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CLINICAL CASE

Primary meningococcal arthritis of the hip due to serogroup W in a pediatric patient

Gabriel Dapueto[1], Patricia Barrios[2], Cristina Zabala[3], Gabriel Peluffo[1], and Gustavo Giachetto[2]*

[1]Clínica Pediátrica B; [2]Clínica Pediátrica C; [3]Clínica Pediátrica A. Universidad de la República, Montevideo, Uruguay

Abstract

Background: *Primary meningococcal arthritis (PMA) is defined as the presence of acute septic arthritis with the identification of Neisseria meningitidis in synovial fluid or blood cultures but no clinical evidence of sepsis or meningitis. This report aimed to describe a clinical case of PMA caused by serogroup W, an uncommon etiology of this disease in Uruguay, and review the available literature.* **Case report:** *We report the case of a 5-year-old female, with no past medical history, admitted to the emergency department with a 12-hour history of fever of 39 °C and a limp. The patient was hemodynamically stable and had no clinical evidence of meningitis. Hip ultrasound showed an increase in synovial fluid. Arthrocentesis showed purulent exudate and synovial fluid culture showed no growth after five days. The blood culture showed isolates of N. meningitidis, serogroup W. The patient received treatment with ceftriaxone, and drainage of the affected joint was performed with excellent clinical response.* **Conclusions:** *Primary meningococcal arthritis is a rare presentation of meningococcal disease. Systematic arthrocentesis and the adequacy of antibiotic therapy when septic arthritis is clinically suspected are essential for confirming the diagnosis and decompressive drainage of the involved joint. This report is the first of PMA caused by serogroup W in Uruguay. Although the most common serogroup involved in meningococcal arthritis is serogroup B in Uruguay, an increase in serogroup W-related diseases has been reported in Chile and Argentina, emphasizing the need for epidemiological surveillance.*

Keywords: *Infectious arthritis. Meningococcal infections. Neisseria meningitidis.*

Artritis meningocócica primaria de cadera por serogrupo W en un paciente pediátrico

Resumen

Introducción: *La artritis meningocócica primaria (AMP) se define como la presencia de artritis séptica aguda sin meningitis ni sepsis meningocócica y con aislamiento de Neisseria meningitidis en líquido articular o sangre. El objetivo de este reporte es presentar un caso clínico de AMP causada por el serogrupo W, una etiología poco frecuente de esta enfermedad en Uruguay, y revisar la literatura disponible.* **Caso clínico:** *Se reporta el caso de una paciente de 5 años, sana, que ingresó por cojera dolorosa y fiebre de 39 °C de 12 horas de evolución. La paciente se encontró hemodinámicamente estable y sin evidencia de meningitis. La ecografía de cadera mostró un aumento del líquido sinovial; la artrocentesis, material purulento . No se observó desarrollo en el cultivo del líquido articular y en el hemocultivo se reportó N. meningitidis del serogrupo W. Se realizó drenaje articular y se administró ceftriaxona intravenosa. La paciente presentó buena evolución.* **Conclusiones:** *La presentación de la enfermedad meningocócica como artritis séptica aguda es extremadamente infrecuente. La*

Correspondence:
*Gabriel Dapueto
E-mail: gdapueto@gmail.com

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punción articular sistemática y la adecuación del tratamiento antibiótico frente a la sospecha de artritis séptica son fundamentales para la confirmación del diagnóstico, además del drenaje descompresivo de la articulación. Este es el primer caso clínico reportado en Uruguay de AMP causada por el serogrupo W. Si bien en nuestro país la mayoría de los casos se deben al serogrupo B, en Chile y Argentina se ha comunicado un aumento del número de casos por el serogrupo W, lo que enfatiza la importancia de la vigilancia epidemiológica.

Palabras clave: *Artritis infecciosa. Infecciones meningocócicas. Neisseria meningitidis.*

Introduction

Acute septic arthritis is a frequent and potentially severe disease with a risk of sequelae at joints. In Uruguay, the most frequent etiology is *Staphylococcus aureus*, with the prevalence of *Kingella kingae* in the group of children under 5 years of age[1].

