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Papular Acrodermatitis of Childhood: The Gianotti-Crosti Syndrome

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Papular acrodermatitis of childhood (PAC), also known as Gianotti-Crosti syndrome, is a self-limited disorder with acute onset generalized lymphadenopathy and monomorphic lentil-sized, dense, nonconfluent, symmetric, flat-topped, nonpruritic papules. We describe 2 patients, one with anicteric hepatitis, lymphocytosis, and positive hepatitis B surface antigenemia, and the other with a cytomegalovirus (CMV) infection.

Papular acrodermatitis of childhood (PAC) was first described separately by Gianotti and Crosti in 1955.[1-4] Also called *Gianotti-Crosti syndrome*, PAC is a self-limited disease that manifests as an acute onset generalized lymphadenopathy and monomorphic lentil-sized, dense, nonconfluent, symmetric, flat-topped papules that range from flesh colored to erythematous, measure between 2 to 5 mm in diameter, and persist for 3 to 5 weeks. Typically, the papules are localized on the face and limbs, with sparing of the flexoral surfaces; they are nonpruritic, well circumscribed, nonrelapsing, and may köbnerize. Occasionally, the papules may appear to be lichenoid or purpuric. They do not affect the mucous membranes. They were originally associated with acute hepatitis, which is anicteric, and the detection of hepatitis B surface antigen (HBsAg) in blood.[1,5]

PAC and a similar process called *papulovesicular acrolocated syndrome* are basically indistinguishable.[2-4] The latter more likely appears as vesicular, pink pinhead-sized, and occasionally coalescent pruritic papules that sometimes recur and do not köbnerize.[2] It has been linked to other viral infections, such as Epstein-Barr virus, cytomegalovirus (CMV), coxsackievirus, human immunodeficiency virus (HIV), and parainfluenza, and is well-known today as the PAC/Gianotti-Crosti syndrome. We describe 2 patients with PAC, one with anicteric hepatitis, lymphocytosis, and positive hepatitis B virus (HBV) surface antigenemia, and the other with a CMV infection.

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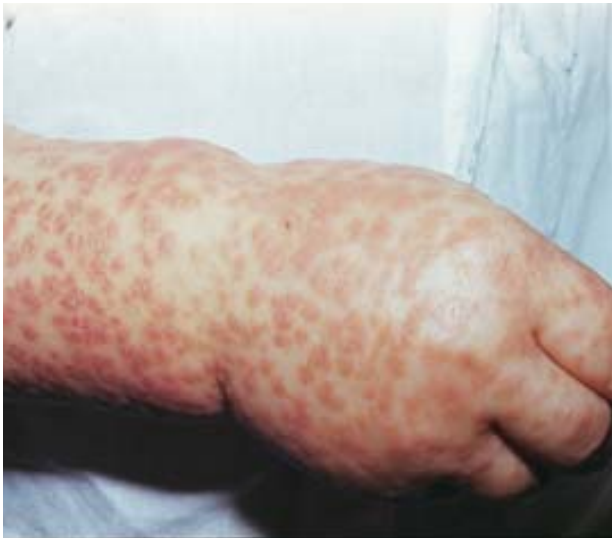

Figure 1. Symmetric monomorphic papules on the upper extremities of patient 1.

Case Reports

Patient 1—A 13-month-old boy had a papular eruption of 6 days' duration. This was preceded by an upper respiratory tract infection with diarrhea, fever (41°C), and general malaise 21 days earlier. The papules developed on the trunk and spread to the extremities and face within a few days.

Physical examination revealed an anicteric boy with a symmetric, monomorphic papular skin eruption over the extremities, face, and trunk (Figures 1 and 2). The papules were most prominent on the

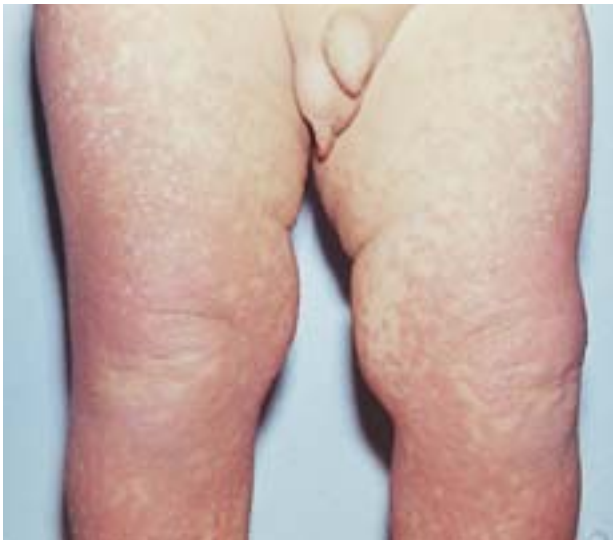

Figure 2. Symmetric monomorphic papules on the lower extremities of patient 1.

