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CASE REPORTS
REPORTES DE CASO

ENVENOMATION CAUSED BY THE BITE OF BOTHRIECHIS SCHLEGELII

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Editorial:

CASE REPORT: ACTIVE PROGRESSIVE BASED ON CLINICAL PRACTICE LEARNING (APB-C)

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Clinical case reports date back to 1600 B. C., when Egyptian papyri first described injuries or disorders of the head and the back (1). Likewise, cases reported by Hippocrates, 460 B.C (2), or the first uterus (3) and face transplants (4) can be found in the literature, as well as cases on the recent Zika epidemic and its relation to microcephaly (5). All of them have greatly contributed to the evolution of medical science during different periods, both in research and learning processes.

Case reports can be considered as scientific publications that represent the simplest form of research in the clinical area (6); however, they are the evidence of what actually happens in each case. That its usefulness is purely investigative is debatable. Case reports have a low profile in relation to the classification of other scientific works, but their contribution to the understanding of history (1), meaningful learning of medicine and a more humanized view of health care is evident (7).

Regardless of the current discussion on the hierarchical place of case reports as a scientific evidence, it is clear that it has always been present in medical literature, not only because of its scientific value, but because it has always been a part of medical learning.

The medicine learning process has evolved, moving from positivist and behaviorist theoretical strategies to the current cognitive, constructivist and socioconstructivist learning processes. These approaches have allowed an active progressive based on clinical practice (APB-C) learning, leaving passive knowledge acquisition processes behind and fostering active, progressive, participatory and integrative processes for logical and constructive reasoning based on each clinical case. Cases are the essence of clinical medicine, even more when they report a new disease, are rare and little known, show a new treatment or intervention, or describe some event that is unknown (8).

APB-C learning is an apprentice-centered strategy that not only considers students as apprentices, but also considers any health professional who progressively builds critical, autonomous, and creative thinking in an open and malleable way, according to the context, and based on new research works. It also includes professionals with an analytical and resolute capacity to apply this knowledge in a specific way to each new clinical case received and, with the potential to broaden their knowledge and experience finding new meanings. In the context of APB-C learning, a clinical case report represents a situation that encourages knowledge, because it not only seeks to solve a problem, but also is, sometimes, the tip of the iceberg for new knowledge.

When the author of a clinical case report incorporates new knowledge into the cognitive structure of the professionals who read it, a meaningful learning process arises, in which each reader gives a personal meaning to the new acquired knowledge. This way, relationships with their cognitive structure are established and new theoretical and methodological elements (9) for teaching-learning processes of future research appear.

One of the most relevant contributions of case reports, and the reason why they are still valid today, is the cognitive dynamics generated when meaning is given to new knowledge, since it could be integrated or diverge from previous knowledge about a specific topic or pathology. This active and progressive dynamic motivates new ventures in scientific research or learning processes in medicine.

Case reports have been proposed as a gateway for undergraduate and graduate students, as well as for professors and research-

ers, to take their first steps into the world of medical literature. This position is not entirely shared by the author of this editorial, since case reports of all kinds have been produced throughout history, and have been submitted by new professionals or experts and researchers of medical science who allow themselves to be astonished by new knowledge and want to share it.

The ability to recognize that which generates new meaning as learning is what allows many authors to detect a case to report and to share it, leaving aside the amount of experience they have. If a case is significant enough for an author, it might be significant for others as well. Then a literature review is initiated, although few cases out of hundreds are actually published; what is meaningful and new for an author, may not be for other professionals.

Historically, this type of articles have shown a complete picture of clinical practice, which evidences the differential empathic process between the attending professional and his patients, showing the comprehensive knowledge that is described in the narrative of the case. Currently, this comprehensiveness in case presentation is increasingly strengthening due to the CARE guidelines (consensus-based development of guidelines for reporting clinical cases) (10), which allow for greater scientific validity and a comprehensive and holistic view of each case presentation.

Writing and analyzing clinical case reports should be part of the APB-C learning strategies for undergraduate and graduate students, as well as for practicing professionals, additionally to historical, academic and humanistic interest generated by the cognitive-constructivist processes of meaningful learning and scientific research.

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ENVENOMATION CAUSED BY THE BITE OF THE SNAKE BOTHRIECHIS SCHLEGELII. REPORT OF TWO CASES IN COLOMBIA

Palabras clave: *Bothriechis schlegelii*; Mordeduras de serpientes; Coagulación sanguínea; Colombia.
Keywords: *Bothriechis schlegelii*; Snake bites; Blood coagulation; Colombia.

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ABSTRACT

The bite by snakes of the *Bothriechis* genus is common in certain areas of Colombia such as the Coffee-growing Region. Due to their arboreal habits and defensiveness, these snakes usually bite farmers in their upper limbs and face. In Colombia, the incidence of accidents caused by these snakes has not been accurately estimated yet because of deficiencies in recording this type of cases, as well as of the ignorance on this reptile by health personnel working in its area of influence.

This paper describes two cases of bites by *B. schlegelii* occurred in Colombia during 2015. The first case is about a 55-year-old man who was bitten on the left hand, and subsequently developed paresthesia and edema until the forearm, with no other findings; the patient underwent treatment with polyvalent antivenin from Probiol®, with complete resolution of the event. The second case portrays a 62-year-old man, bitten on the left hand, presenting with emesis, diaphoresis, edema until shoulder, prolonged clotting times, and no bleeding; the patient required eight vials of polyvalent antivenin from Instituto Nacional de Salud (National Institute of Health, Colombia), thereby normalizing clotting times. Complete resolution of the event was achieved.

INTRODUCTION

The name *Bothriechis schlegelii* derives from the Greek word *bothros*, which means "pit" and *echis*, "snake", referring to the loreal pit that is located between the nostrils and eyes on each side of the face, and also after the German zoologist Hermann Schlegel (1).

The length of *B. schlegelii*, also known as eyelash pit viper, varies between 50 and 120 cm, being females larger than males. The variety of its colors (emerald or dark green, yellow, brown and black), helps it mimic its surroundings. It has prehensile tail, and from two to four small superciliar scales, in the way of "eyelashes". It feeds on baby birds, lizards, frogs and rodents, inhabits tropical forests and corn and coffee crops, at altitudes ranging from 0 to 2600 m; the viper reaches the highest altitude in Colombia (2,3).

In the regions in which it inhabits, it is also known as *cabeza de candado, granadilla, víbora de tierra fría, víbora de pestañas, yaruma, veinticuatro, guacamaya, víbora rayo, mortiñera, colgadora* and *grano de oro* (these are different names to refer to this snake in diverse regions of Latin America) (2,4).

B. schlegelii extends from southern Mexico, throughout Central America, to the east of Venezuela, and in the Pacific through Costa Rica, Panama, El Salvador and Ecuador (5). In Colombia, it lives in the Pacific and Andean regions, and in the Western, Central and Eastern Ranges. In addition, it can be found from the south to the north of the country, on the border with the Venezuelan Andes, and is endemic in the coffee region (2).

Until epidemiological week 32 in 2016, 2 791 cases of snakebite accidents were reported to Sistema Nacional de Vigilancia en Salud Pública (National System of Public Health Surveillance), of which 65.6% corresponded to *Bothrops* (6). However, the number of cases related to snakebites of *Bothriechis* genus specimens was not certain.

CLINICAL CASES

Case 1

Reason for consultation

55-year-old patient, from Pensilvania, Caldas, who was bitten on the back of the left hand by

a 25 cm, thin, triangular head snake during his work in a coffee crop (Figure 1 and 2). The patient denies hypertension, diabetes, kidney disease, bleeding disorders or previous surgeries.

Fig 1. Specimen of *Bothriechis schlegelii* which caused this event, in defensive position.
Source: Own elaboration based on the data obtained in the study.

Fig 2. Head of the specimen. Multiple scales, vertical pupil and loreal pit can be seen.
Note: The specimen was handed over to environmental authorities and returned to its natural habitat.
Source: Own elaboration based on the data obtained in the study.

Clinical manifestations and physical examination

The patient presented with pain when moving the affected hand, paresthesia and 2cm edema in the right hand, which spread to the left forearm. No fang punctures nor local bleeding were observed (Figure 3).

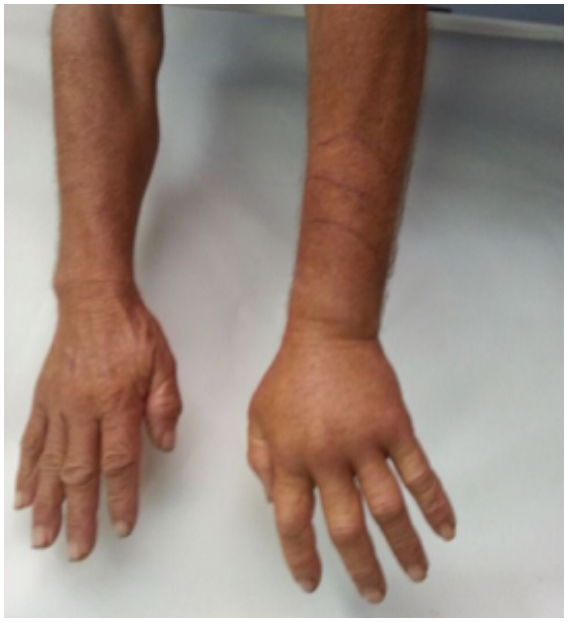

Fig 3. Appearance of the bite by *Bothriechis schlegelii*. Edema in the left hand and part of the forearm is shown.
Source: Own elaboration based on the data obtained in the study.

Laboratory tests

Complete blood count, blood urea nitrogen, creatinine and coagulation tests were performed and no alterations were found. Total CPK was not determined.

Treatment

First, the patient was administered intravenous fluids, analgesia with tramadol, and tetanus

prophylaxis (after confirming normal coagulation tests). Then, he was referred to a nearby hospital where three vials of polyvalent antivenom Probiol® were administered intravenously; afterwards, the patient developed fever, which was controlled with acetaminophen. The pain and edema decreased and, finally, he was discharged after two days of observation.

Case 2

Reason for consultation

62-year-old man, from Fresno, Tolima, who was bitten on the third finger of the left hand during agricultural work by a thin snake, known in the area as *"cabeza de candado* (head lock)" (Figure 4 and 5). He denies hypertension, diabetes, kidney disease, bleeding disorders or previous surgeries.

Clinical manifestations and physical examination

The patient was admitted with pain in the left hand, edema of 1 cm in the right hand, paresthesia in the left shoulder, emesis and diaphoresis (Figure 6).

Laboratory tests

The following tests were performed: unaltered blood count and prolonged prothrombin time, and partial thromboplastin time. Total CPK was not determined.

Fig 4. *Bothriechis schlegelii*. Triangular head.
Source: Own elaboration based on the data obtained in the study.

Fig 5. *Bothriechis schlegelii*. Prehensile tail.
Note: The specimen was sacrificed before consultation with the attending physician.
Source: Own elaboration based on the data obtained in the study.

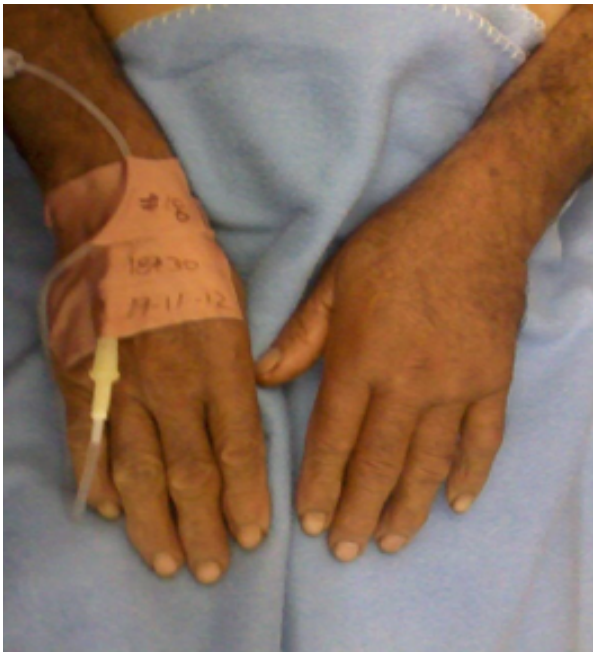

Fig 6. Appearance of *bothriechis schlegelii* bite. Edema in the left hand.
Source: Own elaboration based on the data obtained in the study.

Treatment

The patient received intravenous fluids, analgesia and six vials of polyvalent antivenin produced by Instituto Nacional de Salud intravenously, without adverse reactions. After finding an alteration in clotting, the patient was given two additional vials of polyvalent antivenin, for a total of eight, and was referred to a third level hospital level in Ibagué. In the referral hospital, the patient's condition improved, and coagulation tests were normal 48 hours after the event; finally, he was discharged after 72 hours of observation.

DISCUSSION

The venom of *B. schlegelii* consists, mostly, of phospholipase A2, followed by metalloproteinases, bradykinin potentiating peptides, Kazal type proteinase inhibitor, serine proteinases, L-amino acid oxidase and cysteine-rich secretory proteins (CRISPs), therefore, its properties are hypotensive, edema-forming, procoagulant, myotoxic, necrotizing and hemorrhagic (7).

When dealing with bites by a *Bothriechis* snake, assessing the severity of the bite through the clinical grading adapted by Otero is important (8), which also serves to determine the amount of antivenin to use.

The grades presented by Otero (8) are: Grade 1, absent, only minimal pain; Grade 2, mild, presence of edema (<4 cm) that compromises one or two segments of the bitten limb, ecchymosis, scarce bleeding with normal coagulation or incoagulable blood; Grade 3, moderate, with edema (> 4 cm) that compromises three segments of the bitten limb, blisters, local incoagulable bleeding or presence of systemic hemorrhage; Grade 4, severe, presence of edema beyond the bitten limb, necrosis, compartment syndrome, local hemorrhage with incoagulable blood, systemic hemorrhage (including brain hemorrhage), hypotension or shock, disseminated intravascular coagulation, renal failure and multiple organ dysfunction. According to this, the two cases were considered as mild.

The symptoms manifested by the patient in the first case —localized pain and progressive edema— correspond to the initial symptoms caused by the bite of this snake, which in some cases may be accompanied by hemorrhagic blisters, itching, bruising and necrosis (9, 10). In Colombia, severe poisoning by *Bothrops asper, Bothrops punctatus, Porthidium nasutum and Bothriechis schlegelii* bite has been characterized and includes local necrosis, systemic and local bleeding, hypotension and renal failure (11).

In the second case, although no marked local symptoms were observed, there was a

significant commitment of clotting, which can be explained by two reasons: the direct inoculum of poison inside a blood vessel, and the presence of metalloproteinases in the protein composition of the poison, because their concentration in the venom of *B. schlegelii* (17.7%) is lower compared to that of *B. lateralis* (55.1%). This specimen has shown a wide range of biological activities, such as hemorrhagic fibrinogenolytic degradation of components in the extracellular matrix, and activation of prothrombin and factor X, resulting in extensive local tissue damage and systemic bleeding (12,13).

