Pharyngitis and Exanthema Caused by *Arcanobacterium haemolyticum*

Sir,

Arcanobacterium haemolyticum is a geographically widespread, aerobic, Gram-positive rod isolated most commonly from young pharyngitis patients, in the 15–25-year-old age group, with an isolation frequency of 2%. Beta-haemolytic streptococci have been simultaneously recovered from up to half of the patients (1). One- to two-thirds of the patients also have a diffuse erythematous maculopapular skin eruption on the extremities and trunk, usually disappearing over the course of 2–5 days (2). The patients may also have cervical lymphadenitis, fever and non-productive cough (1). Cases are mostly sporadic and are most likely to spread by direct person-to-person contact via droplets of saliva (3). Although *A. haemolyticum* can also cause infections at other body sites, the characteristic exanthema has been reported together with pharyngeal infections alone (2). When present before pharyngeal symptoms the exanthema is often difficult to diagnose definitively. Here we report a case of exanthema in a previously healthy man who was admitted because of a suspected hypersensitivity reaction. An exudative pharyngitis developed only after admission. Throat-swab culture yielded the causative agent, *A. haemolyticum*.

CASE REPORT

A previously healthy 19-year-old man was admitted to the dermatology ward because of a suspected hypersensitivity reaction. He had a known allergy to penicillin and to dog and cat dander. To improve muscular performance he had used dietary supplements containing maltodextrin and amino acids for 3 weeks. Two days previously he had noticed an exanthema on the upper back and chest spreading centrifugally and becoming intensely pruritic.

The patient complained of a sore throat. His temperature was 38°C, his fingers were slightly swollen and the pharynx showed mild oedema and erythema. A gradually worsening, red maculopapular exanthema over the trunk and proximal extremities was noted (Fig. 1). A hypersensitivity reaction was suspected. The patient then developed an exudative tonsillitis with cervical lympadenopathy, and peroral erythromycin was administered, later changed to intravenous cefuroxime because of difficulties in swallowing.

Blood cultures were negative, as were the results of a streptococcal antigen detection test and antibodies against Epstein–Barr virus (EBV) and parvovirus B19. His level of haemoglobin was 153 g/l, white-cell count was 5.5×10^9/l, platelets 206×10^9/l, C-reactive protein rose to 55 mg/l and serum chemistry was normal. An excisional biopsy of the exanthema was performed. The throat-swab culture yielded *A. haemolyticum* on the second hospital day. On histopathological examination the superficial dermis was oedematous and showed a perivascular infiltrate consisting mainly of lymphocytes with an admixture of neutrophils, eosinophils and plasma cells (Fig. 2) The vascular endothelial cells appeared swollen, but no fibrinoid necrosis was noted.

On the third hospital day the exanthema faded and the pharyngeal discomfort subsided. The patient was discharged with erythromycin. Two weeks later he visited the outpatient dermatology clinic and a mild late desquamation of the skin on the palms and around the fingernails was noted.

DISCUSSION

Exanthema is a symmetric skin eruption caused by infectious agents, drugs, allergens or other as yet unknown mechanisms. Exanthema caused by an infection results either from direct invasion by the organism or due to the host immune response. Because there is a limited profile of response patterns, different organisms and drugs may elicit a similar cutaneous response.

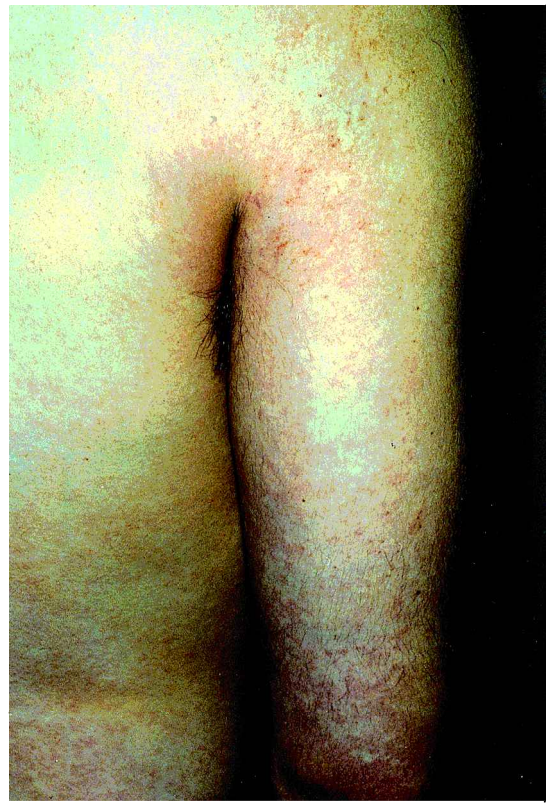

Fig. 1. Exanthema caused by *Arcanobacterium haemolyticum* on the third day. There were numerous Pastia's lines.

Conversely, owing to individual differences in immunological responses, similar microbes can elicit dissimilar responses and skin eruptions. A dermatologist has to consider a wide spectrum of differential diagnostic possibilities. When an infectious exanthema is present before any pharyngeal symptoms, it can lead to diagnostic difficulties.

