RHEUMATOLOGY

Letter to the Editor (Case report)

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Chronic meningococcaemia—a medical oxymoron

Rheumatology key message

- Chronic meningococcaemia should be considered as a rare cause of recurrent fever, arthralgia and maculopapular rash.

SIR, Infections with *Neisseria meningitidis*, a Gram-negative diplococcus, often cause potentially life-threatening meningitis, sepsis, or both, but in rare instances may result in chronic meningococcaemia, characterized by intermittent fever, polyarthralgia and skin efflorescences (usually maculopapular rash) [1]. With early antibiotic treatment, the course of the disease is favourable; otherwise, severe complications, such as meningitis or other organ involvement, might occur. Meningococcaemia can mimic rheumatic diseases, such as vasculitis, lupus, Still's disease or Sweet's syndrome. Given that immunosuppressive treatment may trigger severe complications of meningococcal infection, the latter represents an important, albeit rare, differential diagnosis of rheumatic diseases and should always be considered in patients presenting the above-mentioned triad of symptoms [2].

Here, we present a report of a 51-year-old woman admitted to our hospital with recurrent fever, arthralgia and maculopapular rash (Fig. 1A and C) for 3.5 months. Sweet's syndrome had been diagnosed shortly after onset of symptoms based on clinical presentation and histological examination of one skin biopsy showing papillary dermis oedema and subepithelial infiltration with neutrophils and eosinophils. Systemic CSs (40 mg daily p.o.) were administered without clinical improvement and discontinued after 3 days of intake.

Laboratory tests repeatedly showed elevation of CRP (between 14 and 67 mg/l), ESR (>60 mm/h) and liver enzymes (alanine aminotransferase, aspartate aminotransferase, AP and γ-glutamyl transferase; all up to five times the upper limit of the norm). RF, extractable nuclear antigens, ANA and ANCAs were negative. PCR was negative for HIV, parvovirus B19, HBV and HCV.

Owing to unclear diagnosis in a patient with intermittent fever, a series of peripheral blood cultures was collected during hospitalization in our clinic. *Neisseria meningitidis* serogroup C grew in some of these blood cultures, thus confirming chronic meningococcaemia. Notably, blood cultures had been negative 2 weeks after onset of symptoms. Our patient never showed any signs of meningitis.

Our patient reported recurrent nasopharyngeal herpes simplex infections, which might have served as the portal of entry, because meningococci colonize the nasopharynx and upper respiratory tract in ~10% of the population [3]. Serogroup C is highly transmissible, but rarely causes long-term carriage or chronic meningococcaemia [4]. So far, mechanisms leading from colonization to chronic infection are not fully understood. Deficiencies in antibody production or the complement system, mainly C5–9, but also attributable to SLE, are known risk factors for chronic meningococcaemia. However, the majority of cases have been described in immunocompetent subjects [1, 5]. Notably, nasopharyngeal co-infections predispose to carriage and facilitate bacterial translocation into the bloodstream [4].

We detected perivascular dermatitis in a biopsy of one newly occurring skin lesion (Fig. 1B and C), and also lobular hepatitis with microgranuloma in a liver biopsy. Although no meningococci were detected in either biopsy, we assume that both dermatitis and hepatitis were the result of perivascular bacterial invasion, which was supported by the lymphocytic infiltrate around the dermal vessels (Fig. 1B) [5]. In chronic meningococcaemia, peripheral extravasation of *N. meningitidis* may occur paracellularly, as demonstrated previously in cutaneous lesions [5]. Only one case of chronic meningococcaemia with liver involvement in the form of cholestatic hepatitis has been described so far [6], whereas large numbers of bacteria and a high amount of antigen were detected post mortem in liver tissue of patients who had died from fulminant meningococcal sepsis [7]. *Neisseria meningitidis*-specific PCR analyses (also of biopsy samples) can be useful to confirm meningococcaemia, especially as blood cultures often remain negative because of transient bacteraemia [8].

Our patient was immunized against *N. meningitidis* serotype C in 1984 before making a pilgrimage to Mecca. However, in the 1980s, only polysaccharide meningococcal vaccines were available, which neither provide long-term immunity nor protect against nasopharyngeal carriage [3]. The development of conjugate vaccines inducing immunological memory overcame these deficiencies [3]. It remains open to speculation whether the previous vaccination might have prevented acute and potentially fatal invasive meningococcal disease in our patient.