TREATMENT CONSIDERATIONS

Appropriate initial measures for such events include complete medical history; cardiovascular, respiratory and neurological evaluation; intravenous fluids in a limb other than the affected one; bite site antisepsis; gastric protection and oral rest due to the risk of bleeding; prophylaxis for tetanus with tetanus toxoid when coagulation times are normal or normalized after treatment; broad spectrum antibiotic therapy in case of documented infection, and analgesia with opioids. Non-steroidal anti-inflammatory drugs should be avoided (14).

Currently, three types of antivenins are available in Colombia: one manufactured by Instituto Nacional de Salud, one manufactured by Laboratory Probiol® produced in Colombia, and another manufactured by Bioclon Institute of Mexico. The first two act against the venom of *B. schlegelii* and, according to their availability, should be used taking into account possible adverse reactions such as anaphylaxis, serum sickness, acute renal failure or pyrogenic reactions, which are treated with corticosteroids if they are mild to moderate, or adrenaline if anaphylactic shock occurs (2,8).

The polyvalent antivenin produced by Bioclon Institute of Mexico has also been used to treat this type of envenomation; also, it showed that it can reverse the procoagulant effect of the venom of *B. schlegelii*, as well as the polyvalent serum antivenin produced by Instituto Clodomiro Picado in Costa Rica (15).

CONCLUSIONS

Due to the correct classification of the severity of envenomation cases, the accurate identification of the causative specimens, the adequate dose and the quality of the antivenin used, a satisfactory outcome was achieved in both patients.

B. schlegelii bite produces poisoning, but this fact is underestimated in Colombia, partly because of the ignorance that health personnel have of this snake and because of the characteristics of their venom. Accurate diagnosis and specific treatment with polyvalent antivenin are crucial to prevent further morbidity in these patients.

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CONFLICT OF INTEREST

None declared by the author.

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THROMBOELASTOGRAPHYGUIDED TRANSFUSION THERAPY IN A PREGNANT PATIENT WITH HEMORRHAGIC DENGUE FEVER HOSPITALIZED IN ICU. CASE REPORT

Palabras clave: Dengue hemorrágico; Tromboelastografía; Embarazo
Keywords: Severe Dengue; Thrombelastography; Pregnancy

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ABSTRACT

Dengue fever is the biggest public health issue in tropical countries. A significant percentage of patients who suffer from this disease require admission to the intensive care unit (ICU) due to the severity of the clinical picture. This case reports the clinical evolution of an eight-week pregnant woman with dengue fever associated with thrombocytopenia and leukopenia. The patient comes from an endemic area for tropical diseases, fact that led to diagnose dengue fever with hemorrhagic characteristics.

During her stay in the ICU, the patient presented with first trimester bleeding and placental hematoma. Therefore, and considering the pregnancy and the risk of loss, the hematological function was monitored through thromboelastography. The transfusion of blood products was decided according to the specific findings. Controlling and reversing the obstetric bleeding process was possible, the patient condition evolved favorably, and she was subsequently discharged from the ICU. This article reports on the usefulness of dynamic monitoring the hematological function using thromboelastography in patients with hemorrhagic dengue fever and special conditions such as pregnancy.

INTRODUCTION

Dengue fever is a tropical disease characterized by high fever and bleeding caused by the dengue arbovirus. It is transmitted by the bite of Aedes aegypti, of the flavivirus genus, a species largely found in territories below 1800 masl. According to the World Health Organization (WHO), dengue fever is the biggest public health issue in tropical and subtropical countries, accounting for more than 500 000 hospitalizations per year, with a mortality rate of 1% (1).

In 2012, 54 726 cases of dengue fever were reported in Colombia, of which 1 641 corresponded to severe dengue, and 25 174 to patients under 15 years of age, with a mortality rate of 3.9%. Such figures labeled the country as an endemic territory for dengue fever in the past years (2). Data on its incidence in obstetric population are not clear; however, a susceptibility condition related to the development of infections has been reported, as well as an increase in their severity. In addition, growing evidence on predisposition to the development of activation pictures and severe immune response has been found, especially in cases of *Plasmodium falciparum* and *Listeria monocytogenes* infections, and viral infections such as influenza A(H1N1) (3).

Recently, guided transfusion therapy techniques, such as thromboelastography, have been implemented in patients with critical illnesses to evaluate the different phases of coagulation and clot lysis. The reduction of morbimortality and the cost associated with health care, as a result of the decrease in the number of transfusions, have been described as the main advantages of their use (4). Although reports evidencing the usefulness of thromboelastography in sepsis (5) can be found, its clinical applicability in patients with dengue fever infection and hemorrhagic complications requiring administration of blood products is unknown to date.

Considering the facts exposed above, this article presents the case of a pregnant patient infected with dengue hemorrhagic fever, treated in a university hospital of Colombia. This patient underwent a transfusion therapy through thromboelastography with the purpose of controlling obstetric bleeding and avoiding pregnancy loss.

CASE PRESENTATION

Patient Information

33-year-old pregnant housewife, born in Bogotá D.C.

Clinical findings

33-year-old woman, with no previous medical-surgical history, and eight weeks into her second pregnancy by the time she attends the emergency department. She reported a clinical picture of five days of repeated intermittent fever of 38.3°C, associated with chills, generalized myalgias, musculoskeletal, recto-ocular and headache pain, as well as nausea, asthenia, adynamia and abdominal pain.

She denies any history of trauma and vaginal or urinary tract infections. Likewise, she reported that, by the time of consultation, she was getting prenatal care and that no abnormality had been found. She also reported that seven days before the consultation she had been in an endemic region for multiple tropical diseases, a place located at 300 masl; further investigation revealed that she received multiple insect bites during the trip.

Calendar and diagnostic evaluation

Based on clinical findings, a possible dengue virus infection was suspected and paraclinical tests were requested for admission (Table 1). Physical examination on admission did not show any lesion associated with hemorrhagic phenomena such as ecchymosis, petechia or hematoma. The only abnormal finding developed during her stay in the emergency room after presenting with an episode of acute, sparse and bright genital bleeding. Pelvic examination was omitted, and an obstetric ultrasound was performed, confirming fetal viability and the presence of a retroplacental hematoma of approximately 50%, which could be a sign of threatened abortion. Due to the risk of hemorrhagic complication, the patient was transferred to the ICU, where the dengue infection diagnosis was confirmed after obtaining positive IgG and IgM tests for dengue fever.

THERAPEUTIC MANAGEMENT

On the third day of hospitalization and facing an abrupt reduction of platelet count, a platelet transfusion was indicated and a thromboelastogram (TbEg) was performed to determine the coagulation status. TbEg reported R: 12.5, K: 13.0, alpha: 20.4, MA: 27.2 (Figure 1A). Furthermore, a control complete blood count taken six hours after the platelet transfusion yielded the following results: Hg: 14.4 g/dL, Hct: 42.3%, Polys: 50%, Lymphs: 40.1%, platelet count: 20 700 c/mm3. Taking into account the risk of miscarriage due to persistent vaginal bleeding, a transfusion of blood products was administered again, this time with platelets and fresh frozen plasma (FFP); phytonadione 10mg was initiated intravenously (IV). The control thromboelastograms requested within the next 24 hours are shown below (Figure 1 A, B, C and D).

Monitoring and evolution

During ICU stay, a positive IgM and IgG serum antigen for dengue fever was reported. In addition, the evolution of the patient was satisfactory, and no new episodes of bleeding occurred. On the sixth day of evolution of the disease and with TbEg in the correction phase, the patient was discharged from the ICU without complications. Multidisciplinary follow-up by obstetrics, infectology and psychology was indicated. Seven days after the discharge, an obstetric ultrasound was performed, which showed that retroplacental hematoma persisted with a 50% decrease of the original size and fetal viability.

Table 1. Hemogram and blood chemistry from admission until day five.

Paraclinical exams												
	Leuko-cytes c/mm3	Neutro-phils c/mm3	Platelet count c/mm3	Hgb/ dl	Hct (%)	AST (U/L)	ALT (U/L)	TB (mg/ dl)	DB (mg/ dl)	PT (seg)	PTT (seg)	LDH (mg/ dl)
Day 1	2500	1800	117000	13.6	41	--	--	--	--	--	--	--
Day 2	3250	1340	45000	14	41	1022	1172	0.29	0.15	11 (Ct 10)	46 (Ct 26)	1118
Day 3 (0 hour)	3000	1250	30000	14	42	919	954	--	--	11 (Ct 10)	46 (Ct 28)	--
Day 3 (6 hour)*	--	--	20700	14.2	42	--	--	--	--	--	--	--
Day 4	4250	2300	42000	13	43	382	457	0.5	0.29	11 (Ct 10)	28 (Ct 26)	320
Day 5	5300	2700	65000	13	40	--	--	--	--	--	--	--

AST: Aspartato transferasa; ALT: Alanino transferasa; BT: Bilirrubina Total; BD: Bilirrubina Directa; c: células; Ct: Control; LDH: Lactato Deshidrogenasa; PT: Tiempo de Protrombina; PTT: Tiempo Parcial de Tromboplastina; Rto: Recuento; Hgb: hemoglobina, Hcto: hematocrito; PT: tiempo protrombina; PTT: tiempo de tromboplastina; LDH: deshidrogenasa láctica.

Source: Own elaboration based on the data obtained in the study.

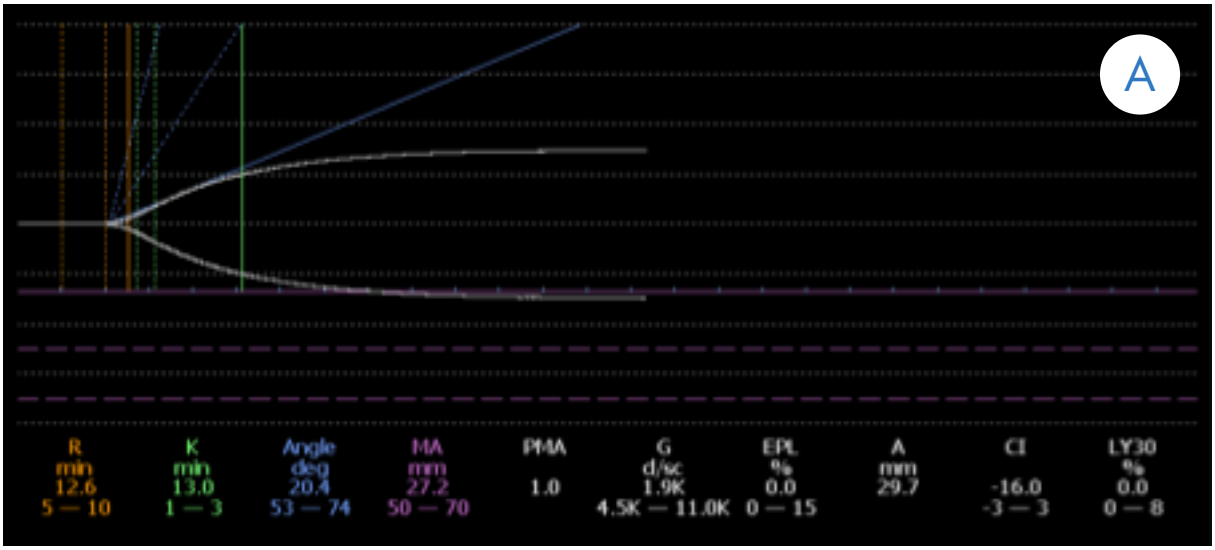
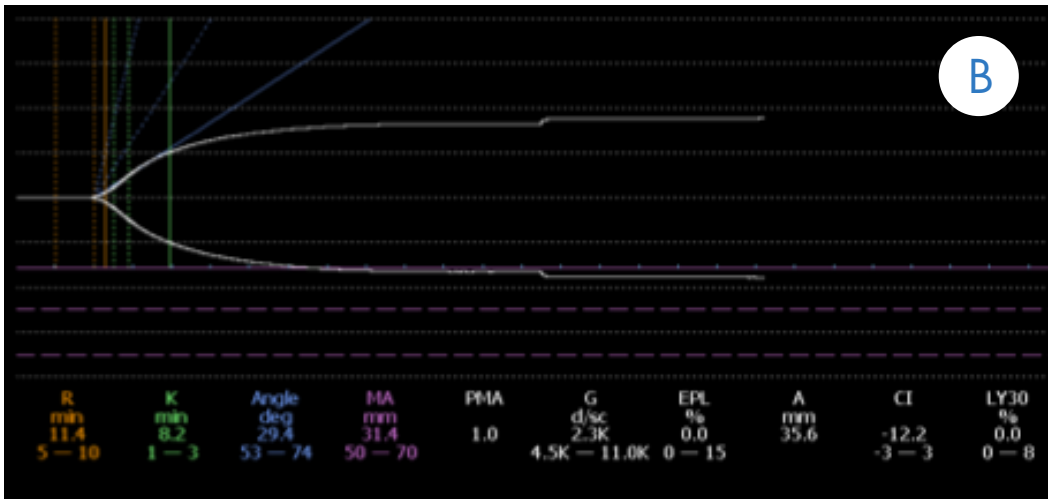
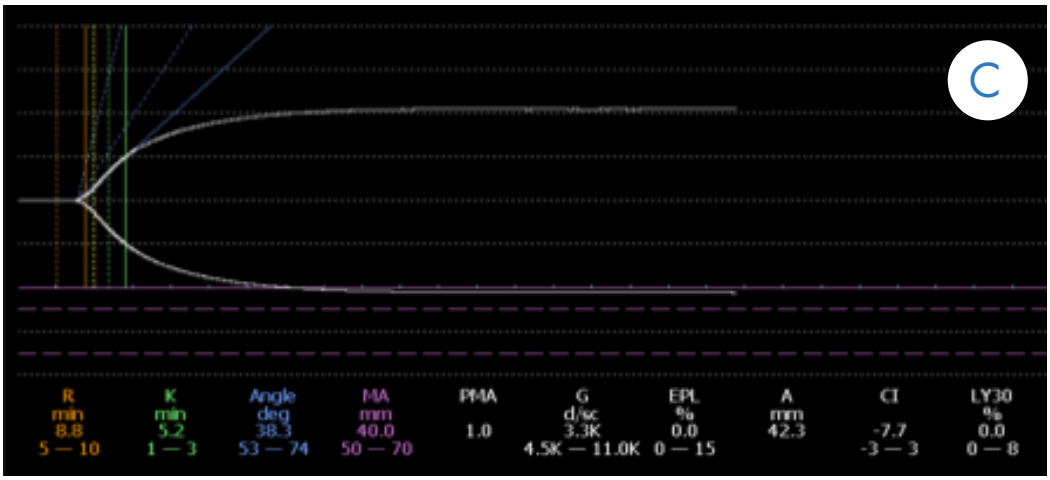


Figure 1 A. Initial thromboelastogram showing an anticoagulation pattern and deficiency of coagulation factors (prolonged k time, decreased alpha angle, and decreased maximum amplitude).





