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Chronic meningococcemia in a vertically HIV-infected adolescent

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ABSTRACT

Chronic meningococcemia is a rare manifestation of meningococcal disease, characterized by a period of more than one week of intermittent or continuous fever, arthralgia and skin lesions without meningitis. It can occur both in previously healthy and immunocompromised patients. The gold standard for the diagnosis is culture isolation of *Neisseria meningitidis* in sterile material. We describe a case of a vertically HIV-infected adolescent with chronic meningococcal disease.

Introduction

Meningococcal disease may present as meningococcal meningitis, meningococcal meningitis with meningococcemia, and isolated meningococcemia. It is a disease caused by the bacterium *Neisseria meningitidis*. Even though there are 12 bacterial serotypes, invasive meningococcal disease is associated with six, classified based on the polysaccharide capsule (A, B, C, W-135, X, Y) [1]. The bacterium colonizes the nasopharynx of asymptomatic carriers up to about 5–10 % of the population, being transmitted from person to person by respiratory secretions [2].

In Brazil, meningococcal disease is endemic with periodic outbreaks of epidemics in several municipalities. The incidence coefficients have remained stable in recent years, with approximately 1.8 cases per 100,000 inhabitants [3]. In São Paulo city, in 2018, 204 cases were confirmed, with 36 deaths, with incidence coefficient being 1.74 and mortality 0.31 [4]. The lethality of the disease in our country has been around 18–20% in recent years, and it may achieve coefficients of almost 50 % in septic presentations [3]. Serotypes B and C cause disease predominantly in Europe and the Americas, being the most common in Brazil [3].

Although the most common clinical manifestations are fever and acute and rapidly progressive petechial and/or purpuric rash, progressing to septic shock within a few hours, there are some chronic, initially more benign presentations, such as chronic meningococcemia [5]. This form represents less than 5% of all cases of meningococcemia, with incidence <0.05 cases per 100,000 inhabitants per year in developed countries [6]. It is a rare manifestation of meningococcal disease without meningitis, of prolonged course of more than one week, with intermittent or continuous fever, arthralgia and cutaneous vasculitis [1]. Few cases of this presentation have been reported, both in previously healthy and immunocompromised patients [5,7].

A case of chronic meningococcemia diagnosed in a vertically infected adolescent with human immunodeficiency virus (HIV) infection will be described, providing a review of the literature on the topic. Its importance lies in the description of a rare disease with atypical manifestation, which is difficult to suspect, and which may be life-threatening if not diagnosed and treated promptly and adequately. This case report was approved by local ethics committee; the patient signed the consent form, with permission to disclose images.

Clinical case

Adolescent, 19 years old, male, vertically HIV-infected, followed up since 3 months of age at our Pediatric Infectious Disease Clinical Care Center. Not adherent to the antiretroviral treatment, he has presented several clinical intercurrences during his life. At the time of this event, there was significant viral replication (HIV viral load

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87,802 copies/μL) and severe immunosuppression (CD4+ count 17 cells/μL).

He came to our medical center with 5 days of prostration, epigastric pain, sparse petechiae, joint pain, ocular pain and conjunctival hyperemia. Fever at the beginning for three days. Initially, he sought another service and the laboratory tests performed detected leukocytosis 19,600/ul (81 % neutrophils), and thrombocytopenia 77,000/ul. He received intravenous hydration and was discharged with symptomatic medication. In our service, he was in good general condition, pale, presenting conjunctival hyperemia, some petechiae on the trunk and limbs, without other signs (see Pictures 1–3). Laboratory tests were performed: leukocytes 4330/ul (53 % neutrophils, 33 % lymphocytes) and improved thrombocytopenia 124,000/uL. As there is epidemiological conditions for arboviruses in our country, serology and blood viral research by polymerase chain reaction (PCR) were done for dengue, zika and chikungunya – all tested negative; serology tested non-reactive for toxoplasmosis and syphilis; for cytomegalovirus serology tested IgG reagent IgM non-reactive. He received symptomatic treatment with partial clinical improvement, keeping skin lesions unchanged. At this time, he was afebrile.