Primary meningococcal arthritis (PMA) is defined as the presence of acute septic arthritis with no association with meningitis or meningococcal sepsis and with isolation of *Neisseria meningitidis* in synovial fluid or blood[2,3].

From a clinical and pathogenic point of view, four forms of joint involvement by meningococcus are described[3]:

- *Early septic arthritis*. It is produced by direct invasion of the microorganism in the context of acute meningococcemia. It generally occurs between the first and second day of evolution. The microorganism grows in joint cultures.
- *Arthritis associated with chronic meningococcemia*. It is also produced by direct invasion during chronic meningococcemia. There may be mono or oligoarticular involvement.
- *Primary meningococcal arthritis*. It is produced by direct invasion of the microorganism without sepsis or meningitis. It constitutes 1.5% of septic arthritis in the pediatric age[4]. In general, it is monoarticular with a preference for large joints as the knee, which is the most common.
- *Allergic arthritis*. It is one of the post-infection inflammatory manifestations of meningococcal disease, including arthritis, vasculitis, pericarditis, and uveitis. It has an immune mechanism due to the deposit of immune complexes at the joint level. It occurs between days 4 and 8 from the beginning of the disease[5].

Within the spectrum of meningococcal disease that ranges from asymptomatic carrier to meningococcal septic shock, joint involvement is frequent, occurring in approximately 10% of patients[2,4,6]. However, most cases of joint involvement occur as a part of systemic disease. PMA is the least common form of joint involvement[3].

In Uruguay, meningococcal disease is low endemic, with an average of 34 cases per year and an incidence of 0.4/100,000 inhabitants[7]. It usually presents as meningitis or septic shock.

N. meningitidis is a Gram-negative coccus bacterium. Meningococci associated with the invasive form of the disease generally have a polysaccharide envelope that characterizes their serogroup. Twelve capsular serogroups have been identified (A, B, C, X, Y, Z, 29E, W135, H, I, J, and L). Serogroups A, B, C, Y, W, and recently X are the most frequently associated with the disease. The others are related to asymptomatic carriers and could very occasionally cause disease[5].

Considering all forms of meningococcal disease, serogroup B is responsible for most of the cases of endemic disease in Uruguay[7]. Of the serogroups that have been involved in epidemic outbreaks, the most frequent is serogroup C, which caused the outbreaks of the 90s. These outbreaks were controlled with the massive application of the A + C polysaccharide vaccine to the group between 2 and 19 years of age. Serogroup B was implicated in an outbreak in 2001 in the town of Santa Lucía, Canelones[8]. The other serogroups have a less frequent incidence. Of the 21 cases reported in 2017, one corresponded to serogroup Y and another to serogroup W[7].

Before 2000, serogroup W was responsible for a small number of cases[9]. Since the outbreak reported in the Arabian Peninsula, an increase in cases attributable to this serogroup has been reported worldwide[9,10]. There are substantial epidemiological differences between the different countries of the region. In Chile, since the epidemic by serogroup W in 2012 and despite vaccination with the conjugate vaccine for serogroups A, C, W, and Y (Men ACWY), serogroup W continues to be the most frequent[11,12]. In Argentina, the most frequent serogroups are B and W, with an increasing trend of the latter since 2008[11]. In Brazil, serogroup C is the most frequent, except in the southern region where, as in Uruguay, serogroup B

predominates[11,13]. The incidence of serogroup C has decreased since the start of vaccination with the conjugate vaccine in 2010. Similar to Chile and Argentina, cases due to serogroup W[13] increased in the southern region of Brazil since 2008.

The exact incidence of PMA in our country is unknown. One case report of PMA caused by serogroup B has been published[14]. In a series of nine cases of PMA published in Argentina, five cases were caused by serogroup W[3].

This study aimed to report a case of PMA caused by serotype W and review the available literature on the matter.