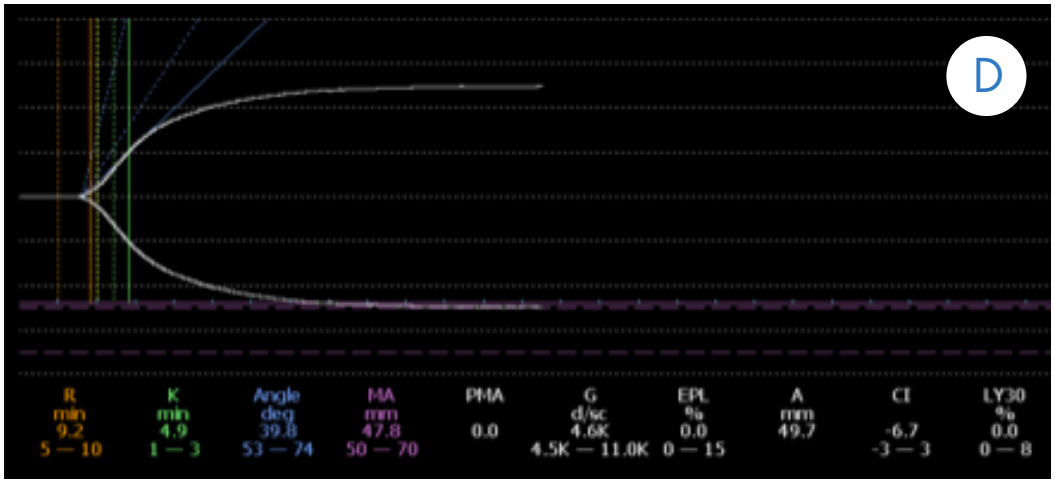


Figure 1 B. Control thromboelastogram (TbEg) # 1 done after the transfusion of platelets and of 10U FFP (gradual correction in K time values, alpha angle, and maximum amplitude). Figure 1 C. Control TbEg # 2 done after the second transfusion of platelet concentrate. Figure 1 D. Control TbEg # 3 done after the FFP transfusion (correction of K time, alpha angle, and maximum amplitude close to reference values).

DISCUSSION

The clinical presentation of dengue is broad and depends on the phases of the disease, which range between asymptomatic or febrile cases during the febrile phase (0-3 days), severe cases of bleeding, shock or organ dysfunction during the critical phase (3-6 days), and the resolution of symptoms in the convalescent phase (>6 days). Recently, a classification of this disease was made according to its clinical presentation to timely identify severe cases and establish proper treatment. Such classification is based on the presence or absence of warning signs and severe dengue states characterized by shock, bleeding or organ involvement such as myocarditis, hepatitis, encephalitis, and renal failure (6).

The risk of hemorrhagic dengue fever during pregnancy is determined according to the trimester in which it is contracted, and includes vaginal bleeding, threatened abortion, and abruptio placentae. In this regard, Carles et al. (7) determined an increased preterm delivery rate of 55% in French Guyana, which is similar to the findings reported by Poli et al. (8). Restrepo et al. (9) reported an increase in the incidence of threatened abortion and preterm delivery in patients with dengue hemorrhagic fever in Colombia.

A more recent study reports that 10% of cases show hemorrhagic events associated with maternal dengue infection, stressing that an association with retroplacental hematoma is observed during the first trimester (10). Evidence suggesting that there is no relationship between dengue and congenital malformations during the first trimester of pregnancy has been compiled. However, in India, Sharma & Gulati (11) have reported some cases of neural tube defects following a regional dengue epidemic, without finding associated chromosomal defects (11).

Most individuals who are infected and develop the disease, evolve to classic dengue fever, a self-limited febrile disease that usually does not represent any complication. Nevertheless, a variable amount of patients develop spontaneous bleeding, decreased platelet count and signs of plasma extravasation; all these manifestations define the dengue hemorrhagic fever.

Hemorrhagic manifestations have been reported in 35-50% of cases, the most common being epistaxis, gingivorrhagia, and gastrointestinal bleeding (12-13). Despite this trend, some authors, such as Chaudhary et al. (14), consider that there is no association between hemorrhagic manifestations and platelet count, although, this claim has not been confirmed yet due to the heterogeneity of patient selection. Deep thrombocytopenia may be strongly related to the severity of dengue in special populations such as children and pregnant women, for whom it is estimated in terms of major and minor bleedings and signs of plasma extravasation.

Discussions around transfusions, particularly about platelets, have been held regarding pregnant women. To date, no information has been published that could certainly associate abortion with dengue infection during the first trimester, whereas an association between the presence of a placental hematoma and the risk of miscarriage has been reported in 5 to 17% of losses in patients with hematomas, with an OR of 2.18 (1.20-3.67) (15-17).

Although multiple etiologic causes of retroplacental hematomas have been found, including fetal malformations, corpus luteum insufficiency, trauma and perinatal infections such as parvovirus and toxoplasmosis, they have also been reported in infections contracted at the uterine and systemic level (18). When considering the

case presented here, it is possible to affirm that the placental hematoma was associated with a systemic viral infection, which worsens due to the presence of hematological dysfunction with severe thrombocytopenia.

In this context, there is no protocol to determine whether the correction of coagulopathy improves obstetric prognosis and reduces the risk of abortion. In a series of 53 patients, Basurko et al. (10) reported two cases of early abortion due to utero-vaginal bleeding and five hemorrhagic complications at the time of delivery. Another study by Chotigeat et al. (19) made a comparison between patients who were transfused platelets before delivery and patients who were not transfused, finding a reduction of associated bleeding events in the first group.

Thromboelastography assesses hemostasis from a functional point of view, and is represented by the interpretation of the cellular coagulation model. Its application in different clinical scenarios, especially in cardiovascular surgery patients and trauma patients, is a proper option to correct acute hematological alterations and to decrease the unnecessary use of blood products. (20). It is worth noting that conventional coagulation tests do not allow managing the underlying coagulation disorder, which often results in unnecessary replacement of blood components. Thus, thromboelastography allows physicians to recognize a coagulopathy and, more importantly, to understand the underlying coagulation disorder (20).

In this case, the alteration was determined at its full extent by using thromboelastography, which allowed transfusing platelets to correct this variable and to ensure adequate platelet function, therefore, resolving the vaginal bleeding. Although determining if this behavior was beneficial to the patient or if the resolution of vaginal bleeding and subsequent reabsorption of the hematoma could have been achieved only through resting and medical management of the viral infection symptoms can be further discussed, this report raises the possibility of including this treatment in the medical practice.

The literature does not provide records regarding the assessment of the performance and the usefulness of thromboelastography as a dynamic test to define the correctness of coagulopathy and, specifically, thrombocytopenia in patients with dengue hemorrhagic fever, as well as in pregnant patients with dengue fever. Its use has been reported in relation to other obstetric conditions, such as acute fatty liver of pregnancy (21), which is another reason to consider this report as relevant.

However, this reports also lacks information on other causes of placental hematoma, such as fetal malformations, which were not determined since the described clinical management was selected due to the gestational age of the patient and the acute course of the disease.

CONCLUSION

Patients with retroplacental hematoma and dengue fever infection associated with severe thrombocytopenia are at increased risk of miscarriage and fetal loss. In consequence, coagulopathy correction may improve pregnancy prognosis. Conventional coagulation tests may underestimate the risk of coagulopathy and increased bleeding secondary to hematoma. Thromboelastography may be a useful tool for identifying patients at high risk of bleeding due to severe thrombocytopenia in cases of dengue fever during pregnancy, so its use in institutions where this technology is available should be considered.

CONFLICT OF INTERESTS

None stated by the authors.

FUNDING

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STUMP APPENDICITIS IN A 2 YEAR-OLD PATIENT. CASE REPORT AND LITERATURE REVIEW

Palabras clave: Apendicitis; Abdomen agudo; Laparoscopia; Complicaciones posoperatorias.
Keywords: Appendicitis; Abdomen, Acute; Laparoscopy; Postoperative complication.

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ABSTRACT

Stump appendicitis is a rare cause of acute abdomen in the pediatric population, therefore, it is not suspected frequently. This paper presents the case report of a 2-year-old child admitted into the emergency room due to vomiting, abdominal pain and fever.

On admission, the patient presented with tachypnea, tachycardia, abdominal bloating and abdominal tenderness; laboratories showed leukocytosis, thrombocytosis and an elevated C-reactive protein (CPR) levels. Abdominal obstruction was considered because of a prior history of peritonitis associated with perforated appendicitis. However, an emergency laparotomy had to be performed during hospitalization due to hemodynamic deterioration and worsening of abdominal pain.

Peritonitis, appendicitis, intestinal perforation and an incidental Meckel's diverticulum were found. After surgery, the patient was taken to the intensive care unit, where antibiotic therapy was administered for 14 days and multiple peritoneal lavages were performed; finally, the patient was discharged.

Even though stump appendicitis is not a common cause of acute abdomen, it should be kept in mind in patients with history of appendectomy accompanied by abdominal pain, who attend the emergency service. Delay in diagnosis and treatment is associated with higher morbidity rates and an increase in medical costs.

INTRODUCCIÓN

Stump appendicitis is a rare entity, characterized by inflammation of the appendicular remnant after an incomplete appendectomy (1, 2); it is not usually considered at first (3), which delays its diagnosis and treatment, causing morbid complications related to an acute abdomen.

The clinical picture is very similar to appendicitis, and it should be suspected in patients with a history of appendectomy. There are several diagnostic aids available in case of doubt, such as ultrasounds and tomography, which in some case series have shown good results. The hypothesis of an increased number of cases in patients undergoing laparoscopic appendectomy generates different opinions and is a controversial issue (4, 5, 6, 7).

This paper presents a case report regarding stump appendicitis in a pediatric patient, as well as a review of the literature. Due to the low incidence of cases, the treatment and recommendations expressed here are based on the experience obtained from case reports; there are no guidelines for the diagnosis and treatment of this entity.

Case report

Two-year old male toddler, admitted to the emergency room with a diagnostic impression of intestinal obstruction. Surgical history included admission to another institution due to acute abdomen six months before the new admission. As a result, he underwent laparotomy, where generalized peritonitis caused by perforated appendicitis was found, as well as intestinal perforation associated with the inflammatory process; in consequence, intestinal resection and end-to-end anastomosis were conducted. Due to sepsis of abdominal origin, the patient required laparostomy with several subsequent peritoneal lavages and hospitalization in the ICU. The patient was discharged in good general conditions, and further data on management are unknown.

At the moment of the consultation, the mother reported symptoms of a day of evolution that began with increasingly diffuse abdominal pain, followed by abdominal distention, multiple episodes of vomiting of gastric contents, and febrile peaks quantified in 39°C, in that order. During physical examination, the patient was found in poor general condition, with grade II dehydration, signs of respiratory distress, alertness, weight of 9.4 kg and vital signs as described in Table 1. The positive findings were enophthalmos; nose with nelaton catheter in permeable right nostril; dry oral mucosa; tachycardia; tachypnea; distended globular abdomen with abolished intestinal noises and tympanic to percussion; voluntary muscular defense, and pain on palpation. Paraclinical tests were requested, yielding the results summarized in Table 2.

Table 1. Vital signs on admission to the emergency room.

Vital signs	
Blood pressure	105/65mmHg
Heart rate	160 beats per minute
Respiratory rate	42 breaths per minute
Temperature	37°C
Oxygen saturation	90% with 21% FiO^2

Source: Own elaboration based on the data obtained in the study.

Table 2. Reports of paraclinical tests performed.

Paraclinical tests	
Test:	Results:
Blood count	▪ Leukocytes 14430/µL ▪ Neutrophils 73,5% ▪ Lymphocytes 19,8% ▪ Monocytes 6,3% ▪ Hemoglobin 11,7g/dL ▪ Hematocrit: 34.7%, Platelets: 654000
Electrolytes	▪ Sodium: 140,6 mmol/L ▪ Potassium: 4,1 mmol/L ▪ Chlorine: 106 mmol/dL ▪ Calcium: 9,2 mg/dL
Renal function	▪ Blood urea nitrogen (BUN): 9.8 mg/dL ▪ Creatinine: 0.17 mg/dL
Serum glucose	27 mg/dL
C-reactive protein	CRP: 48 units
Plain abdominal radiography:	Multiple air-fluid levels with absence of distal gas (Figure 1)

Source: Own elaboration based on the data obtained in the study.

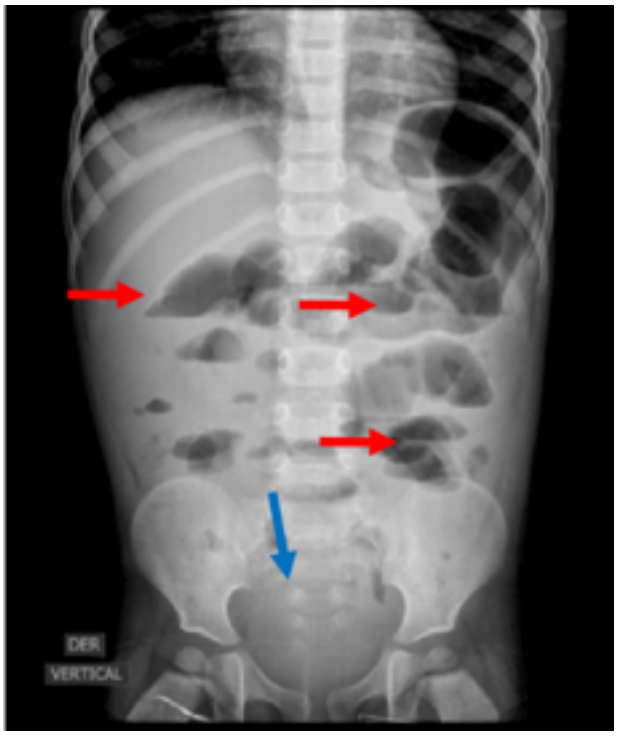

Fig 1. Plain abdominal x-ray (red arrows). Absence of distal gas (blue arrow); air-fluid levels (red levels).
Source: Own elaboration based on the data obtained in the study.

The first suspicion was intestinal obstruction, so a non-surgical medical treatment was initiated. However, the clinical symptoms of the patient were persistent with clinical signs of systemic inflammatory response, and physical examination showed deterioration of abdominal pain despite initial management; for this reason, the patient was referred to the pediatric surgery service for an emergency exploratory laparotomy due to acute abdomen. Performing an abdominal ultrasound or a tomography of the abdomen and pelvis was not possible because of the rapid deterioration of the patient.

The findings during surgery were severe adhesion syndrome, contained intestinal perforation of 5 mm in the anti-mesenteric border at 1 m from the Treitz angle, acute perforated stump appendicitis based on generalized peritonitis (Figure 2), and unperforated Meckel's diverticulum at 50 cm of the ileocecal valve (Figure 3). Based on these findings, laparotomy, appendectomy, generalized peritonitis drainage with cavity lavage, adhesion release, diverticulectomy, enterorrhaphy, and skin closure were performed.

