Severe Necrotizing Otitis and Varicella Associated with Transient Neutrophil Chemotactic Defect

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Varicella is usually a benign disease in immune-competent children. While rare complications have been reported in many organ systems, the skin is the primary target organ in this disease. Secondary infections have been attributed mainly to environmental factors such as poor hygiene and humidity [1]. We describe the case of a healthy child who developed severe necrotizing skin and ear infection during acute varicella illness and in whom a marked transient neutrophil chemotactic defect was noted.

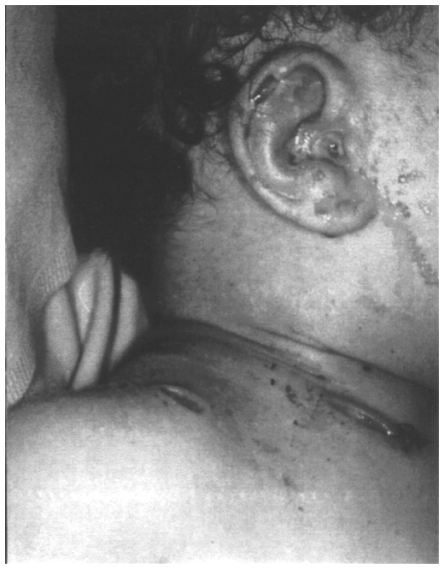
Case Description

A previously healthy 10-month-old boy was admitted to the hospital with fever, ulcerated skin lesions, purulent secretion from the right ear, and a vesicular exanthema characteristic of varicella. On examination, his temperature was 38.9°C, his right ear was drooling and the external meatus was edematous and painful. On otoscopic examination the tympanic membrane was not visible due to the vast amount of secretions. Two large skin lesions (1.5 x 1.0 cm) were noted on his right shoulder and right upper chest [Figure A]. Another small ulcerated skin lesion was seen on the helix of the right ear, and the meatal canal was drooling, swollen and tender. Many vesicular lesions typical of varicella were noted. The rest of the physical examination was unremarkable.

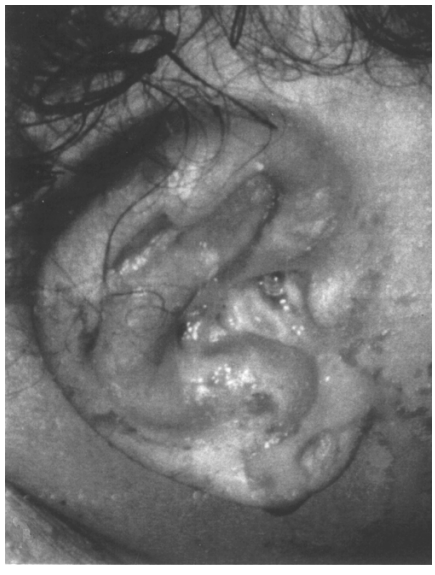
Laboratory data revealed a leukocyte count of 23,700/mm^3 with differential count of 36% neutrophils, 20% band forms, 26% lymphocytes, 14% monocytes and 4% eosinophils. The rest of the laboratory investigation was normal. *Staphylococcus auerus* was cultured several times from the skin lesions. Cefriaxone and cloxacillin were instituted, but during the following 7 days high fever persisted, the amount of ear secretion increased, and the ulceration of the helix of the right ear deepened [Figure B]. On the 8th day, when a culture of the ear secretion yielded *Pseudomonas aeruginosa,* the treatment was changed to ceftazidime. Over the next few days the patient developed necrotizing inflammation of the external ear canal, including the soft tissues, cartilage and bony structures. The patient recovered gradually and was discharged after 3 weeks. Reconstructive surgery was performed 3 months later, but a deformation of the ear and a permanent complete conductive right hearing loss remained.

