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Meningococcemia without Meningitis, Starting with Gastrointestinal Symptoms - Case Report

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Abstract:- Neisseria meningitidis infection is the main etiologic agent of meningitis of bacterial origin in the world, mainly affecting children and young adults, finding up to 15% of the population as asymptomatic carriers. Invasive meningococcal disease has a broad spectrum in its clinical presentation, the most frequent being meningitis and meningococcemia, however, variable foci have been documented such as pneumonia, septic arthritis, endocarditis, among others, the case of Atypical clinical presentation meningococcemia, rarely reported in the literature.

Keywords:- *Neisseria Meningitidis; Meningococcemia; Meningococcal Infections; Diarrhea.*

I. INTRODUCTION

Taking a historical tour of meningococcal disease, we can find references dating back to the 17th century, where it was first reported by Vieusseux, being described as a disease characterized by the typical symptoms of meningococcemia as "fievre cerebrale maligne non contagieuse" (non-contagious malignant brain fever) in 33 patients who died with the condition (4), but it was not until the 20th century that Weichselbaum identified the bacterium, Neisseria meningitidis, in the cerebrospinal fluid of 6 patients with fever (4,7).

Regarding the microorganism N. meningitidis, its microbiological characteristics describe it as a strict, immobile, aerobic gram-negative diplococcus, known as meningococcus (3,4), humans being the only known reservoir of this microorganism (3,5), likewise According to reports, approximately 10 to 15% of the population are asymptomatic carriers of this microorganism both in the nasopharynx and oropharynx, since transmission occurs from one person to another through respiratory secretions (3, 5, 6).

N. meningitidis is classified into different serogroups based on the antigenic differences given by the polysaccharides expressed on the capsular surface, which corresponds to its main virulence factor. Currently, 13 serogroups are known, being groups A, B, C, Y and W135 responsible for approximately 90% of cases of meningococcal disease (1, 2, 4, 21, 22). According to epidemiological reviews, it is found that the most frequently isolated serotype in the United States corresponds to group B and C; while in Colombia serogroup B is the most frequent, however, during 2019 there was an increase in the isolation of serotype C in the country (1, 26, 30).

The current situation of meningococcal disease is that it is estimated to affect 1.2 million cases of invasive meningococcal disease worldwide, with a mortality associated with invasive meningococcal disease of 135,000 cases (1,2), but infection by N. meningitidis It has a wide variability with respect to its incidence in the world, finding variable incidence rates between 20 and 1000 per 100,000 inhabitants in the "meningitis belt" in the sub-Saharan African region (27). In the case of Colombia, an incidence rate of 0.19 cases per 100,000 inhabitants is calculated, having reported up to epidemiological week 48 of 2019, 94 confirmed cases of meningococcal disease; However, reported mortality from meningococcal disease is 27% on average for 2017 (1, 28, 29, 30). Invasive meningococcal disease usually occurs in children under 5 years of age and adolescents (22, 18), especially in infants under 1 year of age, as evidenced in a Spanish study that determined the incidence in 10 years, finding that 47% of the cases correspond to children under 5 years of age and 75% of the cases are reported in children under 20 years of age (18), for Colombia in 2019, it was found that approximately 30.8% of confirmed cases were reported in children under 5 years of age and the highest incidence peak occurred in children under 1 year of age with 2.16 cases per 100,000 inhabitants (28,30).

Likewise, the risk factors are very varied, finding environmental factors such as a psychosocial history of overcrowding, factors inherent to the host such as age (<5 years and >65 years), smoking, complement deficiency, hypogamainimmunoglobulinemia, asplenia, HIV infection, as well as the virulence of the related strain.

In relation to invasive meningococcal disease, a classification of different types was established based on the physiological response generated in the patients, these being Meningitis with sepsis, Bacteremia with sepsis, but without mention of meningitis, Meningitis without sepsis and lastly. place benign chronic meningococcemia (7,9). Given its great genetic and antigenic variability, infection by N. meningitis can present with a wide clinical spectrum, meningitis being its most frequent manifestation with approximately 50% of cases (3), on the other hand, meningococcemia without meningitis occurs in 5 to 20% of people who develop meningococcal disease (in turn finding a high mortality rate that varies between 5 and 20%) (3,7, 9, 27), or other less frequent localized infections such as pneumonia (5-10%) (14), pericarditis, endocarditis, supraglottitis, conjunctivitis, urethritis and otitis media (3, 7).