The patient was referred to the ICU for postoperative care under the diagnosis of abdominal septic shock; piperacillin-tazobactam was used for treatment. Subsequently, the patient underwent a new intervention, and two new abdominal cavity lavages were performed. A 14-day antibiotic scheme was completed, and finally, the patient presented satisfactory evolution and was discharged.

DISCUSSION

The main postoperative complications associated with appendectomy include surgical site infection, intra-abdominal abscesses, intestinal perforation, bleeding and adhesions; nevertheless, the frequency of stump appendicitis is low, since only one case is reported in every 50000 patients (0.002%) with a history of appendectomy (6,8) or even less, 0.0014% (9). This figure may be higher since there are cases that are not reported (10), and because only population in general is mentioned, without making a clear distinction of the pediatric population.

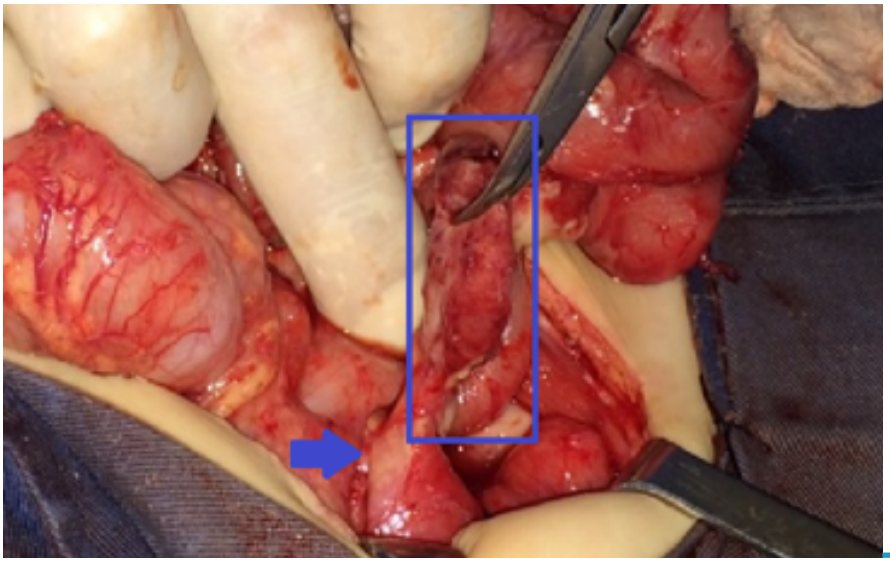

Fig 2. Stump appendicitis, intraoperative findings. The length of the stump, which is greater than 1 cm (blue square), and the cecum (blue arrow) can be seen.
Source: Own elaboration based on the data obtained in the study.

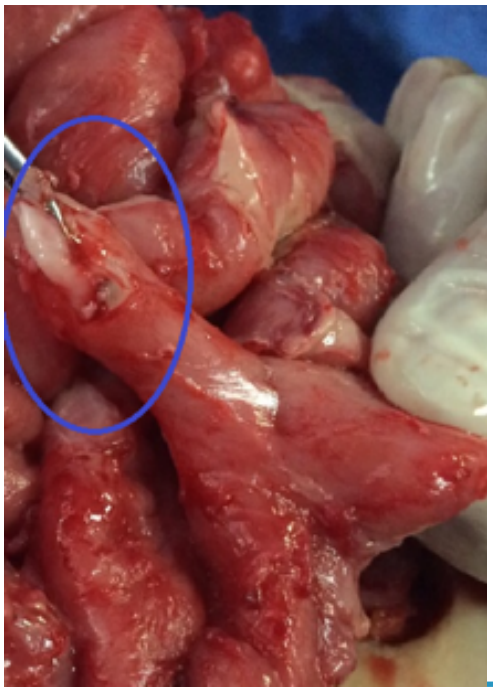

Fig 3. Meckel's diverticulum (blue circle). Intraoperative findings.
Source: Own elaboration based on the data obtained in the study.

Stump appendicitis is a rare cause of acute abdomen in children; therefore, considering this condition is not common for emergency physicians while diagnosing a patient with abdominal pain (5). The length of the appendicular stump (11, 12) is considered as a predisposing factor, when the length is equal to or greater than 6 mm (6, 13, 14). This pathology can appear from 4 days (6, 7, 15) to 50 years after appendectomy, at any age (1). The review by Bing Tang *et al*., shows that, until 2010, there were only 10 cases reported in the English literature regarding the pediatric population, ranging between ages 8 and 15, and with an onset of symptomatology between 2 months and 5 years after surgery (13).

Some causes for atypical stump length include extensive inflammation, inadequate surgical exposure, insufficient surgeon experience, or insufficient stump inversion (13). In the case presented here, the extensive inflammatory and necrotic process presented during the acute appendicitis made it difficult for the surgeon to adequately visualize the base of the appendix and, therefore, a long stump was left.

There is a discussion on whether the increase in this entity is related to laparoscopic surgery (6), although there is no proven evidence. Some authors argue that the absence of tactile perception and two-dimensional view predispose to a long appendiceal stump, thus causing a new process of appendicitis (10); however, a retrospective study by Liang et al. showed that 66% of patients presented with a history of open appendectomy (14, 16, 17, 18). The experience at Fundación Hospital de la Misericordia, a pediatric referral hospital where 1348 appendectomies were performed in 2013 and 1100 in 2014, shows that only one case was presented in the mentioned period.

This pathology has a very similar picture to that of acute appendicitis, characterized by abdominal pain (may be predominant in the lower right quadrant), anorexia, vomiting and fever (2, 3, 5, 10, 15). About 70% of

the cases are associated with perforations generated as complications of the pathology (16), in contrast to 16 to 30% of the perforations caused by acute appendicitis (19). Furthermore, the formation of an infected fistula, inflammatory masses in the lower right quadrant, and presence of signs of peritoneal irritation (13) can be related as well.

In some cases, the condition may present subacute abdominal pain; Roberts *et al.* concluded, after reviewing different case reports, that abdominal pain is the main symptom and that it occurs in up to 77% of cases (15). Diagnosis is based on clinical suspicion, and the use of diagnostic imaging may help increase certainty (17). Diagnostic aids include ultrasound, tomography, and barium enemas (7, 13).

While performing ultrasounds, the same criteria for acute appendicitis can be used to diagnose stump appendicitis: diameter greater than 6 mm in a transverse section of the appendix, edema of the mucosa or presence of a fecolith in the right iliac fossa (2, 13, 20). Meanwhile, during abdominal-pelvic axial tomography, the findings may be non-specific because of appendectomy or abscess, thickening with inflammatory changes at the base of the cecum, inflammatory mass, increased edema in peripheral adipose tissue and tubular thickening, among others. Tomography is recommended as the initial choice because of the speed with which it can be performed and because it is not a dependent operator (5, 7, 11, 13, 14, 21).

Barium enema may be useful when abdominal-pelvic tomography is not conclusive, and especially when the surgical incision has had a torpid evolution; with this imaging modality, a pathognomonic sign of "bird-beak" can be observed as an evidence of appendicular retention, although it actually demonstrates the presence of a long stump and not of inflammation. Barium enema is not recommended in the acute phase of the pathology since it can generate perforation and transitively worsen the condition (13). It is important to consider that the images are not diagnostic, but they help the surgeon in decision-making and should always be accompanied by clinical suspicion.

Management in all case reports is always surgical and may be open or laparoscopic depending on the surgeon's decision and the extent of the condition (13). Since this diagnosis is associated with a high rate of complications, it is best to prevent by leaving a stump smaller than 5 mm, since a greater length may cause a fecolith (15, 18).

Subramanian et al. propose some recommendations to obtain a "critical view" of the anatomical structures during laparoscopic cholecystectomy, for example, thus reducing to the maximum the chances of a long stump. First, they recommend to clearly locate the union of the cecum with the appendix and transitively the base, for which the teniae coli must be followed to the base, and then, to establish the union of three virtual axes corresponding to the terminal ileum, cecal appendix and teniae coli to obtain the "critical view" of the base; the appendix must be located at 10 o'clock, the teniae coli at 3 o'clock and the terminal ileum at 6 o'clock. Finally, the mesoappendix can be dissected and the appendicular base can be located more easily (18, 22).

The use of antibiotics and the correction of other disorders is at the discretion of the attending physician, who must make a decision according to intraoperative findings and patient evolution. However, post-surgical management and complications are very similar to those of an appendectomy, so it all depends on the surgeon's criteria.

It should be noted that, due to the low incidence of cases, there are no guidelines for the diagnosis and treatment of this entity; therefore, the therapeutic management performed and the recommendations formulated are based

on the experience described in the published case reports. The increase in costs is related to the increase in hospitalization days, the need for hospitalization in the ICU in some cases, as well as to surgical reinterventions, and a greater use of medications, among others.

CONCLUSIONS

Stump appendicitis is a rare condition, although it should be considered in patients with abdominal pain and a history of appendectomy, due to the high risk of morbid complications and the possible sequelae, along with increased attention costs. A length greater than 5 mm in the stump has been identified as a risk factor, and some authors associate it with laparoscopic surgery, although there is no evidence to support this assertion.

The clinical picture is similar to classical appendicitis, and some diagnostic images help to reinforce the diagnostic suspicion; tomography is considered the initial examination of choice due to its ease and speed. Management is always surgical and postoperative treatment depends on the surgeon's judgment and surgical findings. As a preventive measure, therefore, leaving a stump equal to or less than 5mm during surgery is advisable, as well as obtaining a critical view of the anatomical structures in order to properly locate the base of the cecum appendix.

CONFLICTS OF INTEREST:

None stated by the authors.

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REYNOLDS SYNDROME: A RARE RHEUMATOLOGIC DISEASE THAT INTERNISTS SHOULD HAVE IN MIND. CASE REPORT

Palabras clave: Síndrome de Reynolds; Esclerodermia Limitada; Cirrosis Biliar; Fenómeno de Reyunad; Hipertensión Pulmonar (DeCS).
Keywords: Reynolds Syndrome; Scleroderma, Limited; Liver Cirrhosis, Biliary; Raynaud phenomenon; Hypertension; Pulmonary (MeSH).

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ABSTRACT

Introduction: Reynolds syndrome (RS) is an autoimmune disorder characterized by overlapping primary biliary cirrhosis (PBC) and limited cutaneous systemic sclerosis (lcSSc). Some published cases do not report pulmonary arterial hypertension (PAH), and diagnoses are usually based on clinical, immunological and histological findings, mainly focused on dermatologic features, on those associated with Sjögren's syndrome, or on an interesting presentation of malignant thymoma; only one case of reported PAH was found, but it was an image report.

Case Presentation: This paper reports the case of a 75-year-old woman who presented with some of the features mentioned above, severe PAH, dyspnea for one month and two weeks of purulent expectoration, as well as generalized pruritus, nasal telangiectasias, Raynaud phenomenon, sclerodactyly, and high levels of alkaline phosphatase and transaminases.

Pulmonary arterial hypertension was documented through a transthoracic echocardiogram, and inmunoflorecence reported mitochondrial and centromere patterns of antinuclear-antibodies. Consequently, RS was diagnosed and phosphodiesterase type-5 inhibitors were started for PAH treatment resulting in the improvement of dyspnea.

Conclusion: Dyspnea could be caused by many conditions, but in the presence of clinical and physical findings, it suggests an autoimmune disorder. Scleroderma should be considered and, additionally, PAH should be investigated since it is present in up to 10% of patients, conferring a worse prognosis. Internists should keep in mind that these disorders may be associated with other autoimmune diseases.

INTRODUCTION

Reynolds syndrome (RS) is an autoimmune disease characterized by overlapping primary biliary cirrhosis (PBC) and limited cutaneous systemic sclerosis (lcSSc); it affects women mainly, and shows an incomplete form of scleroderma. Usually, PBC, in the context of RS, is associated with symptoms that evolve slowly and that are tolerated by patients; it also implies a good prognosis if compared with scleroderma or PBC alone, although diagnosis may be delayed.

While the prevalence of pulmonary arterial hypertension (PAH) in systemic sclerosis patients is about 12% —with a significant related mortality rate at 3 years after the diagnosis of PAH (1)— the prevalence in some studies increases to 26% in RS, negatively affecting prognosis (2). Some published cases do not report PAH, and diagnosis is based on clinical, immunological and histological findings, focusing mainly on dermatologic features (3-9), associated Sjögren's syndrome (10) or as an uncommon presentation of a malignant thymoma (11).

Only one case of reported PAH was found, but it was an image report (12). The case presented here not only some of the features mentioned above, but also severe PAH as part of a study on dyspnea in a woman with both lcSsc and PBC, who was frequently misdiagnosed with an exacerbation of chronic obstructive pulmonary disease.

CASE PRESENTATION

75-year-old woman from Bogotá (Colombia), hospitalized in 2014 due to a history of one month of dyspnea, aggravated by 2 weeks of orthopnea, and purulent expectoration. Further research found that the patient pre-

sented with generalized pruritus, erythema, non-foveal edema in lower limbs and pyrosis the year before. The patient's history showed exposure to tobacco smoke (12.5 pack-year) and alcohol intake once a week since her twenties, as well as chronic bronchitis managed with oxygen (the patient stopped using the oxygen and did not have a prior spirometric test) that required hospitalization with adequate recovery. The patient did not have a diagnosis of diabetes mellitus, systemic arterial hypertension, nephropathy or hepatopathy. No family history was disclosed.

Clinical findings

Since 2009, the patient had persistent cough without expectoration for more than three months, and dyspnea class III according to the functional classification by the New York Heart Association (NYHA), which eventually progressed to NYHA IV, with orthopnea and paroxysmal nocturnal dyspnea; additionally, she experienced productive cough with purulent expectoration for 2 weeks before consultation.

Further investigation revealed that the patient had a previous history of Raynaud's phenomenon and pyrosis. Initial cardiorespiratory examination showed a heart rate of 66 beats per minute, arterial pressure of 108/58 mmHg (systolic/diastolic pressure), respiratory rate of 19 breaths per minute, perioral cyanosis, third degree jugular venous distention, loud tricuspid S2 sound, respiratory distress that required using accessory muscles, coarse crackles in both lungs, hepatomegaly and non-foveal edema in the lower limbs painful on palpation.

Physical examination confirmed secondary Raynaud phenomenon, and generalized pruritus, which was her main symptom, affecting the thorax, abdomen, back and legs. Skin inspection showed nasal telangiectasias, pruritic erythema in abdomen, back and limbs with signs of scratching, red hands, and sclerodactyly (Figure 1).