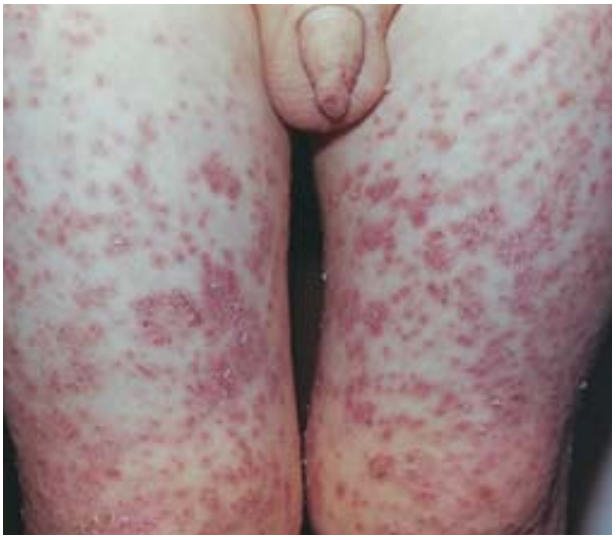

Figure 4. Similar papules on the legs of patient 2.

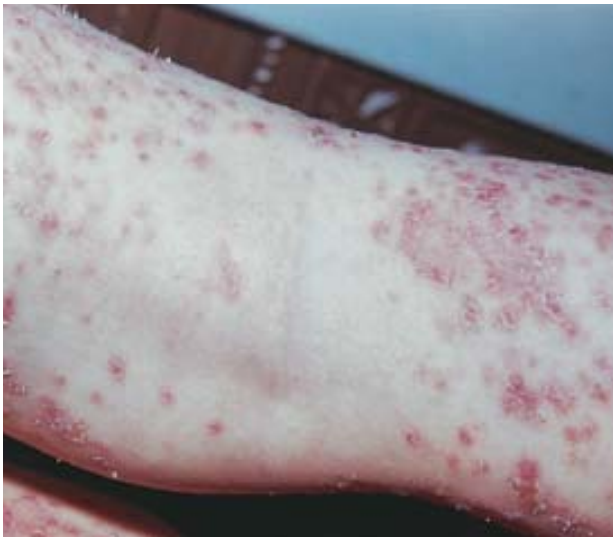

Figure 3. Symmetric monomorphous papules 2 to 3 mm in diameter, flat topped and mildly erythematous, involving the arms of patient 2.

lower and upper extremities and face. Individual lesions consisted of discrete, flat-topped, erythematous papules, 2 to 5 mm in diameter. Mucous membranes, palms, and soles were spared. Generalized lymphadenopathy was noted and was most prominent in the cervical, inguinal, and axillary regions. Abdominal examination revealed an enlarged nontender liver, whose edge was palpable 3 finger breadths below the right costal margin. The skin eruption and lymphadenopathy resolved within 5 weeks.

Laboratory tests performed during the initial visit revealed a hemoglobin level of 11.0 g/dL and a white blood cell count of 12,100/mm^3 (neutrophils, 16%; bands, 7%; lymphocytes, 70%; monocytes, 6%; and eosinophils, 1%). The erythrocyte sedimentation rate (ESR) was 10 mm/h, bilirubin concentration was 6.3 mmol/L, alanine aminotransferase (ALT) concentration was 6.12 mmol/L, and test results for HBsAg were positive. Circulating immune complexes were 0.42 (normal, 0.06). On repeating the complete blood count at day 20, the hemoglobin level was 12.1 g/dL, and the white blood cell count was 12,600/mm^3 (neutrophils, 21%; lymphocytes, 77%; monocytes, 2%; and eosinophils, 0%). The ESR was 5 mm/h.

