

Primary Meningococcal Septic Arthritis

Case Report and Literature Review of an Unusual Manifestation of Meningococcal Disease

Borja Occhi Gómez, MD, César Ramírez Feito, MD, Diego García-Germán Vázquez, PhD, MD, Marta García Vega, MD, and Miguel Ángel García Viejo, PhD, MD

Abstract

Introduction: Primary meningococcal septic arthritis (PMSA) is an unusual manifestation of meningococcal disease. It is defined as the presence of acute septic arthritis without association with meningitis or the classic meningococemia and isolation of *Neisseria meningitidis* in synovial fluid and blood culture. Diagnosis and early treatment, combining antibiotic and joint drainage, are fundamental.

Case Presentation: We present the case of a healthy 17-year-old male who presented with history of an acute onset, painful knee accompanied by fever. *N. meningitidis* was cultured from the synovial fluid. He was treated with arthroscopic lavage and intravenous ceftriaxone for 2 weeks. He was discharged 7 days after admission receiving outpatient intravenous ceftriaxone for 6 days and was ultimately transitioned to oral ciprofloxacin for 2 weeks thereafter. At the final follow-up visit, he had returned to sports activity with a normal knee joint.

Literature Review: We have done an exhaustive literature review in PubMed. Forty-four articles were included, with a total of 46 patients, to which we added ours. We collected the available demographic data, analytical values, culture tests, treatment, and evolution.

Purposes and Clinical Relevance: This case illustrates an unusual presentation of *N. meningitidis* infection. Diagnostic

suspicion is essential. Joint washing and antibiotics are the mainstays of treatment. Early and proper treatment prevents complications and mortality. Our main objective was to evaluate the diagnostics tools and treatment in PMSA. As a secondary objective, we evaluated the cases with negative cultures in order to evaluate the criteria for the diagnostic suspicion of PMSA.

Infection by *Neisseria meningitidis* covers a broad clinical spectrum from carrier status to fulminant sepsis. The most recognized clinical forms are meningitis and septicemia.¹ Joint involvement in meningococcal infection occurs in 1.6% to 16.6% of cases.²⁻⁵ Primary meningococcal septic arthritis (PMSA) is very uncommon. It is defined as the presence of acute septic arthritis without meningitis or meningococcal sepsis and the isolation of *N. meningitidis* in joint fluid or blood.^{2,6,7} It was first described by Sainton on 1919.⁸ In his review, Schaad described 15,387 meningococcal disease cases, among which 1,180 presented with septic arthritis and there were only 25 cases of PMSA.^{2,3,9} It is monoarticular in 52% to 84% of cases, and the knee is the most affected joint.^{2,6,9}

Early diagnosis is essential and is based on diagnostic suspicion and microbiological tests. Treatment combines antibiotic and joint drainage. Prognosis is usually very good.^{1,9,10}

We performed an exhaustive literature review in PubMed. A search was carried out using the following search string: “(((Primary meningococcal arthritis) OR Monoarthritis *Neisseria meningitidis*) OR Primary *Neisseria* arthritis) or *Neisseria* monoarthritis meningitidis) or Isolated meningococcal arthritis.” We found a total of 79 items (Fig. 1). The title and background were reviewed. We included original articles and bibliographic reviews written in English and published in any country between 1979 and April 2017. Articles whose content did not include cases or series of clinical cases were excluded. Forty-four articles were included, with a total of 46

Borja Occhi Gómez, MD, César Ramírez Feito, MD, Diego García-Germán Vázquez, PhD, MD, and Marta García Vega, MD, Department of Orthopaedic Surgery, Servicio de COT, Hospital Universitario de Puerta de Hierro-Majadahonda, Madrid, Spain. Miguel Ángel García Viejo, PhD, MD, Department of Internal Medicine, Hospital Universitario de Puerta de Hierro-Majadahonda, Madrid, Spain.

Correspondence: Borja Occhi Gómez, MD, Department of Orthopaedic Surgery, Servicio de COT, Hospital Universitario de Puerta de Hierro-Majadahonda, C/ Manuel de Falla 1, Majadahonda, 28222 Madrid, Spain; borjaocchi@gmail.com.