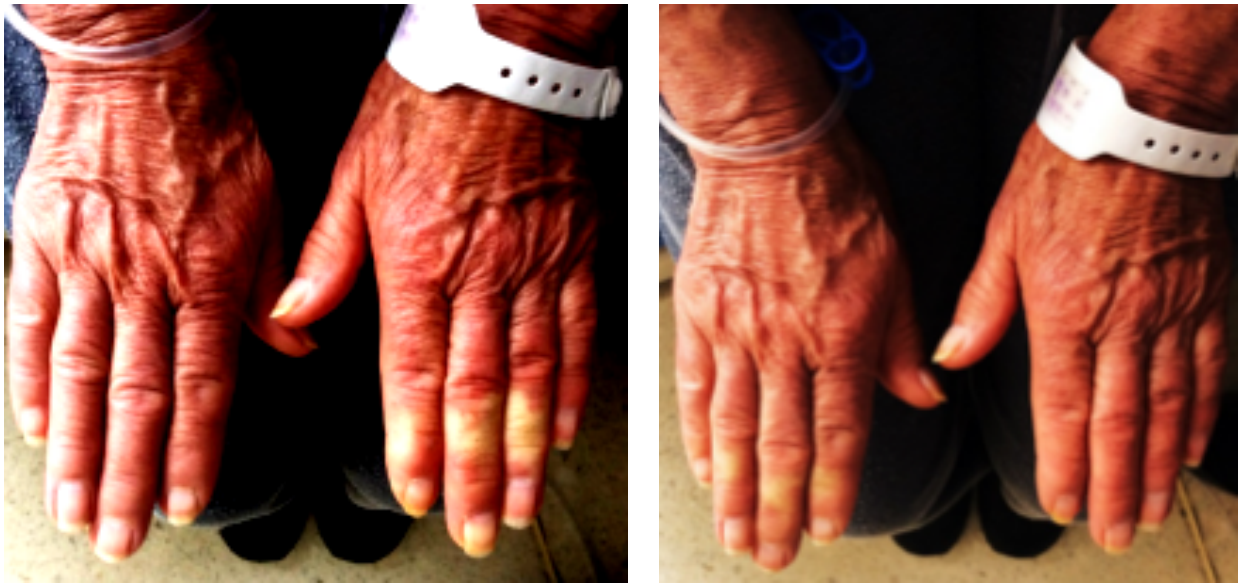

Fig 1. Raynaud's phenomenon.
Source: Own elaboration based on the data obtained in the study.

Initial studies included total blood count (normal), electrolytes (sodium:137 mEq/Lt, potassium: 3.82 mEq/Lt, chlorine:103 mEq/Lt), urine test (normal), arterial blood gases interpreted at 560mmHg atmospheric pressure, which showed a chronic compensated respiratory acidosis without oxygenation disorder (pH 7.38; partial pressure of carbon dioxide (pCO2): 38.9mmHg; bicarbonate (HCO3): 23.6 mEq/L; base excess: -1.7; oxygen partial pressure (pO2): 95.1mmHg; ratio PaO2/FiO2: 297, lactate 0.8 mmol/L), creatinine and blood ureic nitrogen (1.1 mg/dl and 29.25 mg/dl, respectively). Chest radiography showed an increased cardiothoracic index and signs of pre-capillary pulmonary hypertension (Figure 2a and 2b).

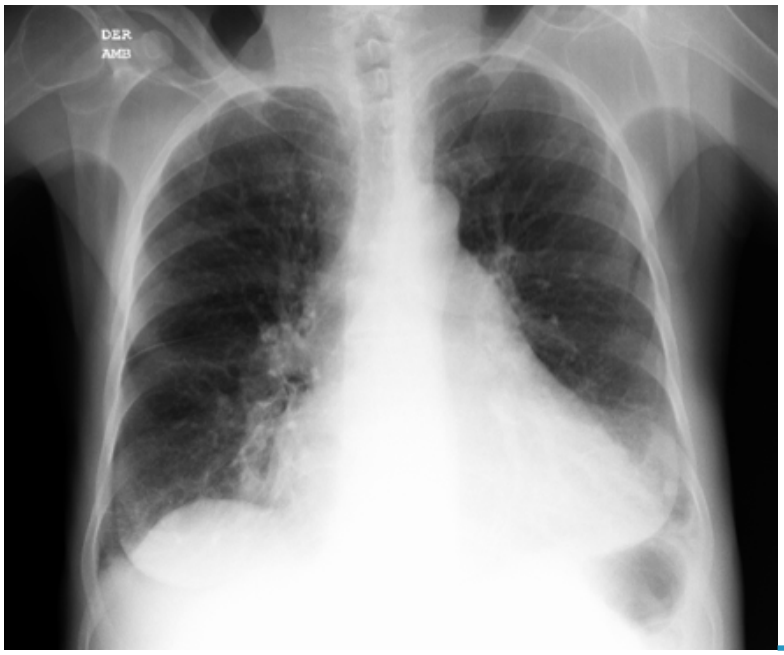

Fig 2A. RChest radiograph. Posteroanterior view.
Source: Own elaboration based on the data obtained in the study.

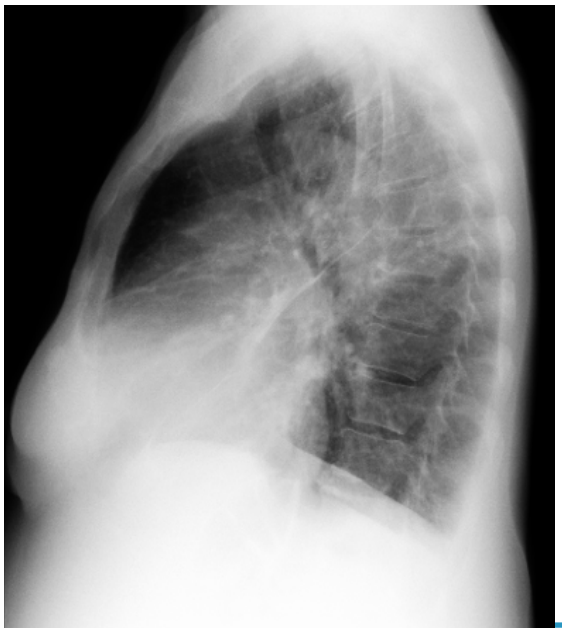

Fig 2B. Left lateral view of chest radiograph. Both projections show pneumonia in the anterobasal segment of the left lower lobe and inferior lingular segment, right middle lobe atelectasis, enlarged cardiac size with pleural effusion and pericardial effusion. Additionally, signs of precapillary pulmonary hypertension can be observed.
Source: Own elaboration based on the data obtained in the study.

Liver profile studies were conducted (Table 1) showing slightly high bilirubin (conjugated: 0.38 mg/dL (47%); unconjugated bilirubin: 0.42 (53%) mg/dL; total: 0.8 mg/dl) and transaminases (ALT 80.5 U/L, AST 82.6 U/L) with high levels of alkaline phosphatase (357 IU/L, reference value: < 250 IU/L); partial thromboplastin time: 34.5 sec (control 32.6), prothrombin time: 16.7sec (control 12.9), and serum albumin test: 3.21 gr/dL.

Table 1. Hepatic and immunological tests.

Test	Value in patient
Bilirubin	Total: 0.8 mg/dl Conjugated: 0.38 mg/dL (47% of total) Unconjugated: 0.42 mg/dL (53% of total)
Transaminases	Alanine transaminase: 80.5 U/L Aspartate transaminase: 82.6 U/L
Gamma-Glutamyl transferase	201 UI/ml (Reference value: women 6-42 UI/ml)
Alkaline phosphatase	357 IU/L (Reference value: < 250 IU/L)
Coagulation test	Partial thromboplastin time: 34.5 sec (control 32.6) Prothrombin time: 16.7 sec (control 12.9).
Serum Albumin Test	3.21 gr/dL
Complement	C3: 118.9 mg/dl reference value 90-180 mg/dl C4: 25.1 mg/dl reference value 10-40 mg/dl).
Antibodies by indirect immunofluorescence	Antinuclear antibodies: 1:2560 dils. ACAs: 1:2560 dils. AMAs: 1:2560 dils.
Hepatitis virus serologic tests	HBSAg: Negative. Anti-HBs IgG and M: Not reactive. Anti HBc: Negative. AntiHC: Negative.

ACAs: anti-centromere antibodies; AMAs: antimitochondrial antibodies; HBSAg: hepatitis B surface antigen; Anti-HBs: hepatitis B surface antibody; Anti HBc: total hepatitis B core antibody; Anti HC: hepatitis C antibody.
Source: Own elaboration based on the data obtained in the study.

An incomplete cholestasis was suspected, and a complete ultrasound of the abdomen was requested, revealing congestive hepatomegaly, free fluid in the peritoneal cavity, and thickening of the gallbladder wall. Measuring GGT levels in blood was determined to confirm intrahepatic cholestatic injury, obtaining a high result (201 UI/ml; reference value: women 6-42 UI/ml).

Initially, decompensated heart failure by an infectious pulmonary process was considered due to the symptoms and the findings obtained during physical examination, which were associated with a chronic pulmonary pathology. The acute infection was treated with antibiotic therapy (piperacillin-tazobactam for seven days) and low-flow oxygen therapy, obtaining some improvement of dyspnea, purulent expectora-

tion cough and absence of crackles on pulmonary auscultation.

A chronic pulmonary pathology was considered as a probably diffuse interstitial process —based on the findings related to nasal telangiectasias, sclerodactyly, Raynaud phenomenon and on the radiographic evidence of pulmonary hypertension (classified as type I)— due to limited systemic scleroderma (or CREST syndrome), which along with incomplete cholestasis, elevated transaminases and pruritus, increases the possibility of an overlapping primary cirrhosis.

A chest radiograph showed increased cardiothoracic index, sign of pre-capillary pulmonary hypertension, which was confirmed by high-resolution computed tomography (HRCT); no pulmonary fibrosis was found. Also, HRTC was compatible with pneumonia in the anterobasal segment of the lower left lobe, with pleural and pericardial effusion. A sputum smear was performed searching for M. tuberculosis, but it yielded negative results.

Cardiovascular studies included an electrocardiogram (Figure 3) with a first-degree atrioventricular block and right bundle branch block without signs of hypertrophy, ischemia or infarction. Transthoracic echocardiography revealed a depressed left ventricular systolic function (ejection fraction of 45%) and relaxation disorder, also confirming cor pulmonale with severe pulmonary hypertension (sPAP=73 mmHg) and tricuspid regurgitation grade IV/IV. By epidemiological nexus with Chagas disease, a Chaga test was requested, but it reported a negative result.

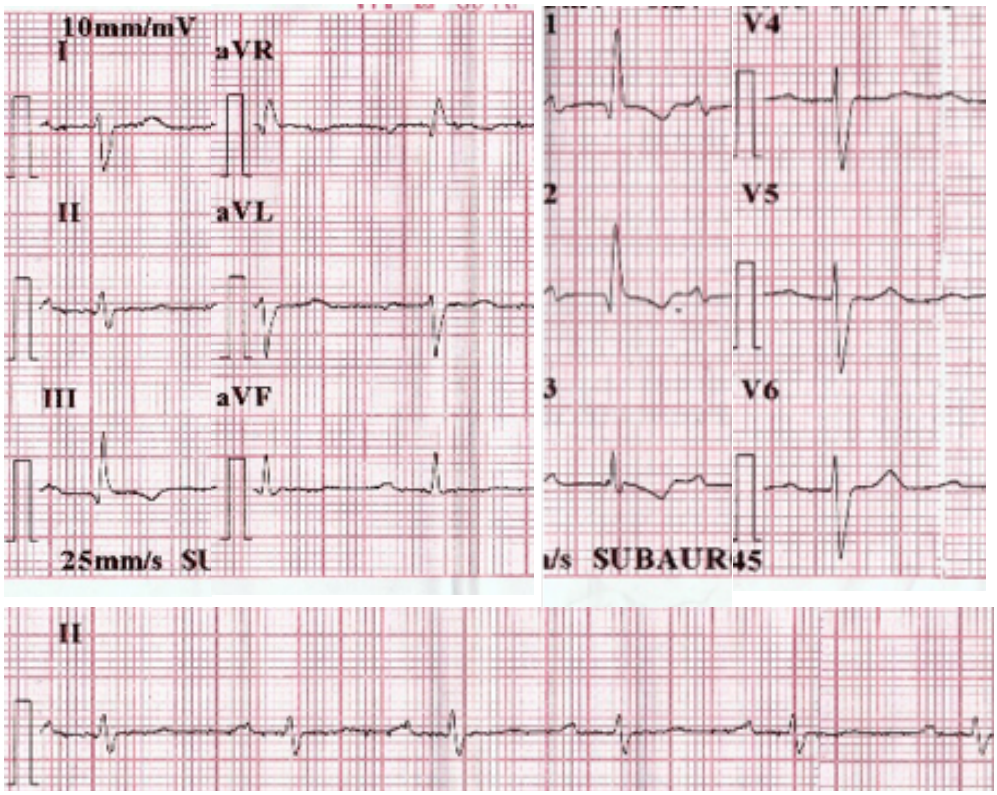

Fig 3. 12-lead electrocardiogram. Findings include first-degree AV block and right bundle branch block.
Source: Own elaboration based on the data obtained in the study.

In addition, an upper gastrointestinal endoscopy test was performed, reporting erythematous mucosa in the esophagus and antral gastritis.

The diagnosis considered limited systemic scleroderma, with the possibility of primary biliary cirrhosis overlap as the cause of intrahepatic cholestasis; immunological tests were performed to confirm a common autoimmune disorder. Also, serum complement levels were measured, showing normal values, which helped ruling out other conditions characterized by complement consumption (C3: 118.9 mg/dl. Reference value: 90-180 mg/dl; C4: 25.1 mg/dl. Reference value 10-40 mg/dl).

Antinuclear antibodies by indirect immunofluorescence showed positive results [antinuclear antibodies: positive with anti-centromere antibodies (ACAs) = 1:2560 dilutions. Anti-mitochondrial antibodies (AMAs) = 1:2560 dilutions)], confirming the presence of two specific patterns of antinuclear antibodies (ANA) for localized scleroderma and primary biliary cirrhosis; viral hepatitis serologic tests were negative.

Based on these findings, the patient was successfully treated with an angiotensin receptor blocker (Losartan), proton pump inhibitors (meprazole) and antihistamines (Loratadine) to minimize the effects of the pathology; also, Sildenafil —a selective phosphodiesterase-5 inhibitor— was administered at 50 mg twice a day for 4 weeks to treat type I PAH, which improved respiratory symptoms. After being discharged, the patient was referred for outpatient monitoring by internal medicine and rheumatology, preserving the treatment and, subsequently, achieving the improvement of symptoms.

DISCUSSION

This patient presented with cor pulmonale secondary to a type 1 pulmonary arterial hypertension, with scleroderma associated to primary biliary cirrhosis or Reynolds syndrome. Systemic sclerosis is a heterogeneous systemic connective tissue disease characterized by vascular endothelial damage in small vessels, autoimmune response associated with specific autoantibodies, and progressive fibroblast dysfunction leading to an increased deposition of the extracellular matrix. The main clinical manifestations include skin thickening and involvement of internal organs (e.g., gastrointestinal tract, lungs, heart, kidney, central nervous system).