Sixteen days after the onset of symptoms, he presented a return of prostration, fever and disseminated hemorrhagic suffusions (see Pictures 4 and 5). He was hospitalized in septic shock, and during the diagnostic investigation, two blood cultures were positive for *Neisseria meningitidis* C, eighteen days since disease onset.

He presented normal cerebrospinal fluid examination with negative bacterioscopy and culture. The patient evolved with acute respiratory distress syndrome and acute renal failure, requiring endotracheal intubation and hemodialysis. He was hospitalized for 46 days, received 10 days of ceftriaxone 2 g 12/12 h. During hospitalization, HIV viral load 382,863 copies/μL and CD4+ count 13 cells/μL. He progressively evolved with improvement, being discharged in good clinical conditions, receiving combined antiretroviral therapy.

The vaccine card was checked, he had received two doses of the meningococcal conjugate vaccine C before this clinical complication: 15 years before with HIV viral load 146,000 copies/μL and CD4+ count 762 cells/μL and 3 years before with HIV viral load 130,214 copies/μL and CD4+ count 75 cells/μL.

Currently, the patient presents good adherence to the antiretroviral medication, with an improvement in CD4+ cell count (445 cells/μL) and a decrease in viral load (155 copies/μL); he has cutaneous scars derived from meningococcal vasculitis (see Picture 6)

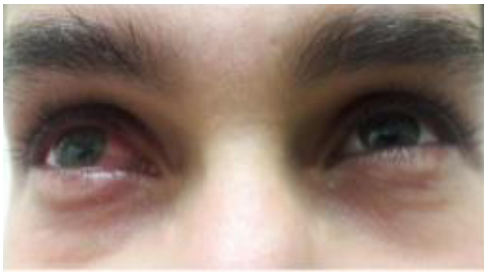
Discussion

We describe a case of a vertically HIV-infected adolescent with chronic meningococcal disease.

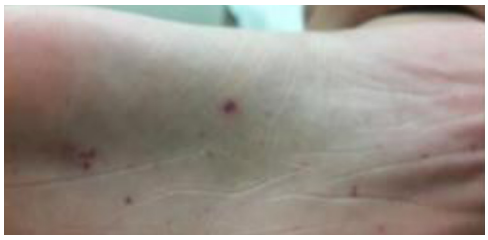
Chronic meningococcemia is a disease caused by the bacterium *Neisseria meningitidis*, characterized by a period of more than one week of intermittent or continuous fever, arthralgia and skin lesions without meningitis [1]. Initial erythema develops to petechiae and purpura due to dermal microvascular thrombosis and perivascular hemorrhage [8]. Other clinical manifestations may occur, such as myalgia, abdominal pain, weight loss, iritis, retinitis [9]. It may be a self-limiting disease, but meningitis and death may occur as late complications [10]. These manifestations mimic several other infections, namely arboviruses, which was a confounding factor in our patient, delaying the diagnosis.

The gold standard diagnostic method is culture isolation of *Neisseria meningitidis* in sterile material [11].

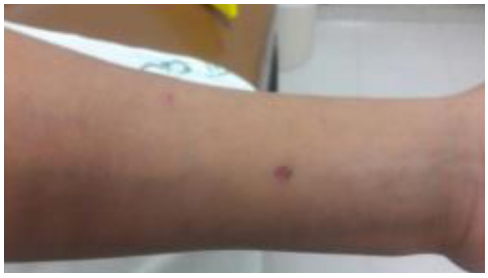
Even if the course seems to be self-limited, the fact that the patient may remain as an asymptomatic carrier and thus develop an invasive disease or spread the agent has tended to favor antimicrobial treatment [12]. The suggested treatment is based on



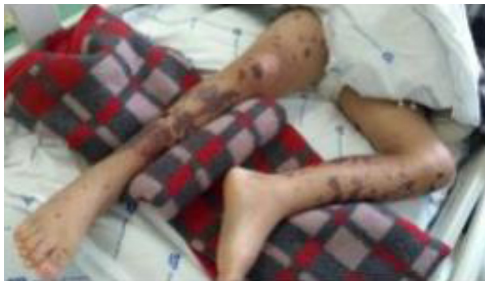
Picture 1. Right eye conjunctival hyperemia.