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It must be taken into account that the clinical picture is characterized by a rapid incubation period, from 2 to 10 days (3), initially expressing itself with general and non-specific symptoms such as fever, headache, asthenia, and adynamia, while the classic triad for the disease Meningococcal sepsis corresponding to a meningeal focus of fever, meningismus, and altered state of consciousness occurs in only 33% of cases (3), and among these, 5 to 20% evolve to meningococcal sepsis; On the other hand, the petechial or purpuric rash is more specific, found in 45 to 65% of cases and has a rapid onset, which begins to become evident in approximately 12 to 18 hours from the onset of symptoms (3,7), on the other hand, neurological focalization in patients with meningococcal meningitis is a late finding (3), therefore it is important to have a high index of suspicion given the non-specificity of the symptoms and the rapid progression to ominous outcomes of the disease that are not has been adequately treated.

The rapid progression and deterioration of invasive meningococcal disease, it is vitally important to initiate early administration of appropriate antibiotic therapy, ideally within the first hour; N meningitidis is highly sensitive to penicillin, the intermediate sensitivity rate (MIC: 0.12–0.25 mg/mL) is low between 5% and 40%, and resistance to penicillin is rare because the empirical treatment of choice in the infection meningococcal infection, high-dose penicillin G or third-generation cephalosporins are recommended for 7 days. (3,4,32)

Indeed, long-term sequelae are frequent, ranging from 11 to 19% (7), the main sequelae being cognitive deficit 7 in 12% of cases (6), bilateral hearing loss/deafness in 4%, epilepsy, motor deficit and amputations secondary to sepsis-associated necrosis (2, 3, 6, 9)

The objective of this review is to report a case of meningococcemia without a meningeal focus in an immunocompetent adult patient, with an atypical presentation of the disease, and adequate response to treatment without subsequent complications.

II. CLINICAL CASE

We found a 46-year-old male patient with a history of Still's disease without pharmacological management and grade 2 obesity, with no other known history, who consulted the emergency department, with a clinical picture of approximately 24 hours of evolution of general malaise, peaks quantified febrile >38°C, abdominal pain located in the epigastrium, multiple emetic episodes, multiple foul-smelling liquid diarrheal stools, and the appearance of violaceous skin lesions on the upper and lower extremities and abdomen. The patient on physical examination found a patient in regular general condition with a toxic appearance, tachycardic (114lpm), febrile (39.2°C), with blood pressure figures within targets (128/77mmHg), dry oral mucosa, abdomen with abundant Panniculus adipose tissue, voluntary abdominal defense, pain on abdominal palpation in the epigastrium without masses, without hepatomegaly or splenomegaly, without signs of peritoneal irritation, on the skin violaceous, hard, irregular and painful lesions on palpation, which do not reduce to acupressure in limbs distal upper and lower legs involving palms and soles (Figure 1), without altered state of consciousness, without neurological focus, without nuchal rigidity or signs of meningeal irritation. Upon review by systems, the patient emphatically denies traveling outside the country or the city, denies contact with people with meningitis.

Fig 1. Skin lesions characteristic of meningococcemia.

Taking into account the evolution and the main complaint of the patient, an approach is carried out with a study of abdominal pain, for which paraclinical studies are requested whose results are referenced in Table 1, in which leukocytosis is evident with a clear predominance of neutrophils, significant elevation of acute phase reactants and impaired renal function, confirming the presence of an infectious process, associated with altered coagulation times, with prolongation of Partial Thromboplastin Time, prolongation of INR and moderate thrombocytopenia, money D positive, which suggest multiorgan dysfunction; It was decided to screen for Human Immunodeficiency Virus (HIV) with a negative result, so it was decided to start broad-spectrum empirical antibiotic management with Ureidopenicillin in association with glycopeptide, since it was considered the skin symptoms (thrombocytopenic purpura) and the prolongation of coagulation times as signs suggestive of disseminated intravascular coagulation associated with sepsis. Up to now, all of the above has been found in the first 24 hours of in-hospital observation without impaired consciousness or meningeal irritative symptoms; Given findings in blood cultures reporting Neisseria meningitidis, it was decided to adjust the antimicrobial management, to a directed management in monotherapy with Ceftriaxone, thus a lumbar puncture was performed 24 hours after the start of directed antibiotic management, due to the

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alteration in coagulation times. , with a report of clear colorless cerebrospinal fluid, leukocyte count of 1xmm3, fresh red blood cells 2xmm3, glycorrhachia of 61mg/dL, protein of 23mg/dL, gram without microorganisms and negative culture at 72 hours, the paraclinical follow-up showed marked improvement in coagulation times, increased platelet count and resolution of acute kidney injury with fluid intake and adequate antimicrobial management, without requiring vasopressor support or transfusion of blood products at any time.