According to the ACR-EULAR criteria for the classification of systemic sclerosis, patients with a total score of nine or more are classified as definite systemic sclerosis; skin thickening in the fingers of both hands with extension to the proximal metacarpophalangeal joints completes the criteria for diagnosis (13).

Moreover, the liver is a lymphoid organ involved in the immune response and in the maintenance of tolerance to self-molecules, but it is also a target for autoimmune reactions, as observed in primary biliary cirrhosis (PBC) (14). PBC is a chronic cholestatic disease, of unknown cause, which shows a slow and progressive destruction of small intrahepatic bile ducts, impaired biliary secretion and stasis of bile acids within the liver that can produce liver fibrosis and cirrhosis (15). This disease causes the increase of serum alkaline phosphatase —more than 1.5 times above the normal limit— and is characterized by the presence of anti-mitochondrial antibodies (AMAs), liver histology with non-suppurative destructive cholangitis, and destruction of interlobular bile ducts. A patient who meets two of these three criteria is diagnosed with PBC (16).

Mid and late 50s is the average age of onset in various studies, and women are affected by this condition more frequently (17). Furthermore, PBC can be associated with many

immunological disorders like systemic lupus erythematosus (2.7–15%), Sjögren syndrome (35–57%), serum anti-phospholipid antibodies (75%) and systemic sclerosis (the prevalence of systemic sclerosis among patients with PBC is 7–12%, while PBC has been reported in 2.5% of SSc cases (14)). In the case presented in this paper, the patient had previously shown dermatologic and respiratory symptoms related to scleroderma, and laboratory findings were associated with the mitochondrial pattern of antinuclear antibodies (18); increased phosphatase alkaline without a high level of bilirubin suggests an asymptomatic or an early stage of autoimmune liver pathology (19-21), therefore, PBC was overlapping SSc.

Reynolds syndrome is a rare autoimmune disease with a possible laminopathy genetic substrate (22), and consists in the simultaneous presence of progressive systemic sclerosis and primary biliary cirrhosis. It was first described by Dr. Reynolds in 1970, who reported six female patients with pruritus, jaundice and hepatomegaly with marked elevation of serum alkaline phosphatase activity, and a positive test for serum mitochondrial antibody (23). Lamins are ubiquitous proteins that polymerize to form nuclear lamina, a meshwork of intermediate filaments located under the inner nuclear membrane; they are involved in laminopathies, a heterogeneous group of diseases that share clinical similarities with SSc. A single heterozygous missense mutation in the Lamin B receptor, LBR exon 9 (c.1114C/T; p.R372C), leads to a change from a hydrophilic amino acid (arginine) to a hydrophobic amino acid (cysteine) (24).

According to Stadie (25), the coincidence of progressive systemic sclerosis and primary biliary cirrhosis seems to be a favorable association for the progression of primary biliary cirrhosis; in this case, the good prognosis of RS could be affected by a pulmonary complication (26).

PAH is another aspect included in the ACR-EULAR criteria for the classification of systemic sclerosis. It is defined as an elevated mean pulmonary artery pressure (mPAP) —25 mmHg— with a pulmonary capillary wedge pressure of 15 mm/Hg. The prevalence of PAH among patients with SSc varies among different studies but rounds 10% (27). In a meta-analysis including twelve studies, the pooled prevalence estimate of PAH in patients with systemic sclerosis was 13 % (95% CI, 8.96% to 17.87%) with an I2 figure of 95.5 % (95% CI, 94.1% to 96.4%), using a random-effects model for estimation.

The estimated prevalence of PAH reported in patients with connective tissue diseases was of 13 % (95% CI, 9.18% to 18.16%) ranging between 2.8 % and 32 % (28). In this case, respiratory symptoms were the main complaint of the patient, and pulmonary hypertension was documented in the study because the patient did not tolerate withdrawal of oxygen (since she had clinical signs of pulmonary hypertension, echocardiography was requested evidencing hypertension). Moreover, tomography did not show interstitial lung disease as a cause of PAH.

In consequence, looking for type 1 PAH in a patient with RS is important because this association is related to poor outcomes. Observational studies have demonstrated that mortality remains high in SSc patients with PAH; more specifically, the three-year survival rate for SSc patients with PAH has been estimated in 56%, compared with 94% in those without PAH, therefore, constituting itself as a leading cause of morbidity and mortality (1) (26, 29, 30).

A systematic review suggests that using transthoracic echocardiogram (TTE), pulmonary function tests, and NT-ProBNP for screening and diagnosis of SSc-PAH (31), in the presence of a low lung diffusing capacity for

carbon monoxide (DLCO) (45-70%), is associated with a 5.6-7.4% of PAH development; on the other hand, a decline in DLCO is associated with an increase in the specificity for PAH (DLCO ≤ 50%, specificity = 90%).

In the DETECT study (29), where a population with SSc was studied, nomograms for practical application of the algorithm were proposed to determine the likelihood of pulmonary arterial hypertension and to decide whether to take a TTE, and the subsequent right heart catheterization, with a sensitivity of 97%. This study included seven non-echocardiographic variables (predicted FVC%, predicted DLCO%, current/past telangiectasias, serum anticentromere antibody, serum N-terminal pro-brain natriuretic peptide (NTproBNP), serum urate, and right axis deviation on ECG) with a prediction model for PAH of 84% [area under the receiver operating characteristic curve (ROC AUC) 95% CI: 79.5 to 89.8] (29). In this case, only predicted FVC%, predicted DLCO%, and NTproBNP were not included.

According to ESC/ERS guidelines for pulmonary hypertension (30) "the therapy of PAH patients cannot be considered as a mere prescription of drugs; it is characterized by an interdisciplinary strategy and the combination of different drugs plus interventions" (31); thus, physical activity, nutritional and vaccination recommendations, along with the referral to a rheumatologist and pneumologist, were given to the patient. In addition, a pharmacologic therapy was initiated.

The treatment of PAH begins with the treatment of the underlying cause when possible, but in type 1 PAH, options include endothelin receptor antagonists (Bosetan or Ambrisetan) or phosphodiesterase type-5 (PDE-5) inhibitors (32). PDE-5 inhibitors are involved in this process through the inactivation of cyclic guanosine monophosphate, the second messenger of the nitric oxide pathway (33-35); it is expressed in lung tissue, and may be upregulated in PAH.

Sildenafil citrate is a selective PDE-5 inhibitor, which is orally active and potent according to a clinical trial (SUPER-1) (36) and its extended study (SUPER-2) (37). PAH patients treated with Sildenafil 20, 40, or 80 mg t.i.d. have reported good results on 6-min walk distance, improving and maintaining functional class (38), haemodynamics parameters (37), and renal function (increased glomerular filtration rate, decreased serum creatinine) (38).

Finally, this study reports the following limitations: 1) the right heart catheterization (RHC) was not performed despite the high level of sPAP in the patient, considering that the error estimation of the right echocardiography is ±20mmhg (39); 2) nailfold capillaroscopy was not available in the institution but the 'SSc pattern' was documented, including architectural disorganization, giant capillaries, haemorrhages, loss of capillaries, angiogenesis and avascular areas, which characterize >95% of patients with overt scleroderma (40); 3) magnetic resonance cholangiography of the liver and hepatic biopsy were not performed because they were not available in our second level medical center. In spite of these limitations, this case significantly contributes to knowledge on SR with some unusual clinical features.

In conclusion, dyspnea could be caused by many conditions, but in the presence of clinical and physical findings that suggest an autoimmune disorder, scleroderma should be considered, and PAH should also be investigated since it is present in up to 10% of patients, conferring a worse prognosis if confirmed. Additionally, an internist should keep in mind that, after appropriate clinical review and physical examination, not only the most frequent diagnoses should be considered but also differen-

tial diagnoses bearing in mind autoimmune diseases, especially when there are various organs affected. “Low prevalence” diseases can be overlooked.

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ACCURATE DIAGNOSE AND MANAGEMENT OF ADVANCED NASAL TYPE EXTRANODAL NK/T CELL LYMPHOMA. A CASE REPORT

Palabras clave: Linfoma Extranodal de Células NK-T; Antineoplásicos; Radioterapia; Granuloma Letal de la Línea Media [DeCS].
Keywords: Lymphoma, Extranodal NK-T-Cell; Antineoplastic Protocols; Radiotherapy; Granuloma, Lethal Midline [MeSH].

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ABSTRACT

Extranodal natural killer (NK)/T-cell lymphoma, nasal type, is a rare entity in otorhinolaryngology. Its management requires skilled physicians in order to suspect this disease and making a proper diagnosis at early stages. This paper reports the case of a 31-year-old male patient, with one month of nasal obstruction, recurrent sinusitis, palatal ulceration and a necrotizing lesion. Histopathology reported lymphoid infiltrate polymorph angiocentric growth pattern and extensive areas of necrosis. Immunohistochemistry confirmed the phenotype for T/NK cells: positive CD3, BCL2, CD4 and CD56. IgG for Epstein-Barr virus was also positive.

The initial staging was T4, N1, M0, Eastern Cooperative Oncology Group (ECOG) scale was 1, with intermediate risk, and low International Prognostic Index (IPI); based on this results, the patient was referred to oncology to initiate treatment. After a ten-month follow-up, the patient's condition improved, with complete remission of nasal and palate injuries; no relapse has occurred to date.

This case is a clear example of the importance of early diagnostic through multiple biopsies in order to establish a specific treatment to decrease complication rates and improve prognosis.

INTRODUCTION

Extranodal natural killer/T-cell lymphoma, nasal type (NKTL), was the term endorsed by the Revised European American Lymphoma Classification (REAL) in 2008 (1) to refer to what was previously known as malign granuloma or polymorphic malignant reticulosis. This lymphoma is one of the most lethal midline granulomas, which are characterized for the extensive destructive lesions in the mucosa of the superior airway and middle facial third (1,2).

It is a rare disease that accounts for 7-10% of non-Hodgkin lymphomas in Asia and Latin America (3) and affects mostly adult men aged between 30 to 40 years. Most of the patients affected by this disease present symptoms for six months prior to the first consultation (2-4), with 70% to 90% of cases with a recent or latent infection with Epstein - Barr virus (EBV) (4). The survival rate ranges between 35% and 85% depending on the severity of symptoms and the local extension. Different case series show a high local recurrence rate of 50% (5) and metastasis in only 13% of patients in skin, lungs and gastrointestinal tract, which represents the order of frequency and worst prognosis (6,7). A correct diagnosis is important to define the type of treatment, which may include surgical procedures, chemotherapy or radiotherapy (8).

CASE PRESENTATION

This case presents a 31-year old mestizo male patient, born in Fusagasugá, Colombia, with a history of inhaled cocaine and tobacco abuse. He works as a painter, with constant exposure to inhaled chemicals. The month prior to consultation, he was treated for acute sinusitis with amoxicillin for 10 days due to bilateral nasal obstruction and occasional epistaxis. Three weeks before consultation, he noted a painful ulcer in the hard palate, although, no systemic symptoms were reported. On general examination he was cachectic but stable, and presented with hyponasal speech. Rhinoscopy showed a bilateral mass in the nasal cavity with septal perforation in Cottle zones 2 – 3. Hard and soft palate showed a necrotic lesion with irregular borders, mucosa swelling without active bleeding. He had no palpable adenopathy on head and neck (Figure 1).

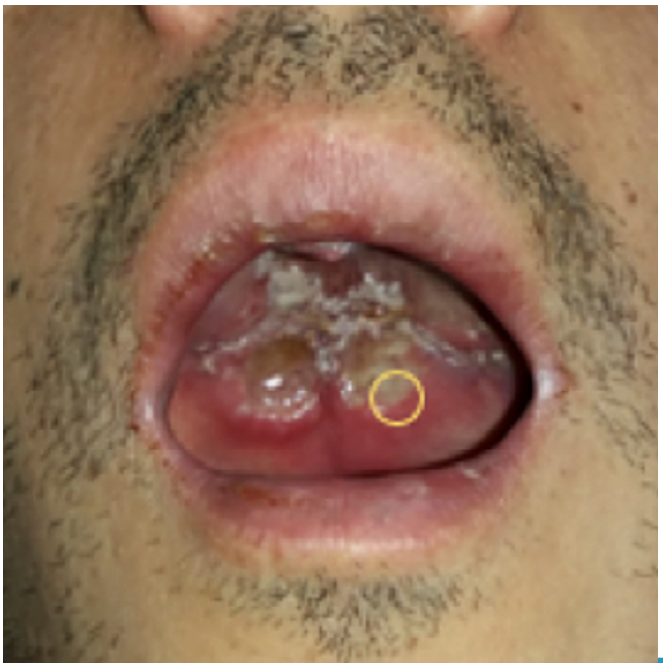

Figure 1. Ulcerated lesion in hard palate with necrotic borders.
Circle: Delimitation of the site of the biopsy.
Source: Own elaboration based on the data obtained in the study.

Blood tests were negative for human immunodeficiency virus (HIV), venereal disease research laboratory (VDRL) and hepatitis B and C, and C-reactive protein test (CRP) was less than 10 mg/L. Computed tomography scan in face and neck showed a mass occupying the nasal cavity, extended to the nasopharynx. The paranasal sinuses were occupied by homogeneous soft tissue density material; left lamina papyracea was eroded and the periorbital fat had inflammatory changes (Figure 2). Lymph nodes of the neck were compromised at zones IIa y IIb. The upper airway was patent. No lesions were identified in CT scans of thorax and abdomen. The patient was hospitalized and multiple punch biopsies of the soft palate were taken.

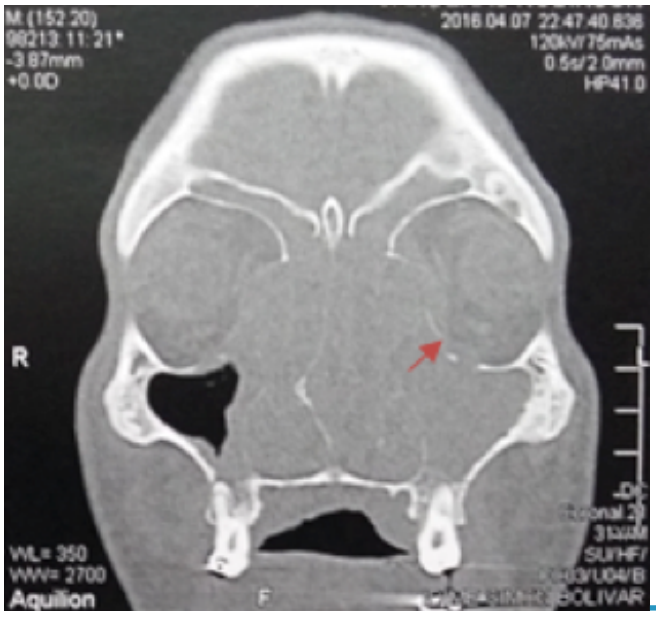

Figure 2. CT scan of nose and paranasal sinuses.
Coronal view: complete occupation of left maxillary sinus, frontal and bilateral ethmoidal sinuses.
Arrow: Eroded left lamina papyracea.
Source: Own elaboration based on the data obtained in the study.