At first, a hypersensitivity reaction was suspected in our patient because of his atopic constitution. His own suspicion focused on the dietary supplements. An exudative pharyngitis developed only after the patient was already on the dermatological ward. Throat-swab culture yielded *A. haemolyticum* on the second hospital day. When specifically asked, the patient told that a friend of his had recently suffered from pharyngitis, during the course of which antibiotic treatment had been switched because of a suspected hypersensitivity reaction. The diagnosis of a hypersensitivity reaction requires more than clinical suspicion and non-specific histopathological findings. In clinical practice, the suspected causative drug is changed to another and later one may try to verify allergy with skin or oral provocation tests. The patient was not tested against the dietary supplements, but the exanthema did not recur once the infection had been treated. No reports were found on allergic reactions caused by maltodextrin.

Up to 75% of patients with symptomatic *A. haemolyticum* pharyngitis develop exanthema, which usually manifests 1–4 days after the appearance of pharyngeal symptoms, but rarely before that. The exanthema can be the presenting feature and

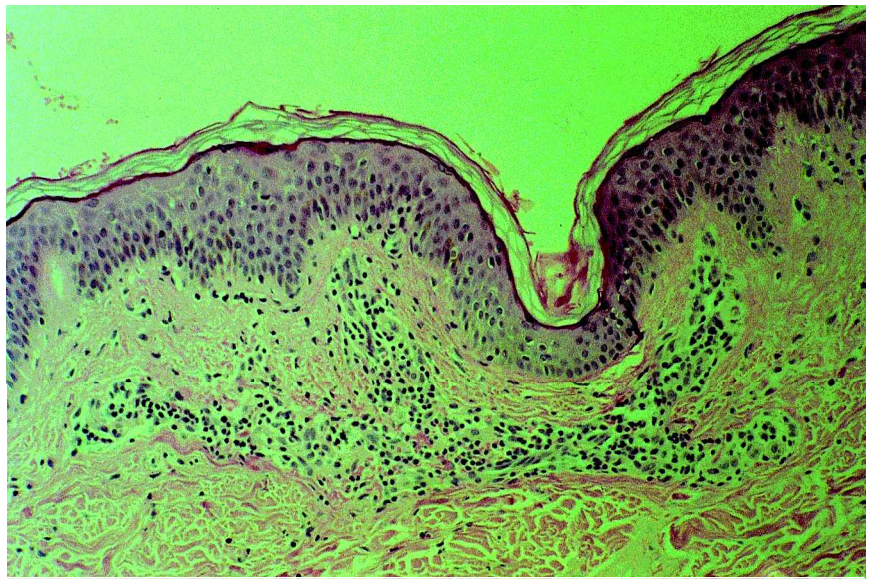

Fig. 2. Histopathological examination of a biopsy from a lesion on the upper arm showed a perivascular infiltration of lymphocytes and histiocytes. (Original magnification ×40.)

appears as a red maculopapular exanthema, mainly on the trunk and the extensor surfaces of the extremities, commonly sparing the face. The exanthema is pruritic in half of the patients and normally fades over 2–5 days (2). Erythema multiforme, urticaria and blistering of palms and soles have also been noted (4, 5). Of the several toxins produced by *A. haemolyticum*, one resembling the erythrogenic toxin of *Streptococcus pyogenes* is suspected of causing the exanthema and desquamation of the skin (2).

Arcanobacterium haemolyticum grows slowly (within 24–48 h) on blood agar, and is not readily apparent in routine cultures if the laboratory has not been informed of the possibility of *A. haemolyticum* infection (5). No routine serological or rapid antigen detection tests are available. *Arcanobacterium haemolyticum* is susceptible *in vitro* to penicillin, cephalosporins, erythromycin, azithromycin, ciprofloxacin and doxycycline, but penicillin tolerance has been reported. Macrolides are considered to be the drugs of choice (6, 7).

Arcanobacterium pharyngitis can at times be severe and closely mimics the life-threatening manifestations of diphtheria (8). The symptoms closely resemble the clinical presentation of pharyngitis caused by group A, C and G streptococci or by various viruses. The presence of skin exanthema with pharyngitis suggests the possibility of infection with *S. pyogenes*, human immunodeficiency virus (primary HIV), EBV, *A. haemolyticum* or Kawasaki disease. The possibility of toxic shock syndrome and secondary syphilis should be kept in mind. Clinically, it is impossible to distinguish between scarlet fever and *A. haemolyticum* infection. The characteristic circumoral pallor or strawberry tongue of scarlet fever are lacking in *A. haemolyticum* infection. Haemorrhagic Pastia's lines, earlier suggested to be typical of scarlet fever, were also seen in our patient (Fig. 1). This feature has not previously been described in infectious diseases other than scarlet fever. Histopathological findings in exanthemas show non-specific perivascular lymphohistiocytic infiltration, where no causative agents can be detected. For an exact diagnosis, in addition to throat-swab culture, a serum treponemal antigen test as well as HIV antibodies and plasma HIV RNA testing should be performed to exclude these when appropriate.

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