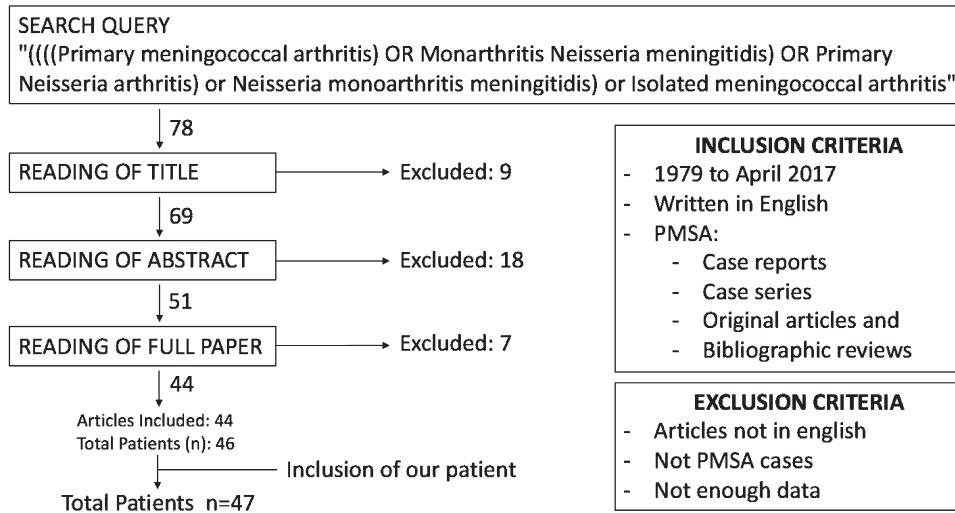


Figure 1 Search terms and articles eliminated or included during our review.

patients, to which we added ours. We collected the available demographic data, analytical values, culture tests, treatment, and evolution. Articles were reviewed by two independent researchers. Data was analyzed with Stata/MP software version 14.2 (StataCorp, LLC, College Station, Texas, USA).

Our main objective was to evaluate the diagnostics tools and treatment in PMSA. As a secondary objective, we evaluated the cases with negative cultures to evaluate the diagnostic suspicion criteria of PMSA.

Clinical Case

A healthy 17-year-old male was admitted into our hospital due to a left knee pain of 3 hours duration. He had a 102° F fever and was vomiting. He denied other symptoms and prior sexual relations and risk contacts. His vaccinations were up to date.

His knee was edematous and warm and was painful to mobilization. No skin rash was noted. Laboratory findings revealed an elevated white blood cell count (10.2×10^9 leukocytes/L) with a left shift (polymorphs 80.4%). C Reactive protein was 48.3 mg/dL. Levels of IgA, IgG, and IgM were normal, as well as a complement C4 level of 33.2 mg/dL.

Aspiration of the joint yielded 112,800 leukocytes/mm³ (92% polymorphs), glucose less than 10 mg/dL, and protein measured 3.6 g/dL. The Gram stain showed Gram-negative diplococci. Intravenous ceftriaxone and cloxacillin treatment was begun, pending culture results.

Arthroscopic lavage was performed. We found synovial inflammation but no other findings. Blood and pharynx cultures were negative, although the latter was taken after the administration of antibiotics.

N. meningitidis was isolated from synovial fluid aspiration. The antibiotic was changed to ceftriaxone 1g/24h for 14 days.

He remained afebrile and asymptomatic during his admission. He was discharged 7 days after admission receiving outpatient intravenous ceftriaxone 1g/24h for 6 days and

was ultimately transitioned to oral ciprofloxacin for 2 additional weeks.

A year and a half later, the patient is asymptomatic and has resumed his normal activities.

Discussion

N. meningitidis is associated with severe invasive infections such as meningitis and fulminant septicemia. Up to 3% of *N. meningitidis* cases have an atypical presentation (arthritis, pericarditis, or pneumonia).^{2,11-13} Meningococcal arthritis accounts for 1% to 2% of all septic arthritis.¹⁰ Among them, PMSA is exceptional, and as far as we know, there are only 47 cases described in English literature, including our patient.