III. DISCUSSION

The case described is an example of invasive meningococcal disease, presenting meningococcemia without meningitis, so this case can be classified in Group 2, according to the pathophysiological classification, with respect to meningococcemia without meningitis it is found to occur in 5 to 20 % of cases of invasive meningococcal disease and is characterized by sudden onset of fever and petechial lesions as corresponds to the natural history of the disease found in the previously described patient (9), this pattern of presentation is the least frequently observed, according to the Statistics for the year 2019 for Colombia, in which 21 confirmed cases were found, corresponding to 22% of the confirmed cases of meningococcemia, in accordance with the incidence found in the international literature (30). The presentation of invasive meningococcal disease associated with abdominal pain and gastrointestinal symptoms, such as nausea, vomiting, and diarrhea is rare, as well as not very specific, leading to a different approach to the pathology and possibly underreporting and even underdiagnosis of it, due to Therefore, we decided to carry out a systematic search in the databases on cases of invasive meningococcal disease associated with gastrointestinal symptoms, after which sporadic reports were found, mainly in children and adolescents, with a clear association between the presentation of meningococcal disease with gastrointestinal symptoms and the isolation of the W serotype of the germ in series of cases in Europe (France and United Kingdom), however in the case of this patient it was not possible to perform the typing of the serotype causing the infection. The mechanism by which it starts with an extrameningeal focus is not clear, given the tropism of the germ. Physiopathological processes have been described in which the greater the load of the germ in the bloodstream, the interaction with the vascular endothelium increases, causing septic microemboli, the main one being cause of complications associated with the disease (10, 12, 21), this atypical presentation frequently leads to delays in the initiation of adequate antibiotic therapy and also to a high rate of morbidity and mortality.

IV. CONCLUSION

It is important to be aware that in young adult patients, the initial presentation of meningococcal sepsis can be very non-specific in a high percentage that may correspond to almost 1 in 5 patients with the pathology, so early clinical suspicion, rapid initiation of immediate antibiotic treatment and supportive care are the fundamental pillars on which treatment is based, thereby avoiding difficult complications in such a young age group that can clearly affect their quality of life and sphere biopsychosocial, as well as the high mortality associated with these pathologies.

Laboratorio	Resultado (valores de referencia)
Glicemia central (mg/dL)	96.6 (70.0 – 110.0)
BUN (mg/dL)	30.3 (6.0 – 20.0)
Creatinina (mg/dL)	2.14 (0.70 – 1.20)
Perfil Hepático	
Bilirrubina total (mg/dL)	1.02 (0.00 – 1.20)
Bilirrubina directa (mg/dL)	0.54 (0.00 – 0.20)
Bilirrubina indirecta (mg/dL)	0.48 (0.00 – 0.80)
Fosfatasa Alcalina (U/L)	81 (40.0 – 129.0)
TGO/ASAT (U/L)	22 (0.0 – 40.0)
TGP/ALAT	15 (0.0 – 40.0)
Proteína C Reactiva (mg/dL)	27.500 (0.00 – 0.500)
Sodio Serico (mmol/L)	137.4 (136.00 - 145.00)
Potasio Serico (mmol/L)	3.58 (3.50 - 5.10)
Hemograma	
Recuento Leucocitos	17610 (4.50 - 11.00 x 10^3/µL)
Neutrófilos % (conteo absoluto)	92.2 (16250) (1.90 - 8.00 x 10^3/µL)
Linfocitos % (conteo absoluto)	5 (0,91) (0.90 - 5.20 x 10^3/µL)
Monocitos % (conteo absoluto)	3 (0,70) (0.00 – 1.00 x 10^3/µL)
Hemoglobina (g/dL)	15.7 (12.0 – 18.0)
Hematocrito (%)	45.6 (36.0 – 54.0)
Plaquetas	145.000 (150 – 450 x 10^3/µL)
PT	23
INR	2.024
PTT	32.2
VIH - PR	No Reactiva

Table 1. Paraclinical report.
PT: Prothrombin Time. PTT: Partial Thromboplastin Time. INR: International Normalized Ratio
TGO/ASAT: aspartate aminotransferase, TGP/ALAT: alanine aminotransferase

- *Declaration on Ethical Aspects*

In order to carry out this report, verbal informed consent was obtained from the patient, authorizing the use of data from his medical history and photographs that did not compromise his identity. Taking into account Resolution 8430 of 1993 of the Ministry of Health and Social Protection of Colombia and the Declaration of Helsinki that determine the guidelines for research in human beings.

➢ *Conflict of Interest Statement*

The authors declare that they have no conflict of interest in the preparation of this article.

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