Erythema Multiforme Major in a Female with Acute Systemic Meningococcal Disease

Sir,

To our knowledge a connexion between systemic meningococcal disease and erythema multiforme (EM) major has not been described before. In the literature we have found only one case report describing chronic meningococcaemia and a maculopapular exanthema, initially misdiagnosed as EM major (1). We report this case to stress that meningococcal disease can present with unusual cutaneous manifestations, including EM major, and that meningococcal disease should be considered whenever a patient presents with fever and exanthema.

CASE REPORT

A 21-year-old female, previously healthy, presented with a 3-day history of shivering attacks, muscle pains, flitting joint pains, and an exanthema located on her hands and feet and spreading to her limbs. Twelve hours before admission she had received amoxicillin.

On admission the patient appeared septic. She had bilateral conjunctivitis, bright-red tongue, haemorrhagic crusts in both sides of the nasal cavity, and indurations with crusts on the prolabium. A symmetrical rash was seen on her hands, feet and limbs, but her trunk, neck and head were unaffected. The rash was confluent in her soles, palms and around her nails. On her limbs and feet and on the dorsal parts of her hands there were several raised atypical target lesions. These elements were round or oval, 1–3 cm in diameter, more or less demarcated, oedematously elevated, with one concentric ring around a central disc. Some of these lesions had small central necroses. No petechiae or typical EM lesions were observed. The diagnosis of EM major was suspected, and the patient was examined by a dermatologist, who confirmed the diagnosis.

Laboratory tests revealed incipient disseminated intravascular coagulation. White blood cell count was 5.6×10^9/l with 41% band neutrophils (normal <5%) out of 76% neutrophils. C-reactive protein was raised at 686 nmol/l (normal <84 nmol/l).

The patient was immediately treated with parenteral penicillin G, gentamicin and metronidazole. After a few days gentamicin was replaced by ciprofloxacin, since EM major due to infection with *Mycoplasma pneumoniae* was suspected.

Repeated blood cultures (BACTEC PLUS aerobic and anaerobic media without penicillinase) were sterile, including special blood cultures for *M. pneumoniae*. Specimens from the cerebrospinal fluid, throat, sputum, urine, faeces, cervix and vagina did not grow pathogenic bacteria. Antibodies to *Neisseria gonorrhoeae, M. pneumoniae* and herpes simplex virus were not found on repeated occasions.

However, at the time of admission, the meningococcal antibody test (MAT, complement fixation test, the Neisseria Department, Statens Serum Institute, Copenhagen) showed a titre of 1:36, after 1 week 1:75, after 8 weeks 1:25 and 1 year later <1:12, a more than sixfold change. Owing to the clinical symptoms and signs and the MAT results, the diagnosis of acute systemic meningococcal disease was strongly suggested, and the case was reported to the health authorities as a case of systemic meningococcal disease.

The patient was treated with penicillin for 3 weeks. During the first 10 days the rash gradually faded and the skin in her palms and soles peeled off, leaving no scars. Laboratory tests normalized, the patient recovered gradually and was discharged from hospital. Six weeks later she was healthy without sequelae.

DISCUSSION

It has been suggested that EM major and Stevens-Johnson syndrome (SJS) are two different disease entities, regarding both clinical manifestations and aetiology (2).

EM major is an acute self-limited inflammatory cutaneous disease, lasting a few weeks and involving at least one mucosal region. The exanthema is characterized by symmetrically and acrally distributed typical concentric lesions or raised (i.e. palpable) atypical targets. The typical concentric lesions are almost pathognomonic of EM. The mucosal erosions often include two or more regions, especially the lips, oral cavity and conjunctivae. SJS is characterized by centrally or diffusely distributed flat atypical targets and/or maculae. Typical concentric lesions or raised atypical targets are never seen. EM major and SJS are thus classified according to different patterns of cutaneous lesions. Both diseases present with epidermal detachment less than 10% of the body surface area, and with similar mucosal lesions, the extent of which cannot be used to differentiate between EM and SJS (2).

EM is mainly caused by infections. Herpes simplex virus is believed to be involved in up to 80% of the cases. It is rarely, if ever, caused by drugs. SJS, on the other hand, is believed to be precipitated mainly, if not exclusively, by drugs (2). The pathogenesis of EM remains unsolved, but a cell-mediated immune response directed against antigens of the precipitating microorganism is probably involved.

Clinically, our patient had EM major, no drugs were administered and some of the most important pathogens could be ruled out. What could be documented, however, was a more than sixfold titre change in MAT. MAT is a complement fixation test, which has been performed routinely at the Neisseria Department, Statens Serum Institute, Copenhagen, for more than 50 years (3, 4). Cross-reacting antibodies induced by *N. gonorrhoeae* may occasionally cause a weakly positive MAT (3). In our patient there was no evidence of infection caused by *N. gonorrhoeae,* and the gonococcal antibody test was negative on repeated occasions. The more than sixfold titre change in MAT in our patient thus strongly suggested the diagnosis of acute systemic meningococcal disease. Probably *N. meningitidis* was not found in the blood because the patient had received amoxicillin before admission and additionally our blood culture system does not contain penicillinase.

We suggest that *N. meningitidis* should be added to the list of possible causes of EM major.

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Jens Hedegaard Kristensen[1], Lena Hesselvig Hagelskjær[1] and Jørgen Prag[2], [1]Medical Department and [2]Department of Clinical Microbiology, Viborg Sygehus, Heibergs Allé 4, DK-8800 Viborg, Denmark.