Epidemiology and Risk Factors

In our review, PMSA shows three peaks of incidence, as it occurs with meningococcal infection. The highest incidence peak occurs around age 20, while the highest meningococcal infection occurs in the early years of life. The third peak will correspond to the population over 65 years of age (Fig. 2). Our review coincides in this aspect with that of Schaad, but not with Wells.^{9,14} Given the small number of patients, we believe that it is early to draw conclusions, but it seems that PMSA affects mainly the young population around the age of 20.

Monoarticular involvement occurs in 66% while polyarticular forms occurs in 34% of cases.

In adults, the knee is involved in 75% of the monoarticular forms. In children under 18 years old, the joint distribution is more heterogeneous with the knee being affected in 46.7%, ankle 20%, hip and elbow (13.3% both), and a sacroiliac involvement in 6.7% of cases. Therefore, PMSA should not be ruled out if it affects other joints rather than the knee, especially in patients under 18 years of age.^{4,12,15,16}

It is important to ask the patient about risk contacts. Respiratory symptoms occur in nearly one-third of patients (29.8%) and dermatitis-arthritis syndrome in almost half of

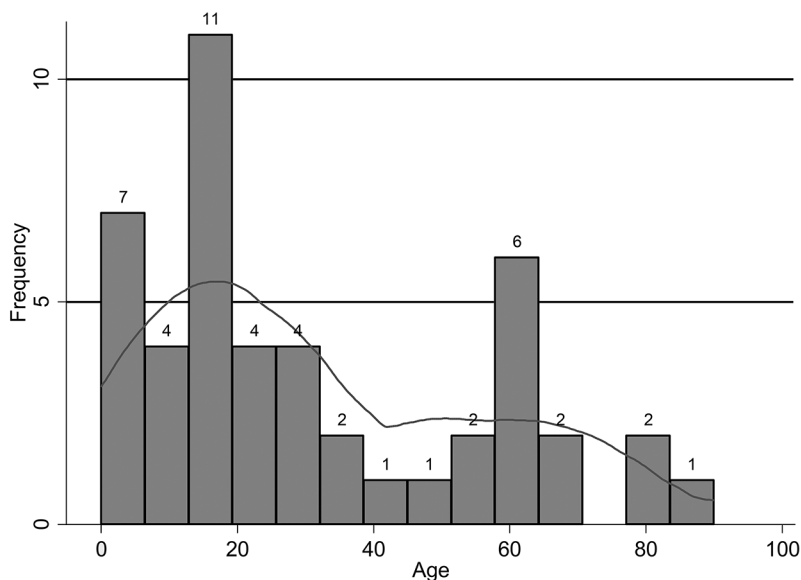


Figure 2 PMSA age distribution.

them (46.8%). Differential diagnosis with a high degree of suspicion for gonococcal disease must be considered.^{9,17,18}

The association between PMSA and immunosuppression, complement deficiencies, and immunoglobulin biosynthesis has not been demonstrated. Even so, given their predisposition to meningococcal disease, it seems reasonable to rule out an immunodeficiency, especially in children or in X, Y, W135, and non-serotypeable serogroups.^{6,12,18-27}

Diagnosis

Culture-Negative Synovial Fluid

Synovial culture-negative septic arthritis is a diagnostic and therapeutic challenge given that in these cases morbidity and mortality can increase.²⁸ Meningococci are fastidious organisms and the scant number of organisms seen on microscopy may not survive culture.²⁹⁻³¹ In our review, synovial cultures were negative in 16% of the cases, similar to Schaad’s findings (10% to 20%).² Diagnostic suspicion is essential in these cases (Table 1).