Broad spectrum antibiotic and pain control treatment were administrated, but during the first week of hospitalization the patient presented left proptosis and gradual loss of vision. He was taken to the operation room for a left lateral canthotomy, but three days later, the patient developed irreversible left amaurosis. The histopathology test for the soft palate biopsy reported polymorphous lymphoid infiltrate with angiocentric distribution and extensive necrosis (Figure 3). Immunohistochemistry confirmed lymphoid phenotype with positive T/NK CD3, CD4, BCL2 and CD56; lactate dehydrogenase (LDH) was negative, and IgG for EBV was positive.

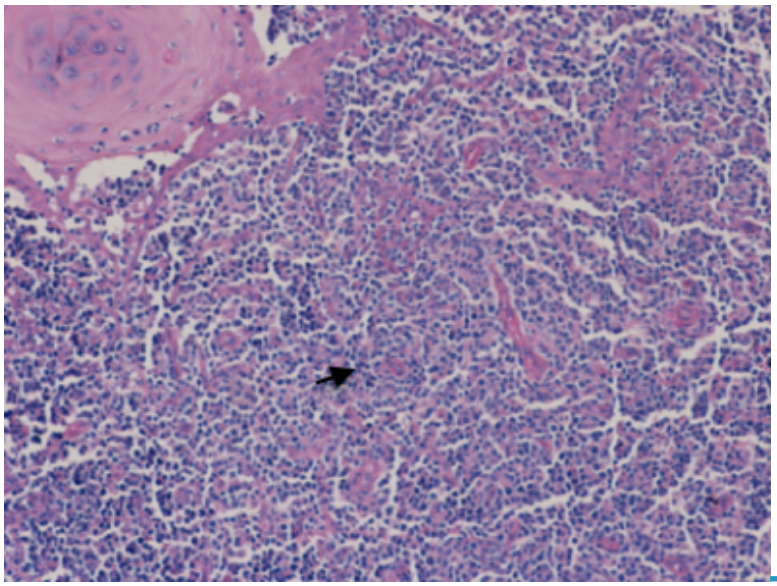

Figure 3. Soft palate biopsy. NK/T extranodal nasal type lymphoma. Arrow. Polymorphous lymphoid infiltrate with angiocentric distribution.
Source: Own elaboration based on the data obtained in the study.

The final staging was T4, N1, M0, ECOG 1, IPI of low/intermediate-risk in a patient with poor health condition. The patient underwent chemotherapy with SMILE protocol (Table 1). Only 2 courses of SMILE were administered with adequate tolerance and some side effects, which were easily managed, such as queasiness, vomiting, weight loss and alopecia. Figure 4 shows the improvement of the lesion seven months after initiation of treatment; finally, after ten months of clinical and radiological surveillance, there was a complete remission of the lesions in oral and nasal cavity. In addition, the patient reported improvement of nasal obstruction and pain in the palate by 90%, but left amaurosis was persistent.

Table 1. SMILE chemotherapy regimen (8).

SMILE Chemotherapy regimen	
Etoposide	100mg/m2 on days 2-4
Cyclophosphamide	1g/ m2 on days 2-4
Mesna	900 mg/m2 on days 2-4
Dexamethasone	40 mg/ m2 on day 2-4
Methotrexate	2g/ m2 on day 1
Asparginase	6000 U/m2 on days 8, 10,12,14,16,18,20

DISCUSSION

Most of the lethal midline granulomas correspond to NK-cell lymphomas, in which an angiocentric and angiodestructive lymphocytic

proliferation occurs along the midline tissue with a fast growing rate. Despite being a low-prevalence pathology in our continent, the NK-cell lymphoma is being more frequently diagnosed and patient's survival rate has increased. The initial symptoms are non-specific and include nasal obstruction and rhinorrhea with recurrent bacterial sinusitis (5,6). As the disease progresses, a unilateral collapse of the nasal cavity and oronasal fistula may appear due to edema, necrosis and major destruction of the tissue in the facial midline (6). Cutaneous manifestations have the highest prevalence among systemic symptoms.

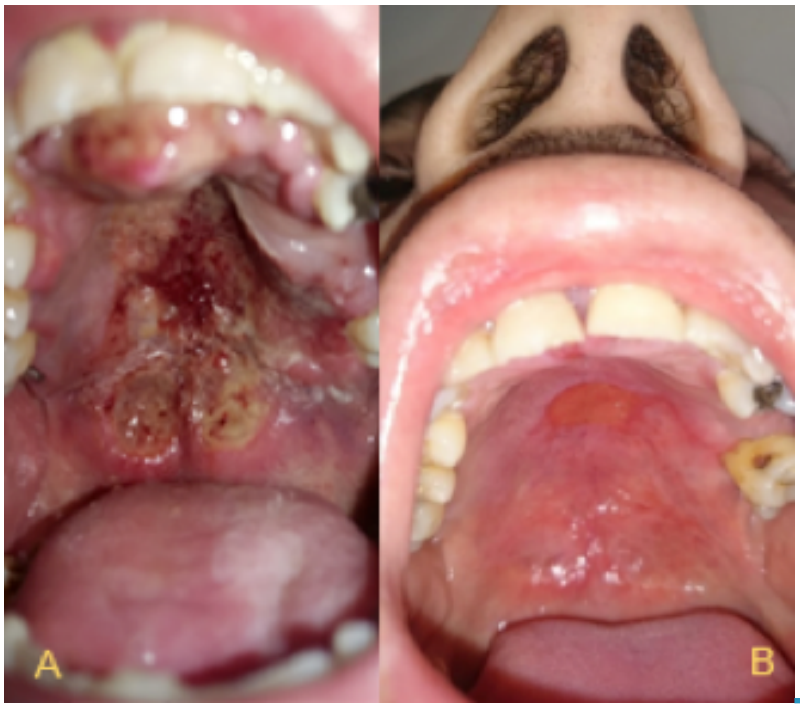

Figure 4. A. Initial lesion in the palate. B. 7 months after SMILE protocol chemotherapy.
Source: Own elaboration based on the data obtained in the study.

The most accurate test for diagnosis in order to find atypical lymphocytic infiltrates with angiocentric distribution is biopsy, and immunohistochemistry is always positive for tumoral markers CD3, CD4, CD56, CD40, CD40 RO. Infection with EBV and high levels of LDH can be found and constitute findings of poor prognosis (8). Medical imaging with computed tomography and magnetic resonance are useful for determining the size of the lesion, the presence of osteolysis, as well as extension to adjacent structures (8,9). In Latin America, discarding infectious diseases such as fungal infections, tuberculosis or tertiary syphilis, and granulomatous diseases like Wegener's granulomatosis, other non-Hodgkin's lymphomas, aggressive NK cell leukemia and malignant epithelial midline tumors is highly important (1,4).

Early diagnosis is of great relevance for better prognosis in order to achieve a higher survival rate. Bad prognosis markers at the time of diagnosis are extensive local invasion, lymph nodes compromise, metastases, high levels of LDH, history of EVB infection and systemic inflammatory response syndrome (6). Likewise, classifying the disease based on the TNM system is essential to define the treatment and the prognosis (10) (Table 2). Numerous scales of functionality for oncologic patients have been described; therefore,

ECOG performance status and NCCN–IPI are recommended since they are the most effective and practical ways to define the stage and prognosis of a lymphoma (11,12).

Table 2. TNM classification for Extranodal NK/T cell lymphoma, nasal type, (10).

Stage	Features
T1	Confined to nasal cavity
T2	Anterior ethmoidal sinus, maxilar sinus, hard palate
T3	Posterior ethmoidal sinus, sphenoid sinus, frontal sinus, oral cavity
T4	Alveolar process, infratemporal fossa, intracraneal fossa
N0-N1	With or without nodular compromise
M0-M1	Local or far metastases

The treatment depends on the staging of the disease. NKTL staged as low risk, stage I or II, is treated with chemotherapy and radiotherapy with a 5 year survival rate of 91%, compared to 54% for only chemotherapy and 76% for only radiotherapy (13). Better results have been accomplished with doses higher than 50 Gy (8-15). Advanced stages III or IV, or with NCCN–IPI greater than 4, with or without extra nasal compromise, show better response to only chemotherapy.

Multiple protocols of chemotherapy are described with asparaginase, cyclophosphamide, etoposide, among others, which can be used in advanced stages, but survival rates have a clear decrease (8-14). Stem cell transplant in advanced stages and relapses is currently being considered as an alternative therapy with good results for improving quality of life and higher survival rates (14,15). Multidisciplinary approaches of this disease are fundamental for the treatment of the patients; new studies are required to evaluate possible alternatives for mid-face reconstruction in patients without relapse.

CONCLUSIONS

Emphasizing on the early diagnosis of one of the most lethal midline pathologies can improve prognosis and quality of life. Although, diagnosis is made based on the first biopsy, usually, more than two or three biopsies are necessary. For advanced stages, only chemotherapy is mandatory in order to reduce mortality probabilities.

CONFLICT OF INTEREST

None stated by the authors.

INFORMED CONSENT

All images have been published with the authorization of the patient.

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INFECTED PULMONARY INFARCTION CASE REPORT

Palabras clave: Infarto pulmonar; Embolismo pulmonar; Anticoagulación.
Keywords: Pulmonary infarction; Pulmonary embolism; Anticoagulation.

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ABSTRACT

Introduction: Pulmonary infarction occurs in 29% to 32% of patients with pulmonary thromboembolism (PTE). The infection of a pulmonary infarction is a complication in approximately 2 to 7% of the cases, which makes it a rare entity.

Case Presentation: 49-year-old woman with pleuritic pain in the left hemithorax that irradiated to the dorsal region, associated with dyspnea and painful edema in the left lower limb of two days of evolution. Two weeks prior to admission, the patient suffered from a left knee trauma that required surgical intervention; however, due to unknown reasons, she did not receive antithrombotic prophylaxis. Physical examination showed tachycardia, tachypnea and painful edema with erythema in the left leg. After suspecting a pulmonary thromboembolism, anticoagulation medication was administered and a chest angiotomography was requested to confirm the diagnosis.

The patient experienced signs of systemic inflammatory response, and respiratory deterioration. A control tomography was performed, suggesting infected pulmonary infarction. Antibiotic treatment was initiated, obtaining progressive improvement; the patient was subsequently discharged, and continued with anticoagulation medication and follow-up on an outpatient basis.

Conclusions: Pulmonary infarction is a frequent complication in patients with PTE. Therefore, infected pulmonary infarction should be suspected in patients with clinical deterioration and systemic inflammatory response. The radiological difference between pulmonary infarction and pneumonia is not easily identified, thus the diagnostic approach is clinical, and anticoagulant and antimicrobial treatment should be initiated in a timely manner.

INTRODUCTION

Pulmonary thromboembolism (PTE) is the third leading cause of death related to cardiovascular disease, in which acute right ventricular failure and pulmonary infarction are the main complications (1). Some studies have reported that pulmonary infarction occurs in 29% to 32% of patients with PTE (1-3).

Pulmonary infarction secondary to pulmonary embolism is more common in patients with low cardiopulmonary reserve (4). A study showed that pulmonary infarctions in patients with PTE occurred in 36% of congestive heart failure cases, and in 54% of patients with hypotension and shock (5). Nevertheless, more recent studies have indicated that young patients with good health status prior to PTE can have a higher incidence of pulmonary infarction (6,3). In addition, a high thrombotic burden has been associated with an increased probability of pulmonary infarction, although this is observed in small pulmonary arteries (7).

In general, pulmonary infarction causes pleuritic pain, tachypnea, dyspnoea and, in extremely rare cases, coughing with hemoptysis (8); therefore, radiological differentiation from other entities such as masses, atelectasis and pneumonia is difficult.

Pulmonary infarction is usually observed in subpleural regions and occurs predominantly in the lower lobes, especially the right lobe. The most common radiological finding is a triangular consolidation of the pulmonary parenchyma (50%), although segments with a ground glass pattern (35.9%) and Hampton sign (14.5%) can also be observed, which help to differentiate it from masses and pneumonia (6,9,10).

Multiple complications have been associated with pulmonary infarction, including pneumonia, pneumothorax, bronchopulmonary fistula, alveolar hemorrhage, cavitations, empyema and pulmonary abscess (11). Infection associated with pulmonary infarction is a rare but important complication, as it may result in the formation of abscesses and empyemas that may require surgical drainage.

The obstruction of a pulmonary vessel secondary to a sterile plunger is suggested to be the cause of blood extravasation into the surrounding tissues, of edema in adjacent bronchial walls, and of the increase of endobronchial secretion, which forms a favorable environment for colonization and bacterial infection by air or blood (12). Bashir & Benson (13), based on a series of postmortem studies, estimated the incidence of lung infarction infection in 2 to 7% (13). The presence of fever, sweating, tachycardia, purulent sputum, as well as of deterioration of the general condition and leukocytosis after pulmonary infarction, is highly suggestive of infection, which is why the spectrum of etiological agents is considered similar to that described in nosocomial pneumonia (11). In cases of infected pulmonary infarction, anticoagulant and antibiotic therapies should be initiated timely and selected according to local resistance patterns, associated pathogens, patient characteristics and clinical context in general (5).

This paper reports a case compatible with pulmonary thromboembolism complicated by infected pulmonary infarction.

CASE PRESENTATION

49-year-old female, public accountant, from Bogotá, Colombia who consulted due to a two-day long clinical picture involving pleuritic pain in the left hemithorax, irradiated to the dorsal region, associated with sudden dyspnea, edema, and warm sensation on the lower left limb; no fever, coughing or hemoptysis were reported. Two weeks prior to consultation, the patient underwent meniscus reconstruction, and anterior and posterior cruciate ligament and left knee chondroplasty secondary to a closed trauma. No postoperative antithrombotic prophylaxis was performed after the procedure due to unknown reasons. The patient had an important history of class 1 obesity, with no previous pathological, toxic or allergic symptoms nor previous hospitalizations.

Physical examination on admission showed a normal general condition, with blood pressure of 97/63 mmHg, heart rate of 106 bpm, respiratory rate of 20 rpm, oxygen saturation at 96%, oxygen inspired fraction of 0.21, and axillary temperature of 36.5°C. Her height was 160 cm and weight 83 kg, which showed a body mass index (BMI) of 32.4 kg/m^2. Thorax auscultation showed P2> A2 without murmurs; fine crackles were also identified in the base of the left lung. Edema in the foot and proximal third of the leg was found in the lower left limb, with local erythema and superficial pain on palpation.

The following tests were performed: blood count, electrolytes, blood urea nitrogen (BUN) and creatinine, which were within normal limits. On the other hand, the electrocardiogram showed sinus tachycardia, while the echocardiogram had a structural and functionally normal heart. Finally, the chest X-ray revealed left basal lamellar atelectasis and right atrium growth (Figure 1).