Under treatment with penicillin G (25 million IE/day for 10 days) according to antibiotic susceptibility testing, fever and skin lesions vanished within the first days of treatment (Fig. 1C–E), transaminases decreased and CRP normalized. At the time of discharge, we started secondary prophylaxis with valaciclovir because of the suspected role of herpes simplex infection in providing a portal of entry for *N. meningitidis*.

It is known that chronic meningococcaemia usually responds well to treatment, without leaving any sequel. Nevertheless, in cases of delayed diagnosis, patients may develop organ involvement, most commonly meningitis, but endocarditis, glomerulonephritis, cholestatic hepatitis and ocular manifestations also have been described [1, 6]. Immunosuppressive treatment with CSs

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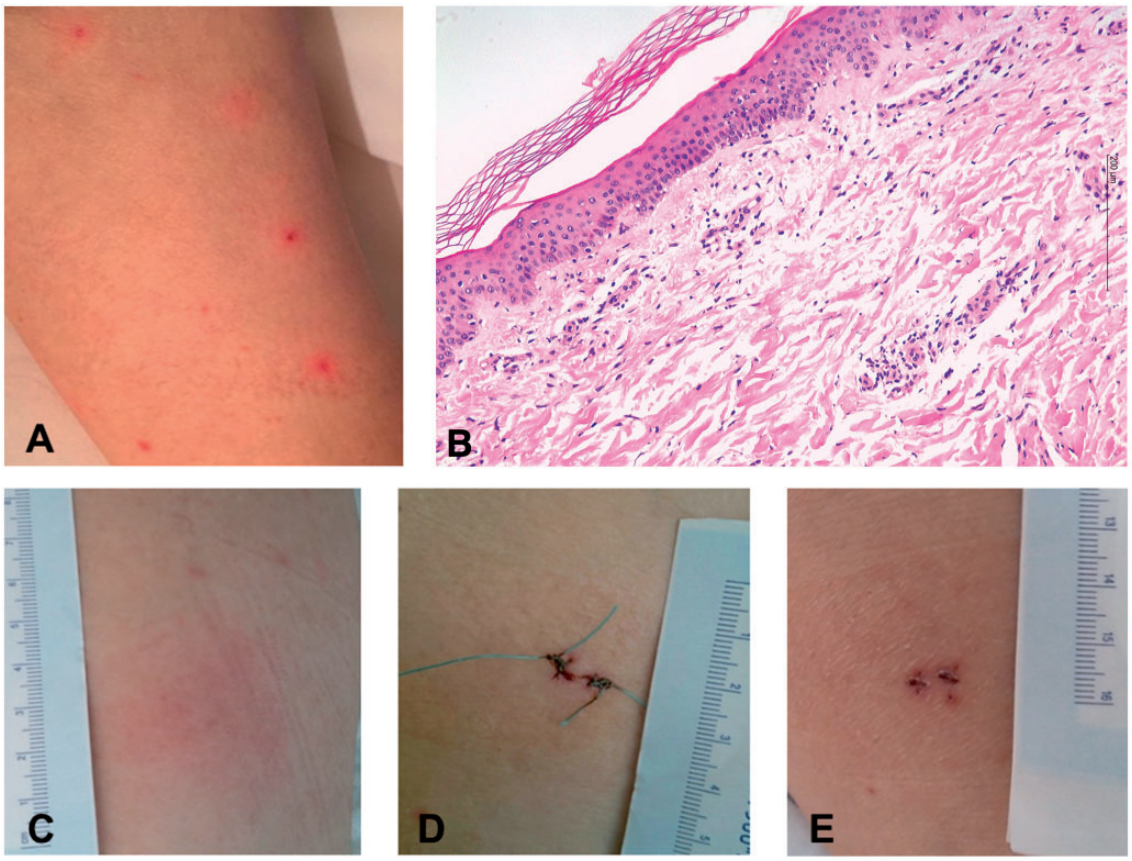
Fig. 1 Vasculitis-like skin lesions in chronic meningococcaemia



(**A** and **C**) Newly occurring skin lesions during hospitalization. (**B**) Biopsy of skin lesion (**C**) stained with haematoxylin and eosin, 100×: lymphocytic infiltrate around dermal vessels and oedema of the upper dermis. (**D**) Skin lesion 1 day after start of antibiotic treatment. (**E**) Skin lesion at discharge.

erroneously administered because of the assumption of rheumatic disease, however, might trigger acute meningitis and result in complications and increased mortality [2].

In conclusion, chronic meningococcaemia might mimic rheumatic diseases. Therefore, in every patient with recurrent fever, especially before starting immunosuppressive treatment, infections should be excluded by serial blood cultures and, in some circumstances, by more sensitive tests, such as PCR assays.

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