In our review, in all cases of culture-negative synovial fluid, at least one of the following was present: risk contact, skin lesions, previous respiratory symptoms, positive nasopharynx and blood culture, or presence of Gram-negative diplococci in a Gram stain (Table 2). We therefore believe that it is important to assess these aspects to increase the suspicion of PMSA. Polymerase chain reaction (PCR) is a very helpful tool in the synovial culture-negative PMSA, especially in those patients who had recently received antibiotics.^{4,29}

Blood and Nasopharyngeal Cultures

In our review, blood cultures were positive in 32.5% of cases, similar to the studies of Schaad² and Wells and Gibbons.⁹ Nasopharyngeal (NF) cultures were positive in 11.5% of cases, far from 30% of Schaad’s findings; NF were

performed only in 55% of the patients.¹⁴ A cause could be the greater use of vaccines today, although this relationship has not been clarified so far.^{25,32,33} Nasopharyngeal cultures, despite a poor performance, can help diagnosis, especially in cases of negative synovial culture.^{2,34}

Serogroups

MenC is the most frequent serogroup in PMSA (40.43%) followed by serogroup B (14.89%). Serogroup B is the most common in meningococcal disease in Europe, USA, and South America, although the incidence of serogroup C is increasing.^{35,36} The greater frequency of serogroup C in PMSA could be due to its greater tendency toward joint involvement.³⁷ It has been proposed that PMSA is caused by less virulent behavior serogroups, with a lower endotoxins release, which generate articular infections instead of causing septicemia.⁴ However, we believe that more studies are needed. In up to 31.9% of cases, the serogroup could not be identified.

Table 1 Diagnostic Key Points in PMSA

Monoarticular involvement (66%)
Mainly around the age of 20
Knee 75% involved in adult monoarticular PMSA
Under 18 years old, joint distribution is more heterogeneous
Respiratory symptoms (29.8%)
Dermatitis-arthritis syndrome (46.8%)
Cultures
+ Synovial cultures (84%)
+ Blood cultures positive (32.5%)
+ Nasopharyngeal cultures (11.5%)
MenC is the most frequent serogroup in PMSA (40.43%)

Table 2 Characteristic Feature of Synovial Culture-Negative Patients (Total 7)*

	Age	NF Culture	Joint Involvement	Skin Lesions	Medical Record	Fever	ESR	CRP	Gram Stain	Blood Culture	Polymerase Chain Reaction	Definitive Treatment
Dillon	12	-	Mono	Purpuric rash	No	Yes	63	N/D	Diploc G-	+	No	Ceftriaxone + Drainage
Verma	19	N/D	Poly	Purpuric rash	No	Yes	58	N/D	Diploc	-	+	G Penicillin + Drainage
Joyce	19	N/D	Mono	Erythematous rash	No	Febricula	N/D	27	Diploc G-	-	+	Ceftriaxone + Drainage
Petty	23	+	Poly	Petechial rash	Sore throat. Bacteriology technologist	Yes	N/D	N/D	Diploc G-	-	+	G Penicillin + Drainage
Edgeworth	24	N/D	Mono	Maculopapular rash	Sore throat	Yes	N/D	389	Diploc G-	-	+	G Penicillin + Arthroscopic Drainage
Bongers	35	-	Poly	Petechial rash	Risk contact	Yes	86	114	-	-	No	Peniciline + Drainage
Garner	79	N/D	Mono	Papular lesion	No	Yes	No	215	-	-	+	Ceftriaxone + Arthroscopic Drainage

*Four were monoarticular and three polyarticular, median age 23 years (range: 12 to 79 years). All had skin lesions. Two (28.6%) had previous respiratory symptoms. Three patients had a risk contact with *N. meningitidis* patients or samples. Six out of seven patients had fever and the latter presented fever the day after admission. Nasopharyngeal cultures were taken only in three patients and was positive in one (33%). In these seven patients an arthrocentesis was performed, obtaining a pus draining in all cases. 71.4% showed Gram-negative diplococci in the Gram stain. In five patients, the polymerase chain reaction was diagnostic. In Bongers et al., the patient's child had a concomitant meningitis, *N. meningitidis*. In Dillon's case, diagnosis was made by the growth of *N. Meningitidis* in blood cultures and presence of Gram-negative diplococci in the Gram stain. NF Culture = nasopharyngeal culture; N/D = No Data; ESR = erythrocyte sedimentation rate (mm/h); Mono: monoarticular; Poly: polyarticular; Diploc: diplococci; G: Gram; CRP: C reactive protein (mg/L).