In order to find a possible explanation for the severe suppurative infection, further laboratory investigations were performed. Immunoglobulin levels were found to be normal, with high IgM and later IgG titers against varicella–zoster virus. Neutrophil opsonophagocytic activity, which was measured by Luminol-enhanced chemiluminescence response, was found to be normal. On the other hand, neutrophil motility was markedly depressed. By using the under-agarose chemotactic assay, a significant defect in both random migration (46%) and net migration (0%) was observed. The defect was confined to the neutrophils and no inhibitory effect was found in the patient's serum (data not shown). The observed defect was of a transient nature. Three months later a marked improvement was noted (random migration 60%, net migration 59%); and 9 months after the acute episode the neutrophils' motility ability returned to normal (random migration 120%, net migration 140%).

Follow-up revealed no new infection episodes and, apart from the complete hearing loss in the right ear and the external ear deformity, the child is healthy.



[A]. Ulcerated skin lesions on right shoulder, right upper chest and helix of the right ear.



[B]. A closer look at the affected ear shows copious secretion and a deep ulceration of the helix.

Comment

Although skin infection is the most common complication in varicella in-

fection, we believe that our case is unique in its severity. Secondary skin infections with *Staphylococcus* or *Streptococcus* occur more commonly under conditions of poor hygiene and elevated temperature and humidity, conditions that did not exist in the present case. Even in the so-called bullous varicella, which is the worst epidermal form of varicella, no serious consequences were reported [1]. In our case the systemic symptoms of the disease were not different from those seen in the normal course of varicella, and no lung or neurological complications were noted.

The unusually severe skin involvement prompted us to look at the patient's neutrophil functions. While several studies were performed regarding the direct role of neutrophils in the host immune response against varicella–zoster virus, the effect of the virus on neutrophil function was not assessed. Previously, it has been shown that several viruses — especially measles, human immunodeficiency virus, cytomegalovirus, and influenza A — may indeed cause neutrophil dysfunction with decreased chemotaxis [2]. A recent study by Abramson and Hudnor [3] revealed that the leukocyte dysfunction in influenza A infection was due, at least in part, to blocking of the sialophorin receptor on the leukocyte surface. Depressed neutrophil motility has been observed also in patients with recurrent herpes simplex virus infections [4]; this defect was due to some intrinsic cell dysfunction without any serum inhibitory factor, as was seen in our case as well. Endotoxin-activated serum from our patient prompted a normal leukotactic activity (data not shown).

We postulate that the defect observed in our patient is due to the interaction of the virus with one or more receptors on the neutrophil surface. This receptor plays a role in neutrophil motility, mainly through sensing chemotactic factors. Once the virus is eliminated, the receptor gradually regains its function and the transient defect disappears. Granulocyte macrophage colony-stimulating factor, which was found to reverse the neutrophil dysfunction due to influenza A [5], may thus be of help in cases of viral infections with severe secondary complication due to neutrophil dysfunction.

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Capsule

ACE inhibitors and response to physical training

The function of local renin-angiotensin systems in skeletal muscle and adipose tissue remains largely unknown. A polymorphism of the human angiotensin-converting enzyme (ACE) gene has been identified in which the insertion *(I)* rather than deletion *(D)* allele is associated with lower ACE activity in body tissues and increased response to some aspects of physical training. In investigating the metabolic effects of local human renin-angiotensin systems, a group from the UK studied the association between the ACE gene insertion or deletion polymorphism and changes in body composition related to an intensive exercise program.

The researchers used three independent methods (bioimpedance, multiple skinfold-thickness assessment of whole-body composition, and magnetic resonance imaging of the mid-thigh) to study changes in body composition in young male army recruits over 10 weeks of intensive physical training. The findings showed that participants with the *II* genotype had a greater anabolic response than those with one or more *D* alleles for fat mass and non-fat mass. Changes in body morphology with training measured by the other methods were also dependent on genotype.

The interpretation of the scientists is that *II* genotype, as a marker of low ACE activity in body tissues, may conserve a positive energy balance during rigorous training, which suggests enhanced metabolic efficiency. This finding may explain some of the survival and functional benefits of therapy with ACE inhibitors.

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