Clinical case

We describe the case of a 5-year-old female patient with no relevant past medical history who did not travel abroad. The patient lives with both parents, adequate housing without overcrowding. According to the national vaccination plan, she received one dose of BCG tuberculosis vaccine, four doses of pentavalent vaccine (diphtheria, cellular pertussis, tetanus, *Haemophilus influenzae* type B, hepatitis B), three doses of 13-valent pneumococcal conjugate vaccine, four doses of the inactivated polio vaccine, two doses of hepatitis A vaccine, two doses of varicella vaccine, and two doses of measles, rubella, and mumps (MMR) vaccine. Twelve hours before admission, she presented a fever of up to 39°C and a painful limp that restricted standing and walking. In the days before the consultation, she reported a runny nose and catarrhal cough. On physical examination, the patient was found to be in good general condition. Glasgow Coma Scale (GCS) 15; immediate capillary refill time; warm limbs, full pulses, skin without lesions. The hip presented with antalgic posture in abduction and external rotation and pain on mobilization with minimal movements. No other joints were involved, neither stiff neck nor meningeal signs. The rest of the physical examination was found with no alterations. She was hospitalized with probable septic arthritis of the hip.

Hip ultrasound reported an increase in synovial fluid with simple characteristics, measured 5 mm at the level of the anterior recess. Synovial membrane thickening and capsule protrusion were associated. The hip X-ray showed no alterations. Blood test results showed leukocytes 7300/mm^3, neutrophils 32%, lymphocytes 48%, hemoglobin 12.1 g/dL, platelets 217,000/mm^3. C-reactive protein (CRP) levels were 70 mg/L, and procalcitonin (PCT), 0.5 mg/L. A sample was collected for blood culture.

Arthrocentesis was performed 5 hours after hospital admission before the start of antibiotic treatment. Purulent material was obtained and sent for culture. Surgical cleaning was performed, maintaining drainage. According to local epidemiology, empirical antibiotic treatment with intravenous clindamycin and cefuroxime was started targeting a possible staphylococcal etiology and less likely *K. kingae*.

The patient presented a good evolution. Twenty-four hours after admission, she was apyretic, with progressive improvement in pain and joint functionality *N. meningitidis* serogroup W no producer of beta-lactamase was found in blood culture 48 hours later. Antibiotic therapy was modified to ceftriaxone, which the patient received for up to 10 days. Subsequently, she completed 21 days of oral amoxicillin. No bacterial growth was reported in the joint fluid culture.

After hospital discharge, complement components C3 and C4 were evaluated due to the infrequent clinical presentation and serogroup and found within normal values.

Discussion

The patient presented PMA given the joint involvement and isolation of *N. meningitidis* in blood culture but no meningeal involvement or sepsis.

The presentation of meningococcal disease as acute septic arthritis is extremely rare[3]. Among the most frequent causes of septic arthritis in our country, *S. aureus* is included in all age ranges, and *K. kingae* in children[1,15]. The empirical treatment, in this case, was directed to these etiologies.

The serogroup of *N. meningitidis* involved in this clinical case is rare. Although most cases are due to serogroup B in our country, an increase in the number of cases caused by serogroup W[11] has been reported in Chile and Argentina. Also, cases of serogroup W have increased in Europe, which has led to adjustments in vaccination programs[16]. We found only two previous reports of PMA caused by this serogroup in PubMed; however, this was the most frequent serogroup in a series of nine cases in Argentina[3,16,17].

Regarding the site, the involvement is generally monoarticular, and the knee is the most frequently involved joint, followed by the hip, as in this case[3,18].

Several factors predispose to invasive meningococcal disease. Age is one of the fundamental risk factors, with children under one year of age being the highest

risk group. However, approximately 40% of cases occur in children under 5 years of age[5,6,19]. The cases caused by serogroup B tend to occur in younger children, while the other less frequent serogroups usually cause disease in older patients[5].

In the present case, the lab study was indicated to rule out complement alterations due to disease caused by other serogroups rather than A, B, and C[5,6]. The deficiency of specific antibodies or terminal complement components (C5-C8) is mainly associated with an increased risk of meningococcal disease, up to 600 times higher[5,6]. The complement deficiency studies performed on this patient were incomplete. The screening method to identify complement alterations is the CH50 test that is altered in the case of any of these factors[20].