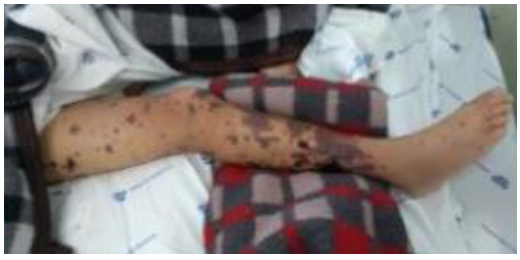
Picture 2. Petechiae on the soles of the feet.



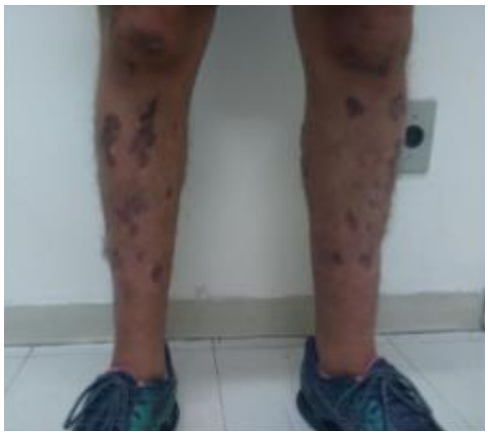
Picture 3. Petechia on the arms.



Pictures 4 and 5. Hemorrhagic suffusions on the limbs.



Pictures 4 and 5. (Continued)



Picture 6. Cutaneous scars on the limbs.

the use of beta-lactams, namely 3rd generation cephalosporin, used in our patient [1,6].

The reason why these less severe forms of the disease occur is unknown; the susceptibility of the host and the virulence of the bacterium are possible explanations [1,13]. Although there seems to be a greater association with serotype B [1], serotype C was isolated in our patient. The disease can occur in previously healthy individuals or with some immunodeficiency [5,7,9].

After a literature review, we identified only four cases of chronic meningococcemia in horizontally HIV-infected adult patients since 1990, none with this serious evolution [6,9,14]. A recent study found a substantial increased risk of meningococcal disease among adults with HIV infection that met AIDS criteria; in this study they observed a similar clinical presentation and outcomes of meningococcal disease compared to those without HIV infection [15]. The increased relative risk observed for meningococcal disease was similar to those observed for HIV-infected individuals in New York City, South Africa and England, ranged from 3.4–6.6 per 100,000 (relative risk = 5–13 compared with HIV-uninfected persons) [15–18]. Among HIV-infected persons, a low CD4 count or high viral load were associated with an increased risk [17]. Considering this increased risk, in 2016 the US Advisory Committees on Immunization Practices approved a recommendation for routine vaccination of HIV-infected person [19]. In Brazil, meningococcal conjugate vaccine type C is routinely recommended for HIV-infected patients.

With this clinical case we intend to highlight the heterogeneity and low specificity of the symptoms that meningococcal disease may present, especially in immunocompromised hosts, leading to a possible diagnostic delay of a potentially fatal disease.

The association between *Neisseria meningitidis* infection and HIV infection is not yet well defined. Due to the potential for progression and the risk of *N. meningitidis* transmission, a better understanding of the association between HIV infection and meningococcal disease is important to prevention strategies.

Ethical approval

Written informed consent was obtained from the patient for publication of this case report and accompanying images. This case report was approved by local ethics committee.

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CRediT authorship contribution statement

Rita S.B. Cardona: Data curation, Formal analysis, Writing - original draft. **Fabiana Bononi do Carmo:** . **Suenia Vasconcelos Beltrão:** . **Aída de Fátima T. Barbosa Gouvêa:** . **Reinaldo Salomão:** . **Regina Célia de Menezes Succi:** Supervision, Writing - review & editing. **Daisy Maria Machado:** Conceptualization, Writing - review & editing.

Declaration of Competing Interest

The authors have no conflict of interests, personal or financial, to declare.

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