The Wells scale was applied, finding a high probability for pulmonary thromboembolism. Anticoagulation was initiated with low molecular weight heparin (enoxaparin) at a dose of 1 mg/kg every 12 hours, and a computed axial angiography (AngioCAT) of the chest was

performed, confirming the diagnostic suspicion by reporting pulmonary artery obstruction in the trunk of the lower left basal segment (Figure 2).

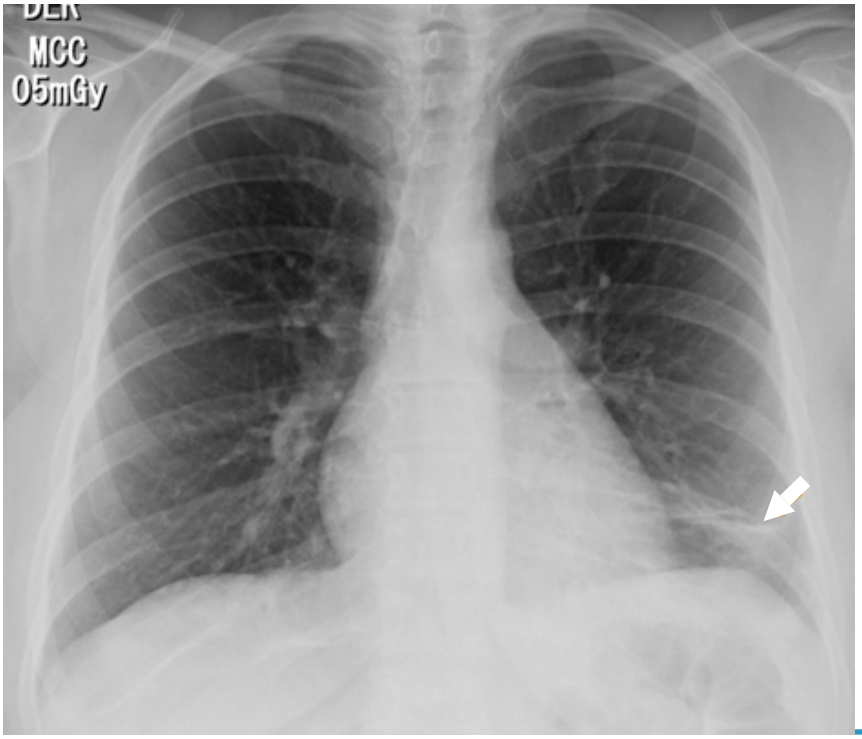

Fig 1. Posteroanterior chest X-ray. Image in left basal band corresponding to atelectasis (arrow).
Source: Own elaboration based on the data obtained in the study.

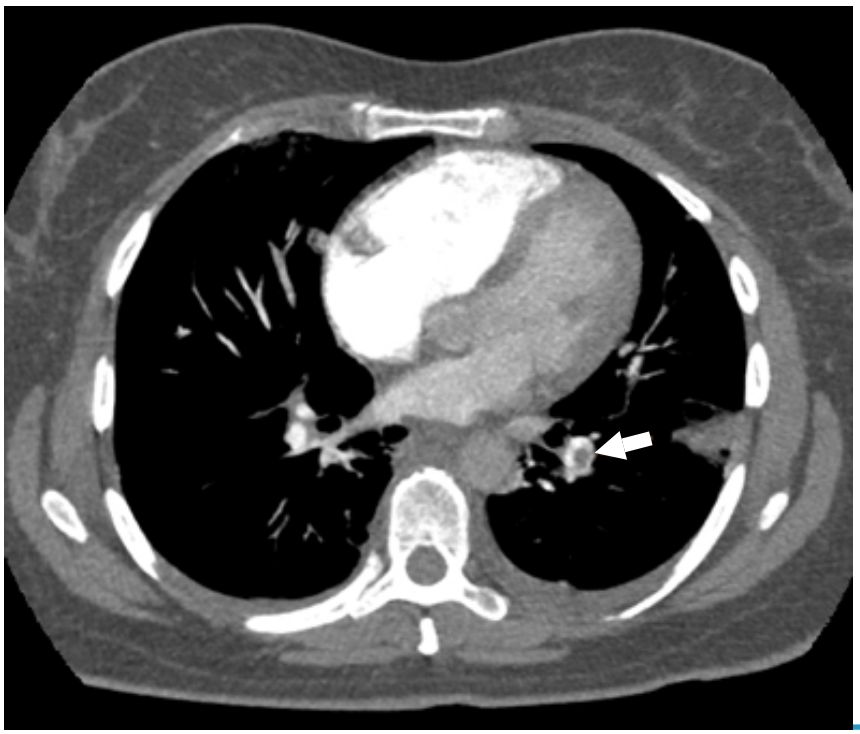

Fig 2. Angiotomography of the chest. Axial plane. Pulmonary embolism, filling defect in the shape of a life preserver sign (arrow).
Source: Own elaboration based on the data obtained in the study.

Surprisingly, after initiating anticoagulation and other general treatment measures indicated for pulmonary thromboembolism, and about three days after her hospitalization, the patient required increased oxygen flow through nasal cannula, her chest pain worsened, and presented with dyspnea, fever, leukocytosis, tachycardia, and tachypnea. Control paraclinical exams were requested, revealing high C-reactive protein and a significant increase in leukocytes at neutrophils expense. A new chest tomographic evaluation was performed, in which wedge densities were identified in the middle and lower right lobes and in the lower left lobe, as well as an aerial bronchogram of the right lower lobe and bilateral pleural effusion (Figure 3 and 4). No blood cultures or sputum cultures were performed.

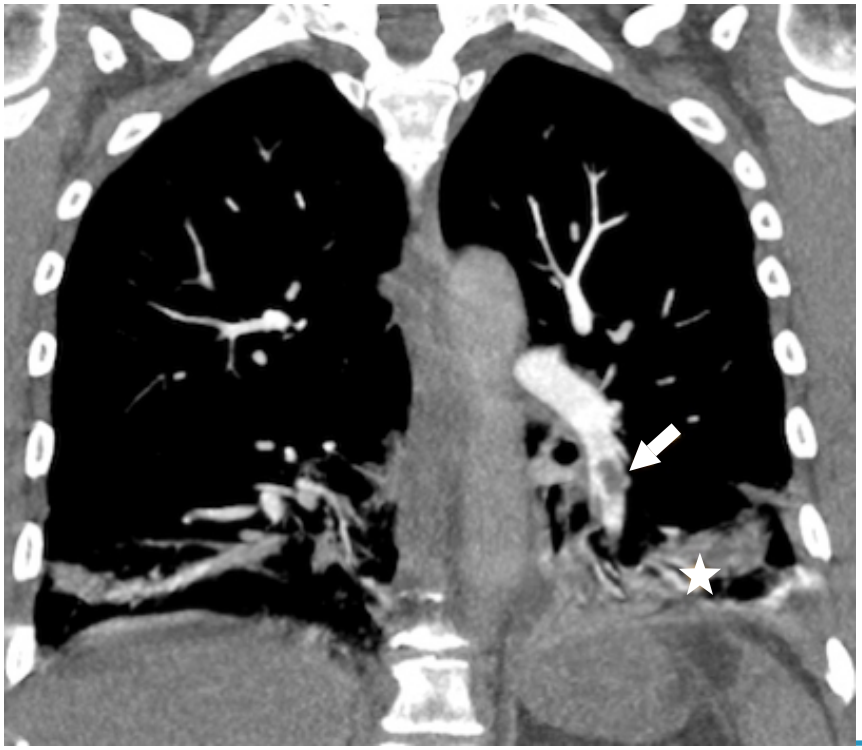

Fig 3. Angiotomography of the chest. Coronal plane. Pulmonary embolism, filling defect configuring the railway track sign (arrow), left basal consolidation of the pleural base and air bronchogram corresponding to pulmonary infarction (star).
Source: Own elaboration based on the data obtained in the study.

With this in mind, infected pulmonary infarction was diagnosed and broad-spectrum antibiotic therapy with piperacillin + tazobactam was initiated at a dose of 4.5 g intravenously every six hours, considering that the infection was nosocomial and that the patient had undergone a recent hospitalization, thus increasing the risk of resistant germs.

The patient improved progressively, and oral anticoagulation with warfarin was initiated at a dose of 5 mg every 24 hours. After completing the seventh day of antibiotic treatment and with INR (International Normalized Ratio) within the therapeutic range, she was discharged with anticoagulation prescription for three months initially, and internal medicine outpatient controls. No adverse reactions to treatments during hospitalization were observed. Figure 4 shows the timeline of the reported case

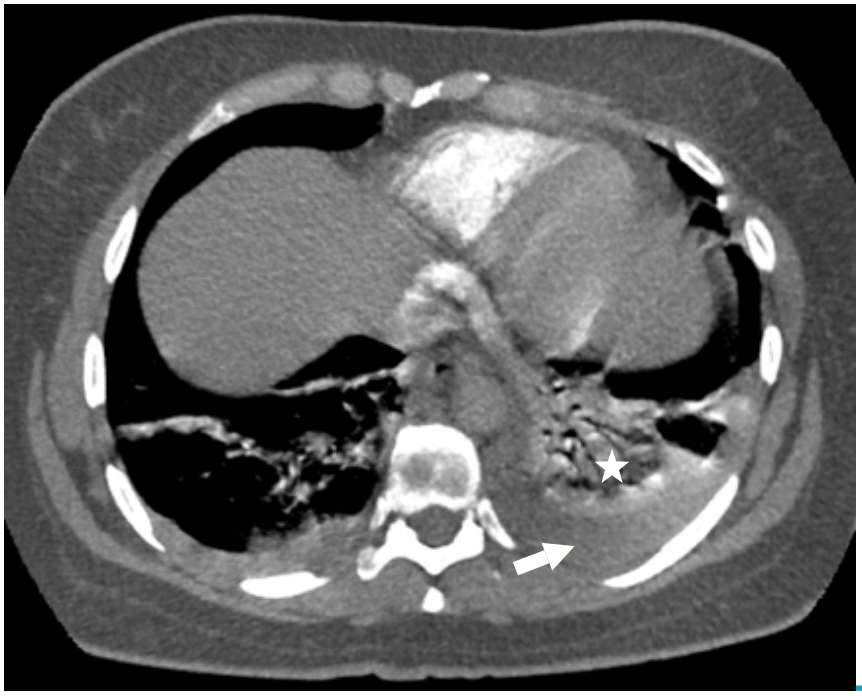

Fig 4. Chest AngioCAT. Broad base consolidation, hilar apex, obtuse borders that coincide with pulmonary infarction (star), pleural effusion (arrow).
Source: Own elaboration based on the data obtained in the study.

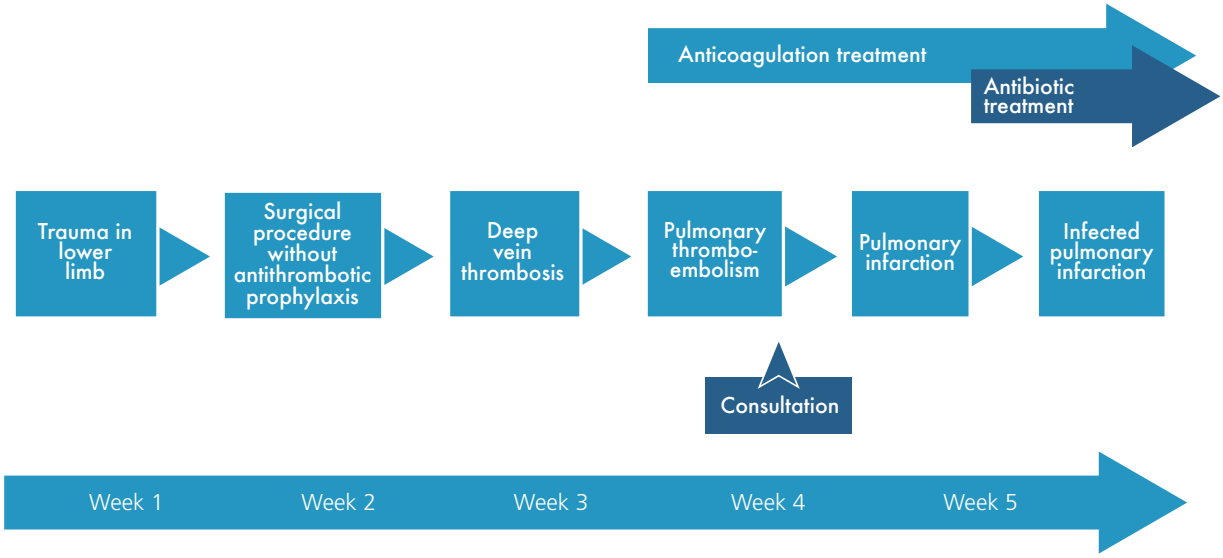

Fig 4. Timeline.
Source: Own elaboration based on the data obtained in the study.

DISCUSSION

This case shows the clinical evolution of a patient with PTE, which progressed to pulmonary infarction and infection of the necrotic lung tissue. This case is relevant from several points of view, since it points the importance of thrombus prophylaxis in patients at risk,

and exposes complications that endanger patients' lives and generate diagnostic, therapeutic and research challenges.

Many risk factors are associated with pulmonary thromboembolism; in this case, the patient presented trauma, surgery, immobility and obesity (14). The incidence of PTE can be reduced by performing thrombus prophylaxis in patients undergoing orthopedic knee surgery, particularly in the presence of additional risk factors (15). Therefore, prophylaxis until patients recover mobility is highly recommended (16).

PTE diagnosis was obtained by following the guidelines for clinical practice (17), that is to say, by classifying the probabilities through Wells scale and confirming the diagnosis with the test of choice, in this case, chest AngioCAT.

On the other hand, the evolution of the patient's clinical picture, besides the development of systemic inflammatory response, elevation of acute phase reactants, exacerbation of pleuritic pain and respiratory deterioration, caused the suspicion of infected pulmonary infarction (8). This clinical presentation, along with compatible diagnostic images, was the basis of the diagnosis. In this case, a significant improvement was achieved, allowing hospital discharge and a good short- and long-term prognosis.

Nevertheless, it is important to mention that this report has significant limitations: the lack of microbiological isolates to determine the etiological agent, the lack of clinical practice guidelines for the diagnosis and treatment of infected pulmonary infarction, and the radiological difficulty to differentiate bacterial pneumonia and pulmonary infarction (11). In addition, antibiotic treatment was selected based on the extrapolation of the local guidelines for the treatment of nosocomial pneumonia. Further research on the subject is necessary to better understand, diagnose, treat and prevent this entity, in order to improve care and clinical outcomes of patients.

In conclusion, pulmonary infarction is a common complication of pulmonary thromboembolism, which can become infected on rare occasions. Consequently, a high degree of clinical suspicion and adequate interpretation of the evolution are necessary to establish the diagnosis and to provide timely management.

Patient Perspective: the patient expressed gratitude for receiving medical care in an appropriate and humanized way.

Informed consent: the patient consented the publication of the information used in this case report.

CONFLICT OF INTEREST

None stated by the authors.

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