The initial selection of antibiotics (clindamycin and cefuroxime) was decided based on national guidelines and directed to the etiological agents of septic arthritis in our country, the most frequent being *S. aureus* and considering *K. kingae* because of its prevalence in this age group. For convenience, the antibiotic plan with ceftriaxone was continued, although penicillin could have been used since the microorganism was sensitive to this antibiotic. *N. meningitidis* generally remains susceptible to penicillin; however, strains with resistance to penicillin but not to cephalosporins have been reported, which has caused therapeutic failures. The mechanism involved in resistance to penicillin is structural changes at the level of penicillin-binding proteins (PBP)[5,6]. The empirical treatment in the patient showed activity against *N. meningitidis*, even against the possible strains with resistance to penicillin. Regarding duration, there are no specific guidelines for the treatment of PMA. Following the national guidelines for treating septic arthritis, a duration of 21 days of antibiotic therapy was chosen[15].

Arthrocentesis was performed early and before the start of antibiotic treatment. Systematic joint puncture in the event of suspected septic arthritis is essential for the study of synovial fluid, confirmation of the diagnosis, and the adjustment of antibiotic treatment, additionally to decompressive drainage of the joint[5]. The need for drainage and debridement of the joint should be decided with a pediatric orthopedic surgeon. At the hip joint, the standard open approach is indicated.

PMA is a potentially vaccine-preventable disease. There are two meningococcal vaccines available: Men ACYW is composed of polysaccharides for serogroups A, C, Y, and W135 conjugated to diphtheria toxoid; Men B-4C is formed by three recombinant proteins, NHBA, NadA, FHbp, and by outer membrane vesicles that contain the PorA membrane protein of the P1.4 serosubtype[21]. According to data from the United Kingdom, where this vaccine is used routinely, its effectiveness in preventing invasive meningococcal disease caused by serogroup B is 92.4%[7].

In Uruguay, these vaccines are not part of the national vaccination scheme, and their indication is considered free of charge for risk groups and in the context of outbreak control.

The universal incorporation of meningococcal vaccines is under constant review. As PMA is a disease with high lethality despite treatment, vaccination is a fundamental strategy[9]. However, in developing countries with limited financial resources, vaccination costs against meningococcal diseases limit their universal inclusion. In Uruguay, under the current low endemic epidemiological situation, it has been decided to maintain the vaccination strategy in outbreaks and risk groups[7].

In Uruguay, the current recommendations for these vaccines are the following[22]:

- In cases of outbreaks or epidemics
- High risk of invasive meningococcal disease
- People with C5-C9 complement deficiency (properdin, factor H, or factor D)
- People with functional or anatomical asplenia
- Hematoncological diseases
- Hematopoietic stem and solid organ transplant recipients
- People traveling to endemic or outbreak areas
- Health or laboratory personnel who handle bacteriological samples
- Previous episode of invasive multiple sclerosis
- Leakage of cerebrospinal fluid (due to congenital malformations, skull fracture, or neurosurgical procedure)
- Carriers of human immunodeficiency virus regardless of immune status

The present report is the second PMA case documented in Uruguay. No cases of children with arthritis caused by *N. meningitidis* serogroup W have been reported in our country. Considering the current situation in the region, we must be attentive to epidemiological surveillance and possible changes in serogroups. With appropriate treatment, PMA is a disease that evolves adequately with no sequelae. However, the diagnostic delay is associated with a higher risk of complications. Therefore, high diagnostic suspicion, systematic joint puncture, and timely initiation of antibiotic treatment are fundamental[3,4].

Although the incidence of invasive meningococcal disease is low, its high lethality aims to vaccination as an attractive measure for controlling this disease in the future.

Ethical disclosures

Protection of human and animal subjects. The authors declare that no experiments were performed on humans or animals for this study.

Confidentiality of data. The authors declare that they have followed the protocols of their work center on patient data publication.

Right to privacy and informed consent. The authors have obtained the written informed consent of the patients or subjects mentioned in the article. The corresponding author has this document.

Conflicts of interest

The authors declare no conflict of interest.

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