The serum antibody to the HBsAg (anti-HBs) appeared 2 years later, and the patient's mother became ill 4 months after that. Her illness began with a pruritic urticaria and arthralgia that lasted 3 weeks. Next, she noticed yellowing of her sclera and skin. Results for HBsAg testing were positive; increase in bilirubin reached 230.2 mmol/L (conjugated 159.4 mmol/L), with an ALT concentration of -5.7 mmol/L. Two years later, test results for HBsAg were negative.

Patient 2—A 27-month-old boy was seen for evaluation of widespread papules of 21 days' duration. The eruption began on the face as erythematous papules, with associated rhinorrhea and a sore throat with pharyngeal erythema. Over several days, it spread to the arms, legs, and buttocks. There was a history of fever and diarrhea before the eruption. The patient's parents were unaffected, and there was no known contact with anyone having a similar rash.

Physical examination revealed symmetric, monomorphous papules involving the face, arms, legs, buttocks, and trunk, with sparing of the antecubital and popliteal fossae, palms, and soles. Individual papules were 2 to 3 mm in diameter, flat topped, and erythematous, with mild peripheral desquamation (Figures 3 and 4). These papules were dense, did not

coalesce, and were not pruritic. There was a generalized lymphadenopathy (mainly inguinal and axillary). The liver and spleen were not palpable.

Laboratory studies performed during the initial visit revealed a hemoglobin level of 12.0 g/dL and a white blood cell count of 6210/mm^3 (neutrophils, 61%; bands, 5%; lymphocytes, 27%; monocytes, 7%; and eosinophils, 2%); and platelet count, 356,000/mm^3. The ESR was 2 mm/h. Results for HBsAg and Epstein-Barr virus testing were negative and within normal ranges for bilirubin, serum glutamic-oxaloacetic transaminase, and alkaline phosphate. Antibodies against CMV were detected by immunofluorescence with titers of 1:64. The ratio for early antigen was 1:8.

Comment

We describe 2 boys with PAC, aged 13 and 27 months, respectively. In each, the disease manifested with a prodromal phenomenom of upper respiratory tract infection, diarrhea, fever, and malaise, lasting 2 to 3 weeks before the skin eruptions. Both cases followed with an acute onset of flesh-colored, lichenoid papules measuring 2 to 3 mm in diameter, which generalized within a few days. The lesions were symmetrically distributed, sparing the antecubital and popliteal fossae. The only difference between the cases was that patient 2, who did not have an HBV infection, had papules that tended to desquamate. There was pronounced lymphadenopathy in both cases. Patient 1, the boy with the HBV infection, had an enlarged liver, and the results from HBsAg testing were positive. His mother, also found ill with HBV 4 months later, developed urticaria but not PAC. Patient 2 had a CMV infection.

Although the HBV is the most common infective agent in PAC, other viruses, such as Epstein-Barr, poxvirus, parvovirus B19, human herpesvirus 6, rotavirus, coxsackievirus (A16, B4, B5), HIV, parainfluenza, and CMV, also may be related to a similar cutaneous response (Table).[3-14] PAC also may be linked to vaccinations, eg, influenza, pertussis, diphtheria, and the combination measles, mumps, and rubella.[15,16] Occasionally, PAC may be seen in adults.[11,16]

The prodromal stage of HBV and other viral infections may be associated with cutaneous eruptions, most often urticarial (as seen in the mother of patient 1) or generalized maculopapular rashes. Sometimes, however, PAC develops, typically in young children. Why they are preferentially affected is unclear. The AYW subtype of HBV may be more likely to induce PAC than other subtypes of this virus.[13] An anomalous or immature immunologic response may be important in the pathogenesis of PAC. Although circulating immune complexes may be present,[14] histopathologic studies have not confirmed the evidence of a vasculitis typical of immune complex deposition. Thus, the exact pathogenesis of PAC remains obscure. Nevertheless, PAC should not be overlooked,[16,17] since it may be a marker for serious viral disorders, including infections with HBV and HIV.

Viral Infections or Vaccinations Associated With PAC

Viruses
Epstein-Barr
echoviruses
hepatitis A, B, C
cytomegalovirus
poxvirus
parvovirus B19
human herpesvirus 6
rotavirus
coxsackievirus (A16, B4, B5)
human immunodeficiency virus
Parainfluenza
rubella
adenovirus
respiratory syncytial
Vaccinations
polio
influenza
pertussis
diphtheria
combination measles, mumps, and rubella

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