Table 3 Characteristic Features of Patients Who Presented Medical Complications

Study	Age	MR	Sex	Time to diagnosis	Fever	Culture	Treatment	Estancia	Serogroup	Complications
Samanta 1990	20	No	F	5 hours	+	S +	Open Drain + Benzilpeniciline	21 d	C	Respiratory Distress Syndrome
Cheng 2003	54	No	M	3 days	NO	V +	Ceftriaxone	20 d	N/D	Uveitis, lost monocular vision
Michel 2013	60	HIV, Grout	F	7 days	+	S +	Open Drain + Ceftriaxone	62 d	N/D	Neurologic sequelae

F = female; M = male; MR = medical record; Mono = monoarticular; Poly = polyarticular; S+ = synovial positive culture; V+ = vitreal positive culture; N/D = no data.

Treatment

Intravenous Antibiotic Treatment in PMSA

An empirical antibiotic was used in all cases until microbiological tests were obtained. Choice and duration of antibiotic treatment is controversial. Penicillins have been the classic treatment. In the last 20 years there is a tendency toward the use of third generation cephalosporins since they have a similar efficacy and their administration is more comfortable.

Outpatient Antibiotics

There is no consensus on the type or duration of antibiotic treatment after a patient's discharge; no complications have been found in those patients who did not received antibiotic after discharge.^{15,26,36,38} In our case, the patient received intravenous ceftriaxone on an outpatient basis the first week after discharge followed by oral ciprofloxacin for 2 weeks. In the other four cases where a quinolone was used at the patient's discharge, the antibiotic was given between two and 4 weeks.^{30,39-41} These guidelines are effective and allow for a shorter hospital stay and greater patient's comfort due to the shorter hospital stay. More studies and cases are needed for a consensus in antibiotic guidelines.

Is Arthrocentesis Enough in Monoarticular PMSA?

Treatment of monoarticular PMSA is based on antibiotic and joint drainage, which can be performed by arthrocentesis or through surgery. Joint drainage is usually necessary to lower the bacterial load and reduce proinflammatory factors.²⁶

The advantages of arthrocentesis are its less aggressiveness and easy realization with minimal complications, although in 54% of cases a second arthrocentesis was needed. Arthroscopy allows articulation visualization, having as a disadvantage the need for general anesthesia and second lavage in 25% of the cases. In cases of poor outcome, it is useful to review the joint and release synovial plicae if present.⁴² Arthrotomy, finally, shares the advantages and disadvantages of arthroscopy, but adding its surgical aggression; arthrotomy could be reserved for deep joints like the hip, although arthroscopic washes have been described.^{5,39,43}

Both arthrocentesis and arthroscopic washing, according to our review, were effective in PMSA. The choice will be based on each hospital's protocol, the affected articulation, and surgeon preferences. In any case, the patient should be advised about the possibility of the need to place several drains, as in any septic arthritis.^{10,43-46}

Prognosis

Three out of 47 patients in our review presented medical complications. One patient required ICU admission with neurological sequelae and another lost monocular vision due to a meningococcal uveitis; the third patient experienced respiratory distress syndrome without sequelae (Table 3).^{15,32,47} There was only one case of secondary osteoarthritis after PMSA; it was in a 60-year-old patient who required an ankle arthrotomy.⁴⁸

In our case, joint prognosis was excellent. There is con-

trovery about joint prognosis, although most of the authors in our review suggested an excellent prognosis if treated in time. Despite this, long-term results should be assessed through longer term follow-up.^{1,6,9,10}

Conclusions

Primary meningococcal septic arthritis is an uncommon entity that warrants a high index of suspicion. Joint washing and antibiotics are the mainstays of treatment. Early treatment is essential for achieving a satisfactory outcome. Since it is an uncommon pathology, more cases are needed to continue the study of this pathology, its diagnosis, treatment, and long-term outcomes.

Disclosure Statement

None of the authors have a financial or proprietary interest in the subject matter or materials discussed in the manuscript, including, but not limited to, employment, consultancies, stock ownership, honoraria, and paid expert testimony.

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