CME Article

Twenty-one Cases of Papular Acrodermatitis During the Time of the Systematic VHB Immunization: Suggested Guidelines and Management to Determine the Etiology

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Target Audience

This CME activity is intended for physicians, medical students and nurse practitioners. Primary care physicians will find this information especially useful.

Learning Objectives

After completion of this article, the reader should be able to:
1. Identify the clinical manifestations of papular acrodermatitis
2. Order appropriate tests complementary tests for patients with papular acrodermatitis
3. Determine the prognosis of papular acrodermatitis

Abstract

Papular acrodermatitis (Gianotti-Crosti syndrome) appears often associated to underlying viral infection. Its clinical manifestations are quite clear and include papules or vesicles. Clinical diagnosis is quite easy for the pediatrician, but the discovery of the etiologic agent is not always accessible.

Twenty-one children with papular acrodermatitis were evaluated, between the ages of 11 months and 14 years. Acrolocated papulovesicles were seen in 7 cases, only papules in 11 cases, and macules and papules in 3. Serological investigations revealed positive IgM antibodies against: Epstein-Barr virus(EBV) 7 cases, adenovirus 2 cases, cytomegalovirus 1 case, Mycoplasma pneumoniae 1 case, parvovirus B19 1 case, coxsackie B 1 case. In 8 children no underlying virus or bacterial infection was found.

Since the general implementation of hepatitis B virus (HBV) vaccine in more advanced countries, this etiology is not frequent in papular acrodermatitis. Consequently, a range of other etiologic factors must be considered.

Introduction

Papular acrodermatitis (PA) of childhood, or Gianotti-Crosti syndrome, was first described in 1955 and was found to be associated with hepatitis B virus infection(1). Clinical diagnosis is not difficult for the pediatrician, but the discovery of the etiologic agent is not discovered.

Reported associations with this disease include viral infections (Epstein Barr, enteroviruses, hepatitis A, B, C, cytomegalovirus, poxvirus, parvovirus B19, human herpesvirus 6, rotavirus, HIV, parainfluenza, rubella, respiratory syncytial virus and, adenovirus), vaccinations (poliomyelitis, influenza, pertussis, diphtheria, and measles-mumps-rubella) and bacterial infections (Mycoplasma pneumoniae, Mycobacterium avium, group A β-hemolytic streptococci) (2-7).

During recent years, the association between PA

and all these etiologies has increased while it is the contrary with HBV. The present low incidence of cases associated with HBV in the EU and the US has coincidence with the progressive implantation of the vaccine in children and teenagers.

We present our experience of the last four and a half years and propose some guidelines to establish etiologic agent of PA.

Patients and Methods

All files of patients diagnosed as papular acrodermatitis syndrome who were reviewed in the Department of Pediatrics of the Hospital del Mar of Barcelona during the period from 1999 to June 2003 were evaluated with the same protocol to obtain clinical data and laboratory findings.

The topics studied were: age, vaccination dates, types and place of the eruptions, existence of itch, presence of additional clinical manifestations. Laboratory studies (AST, ALT, alkaline phosphatase). Serological test for viral hepatitis types A, B, and C, Epstein Barr virus (EBV), cytomegalovirus (CMV), parvovirus B19, adenovirus, Coxsackie A/B virus, were performed on all the patients. In some children other serological tests were made in accordance with clinical manifestations.

It was considered a recent infection related to cutaneous eruption when viral titers were positive for IgM-antibodies.

The visits were made until the clinical normalization.

Results

The main clinical features and etiologic agent of our patients are summarized in Table I. Fourteen males and 7 females between the ages of 11 months and 14 years were evaluated. None of the 21 patients diagnosed with PA had any relation with HBV. The etiolgy was demonstrated in 13 (61,9%): EBV in 7 cases, adenovirus in 2 and 1 case cytomegalovirus, 1 of Coxsackie, 1 of Mycoplasma pneumonia and another 1 of Parvovirus B19. From the 8 in which it was impossible to establish any etiology, it can be said that: a) the etiologic studies were only done in the agents known to be related to PA; b) through the anamnesis, no relationship with any immunization was established; c) in order to avoid disturbing the child and because of the favorable resolution of the disease a second serologic study to evaluate the increase of the IgG after 4 weeks was not performed.

Of the 21 patients, 15 boys and 6 girls: 19 (90,47%) were under 8 years and nine (42,85%) were under 4years. The eruptions were papular in 11 cases, papulovesicular in 7 cases and mixed papular and macular in 3 cases. In 8 cases the eruptions were pruritic.

High levels of alkaline phosphatase was seen in one case and high transaminases were seen in two cases of EBV.

In all cases, the skin eruption resolved between 4 and 5 weeks.

Discussion

Gianotti-Crosti syndrome or PA infantile is best considered a reaction pattern associated with viral infections and immunizations. In 1970, the etiological association with the HBV (8,9) based the prognosis and the laboratory investigations for some years. Retrospective analysis of 308 patients made by R.Caputo confirmed that only the 22,4% were caused by HBV (10). Even in high-rate countries, etiologic factors other than HBV have been published (2-6; 11-16).

It is very clear that the spectrum of associated infectious agents may still be incompletely defined. Its clinical manifestation and its spontaneous healing added to the multiple etiologies, suggest that papular acrodermatitis may be an expression of immune dysregulation (12). The pathogenesis of PA is still unclear, although different hypotheses have seen proposed. Cellular reactions and immunohistochemical findings (CD3, CD4, CD8, CD20, TIA, S-100 protein, KP-1, EBV-latent membrana antigen 1 and 2) and ultrestructural studies have demonstrated no evidence of viral antigens or viral particles. Although not proven, the associated infections may depend on inherited patterns of immune dysregulation induced by etiologic agent.

The different demographics of infectious diseases may explain the varied incidence of etiologic incidents in each country. In high-rate HBV countries, since the 1990s, the HBV vaccine has been gradually administrated to the generalization in children and teenagers. This fact could explain partially the low number of PA cases diagnosed

Table 1. Clinical and Serologic Findings

Gender	Age (years)	Clinical appearance	Pruritus	Other Symptoms	IgM antibodies
M	5	Macula and papules	++	None	Ø
M	5	Vesiculopapules	None		EBV
M	4	Papules and Microve-sicules	++	Fever	Ø
M	3	Papules and Microve-sicules	++	Lymphadenopathy	EBV
M	6	Papules and macules	None	Fever	CMV
F	4	Papules and Macules	None	Fever	Mycoplasma pneumoniae
M	10	Papules	None	None	EBV
M	4	Papules	++	Purpuric lesions in the mouth	Ø
M	14	Papules	None	None	Ø
F	5	Vesiculopapules	++	None	Ø
F	7	Papules	None	None	EBV
M	6	Papules and Microve-sicules	None	None	Ø
F	2	Papules	None	None	EBV
M	1	Papules	None	None	Coxsackie B
M	1	Papules	++	None	Ø
M	1	Papules	++	None	Adenovirus
M	3	Vesiculopapules	+++	None	Ø
M	8 (months)	Papules	None	Lymphadenopathy	Adenovirus
M	8	Papules	None	None	Parvovirus B19
F		Vesiculopapules	None	Lymphadenopathy	EBV
F		Papules	None	None	EBV

+ mild ; ++ moderate ; +++ strong
Ø = negative

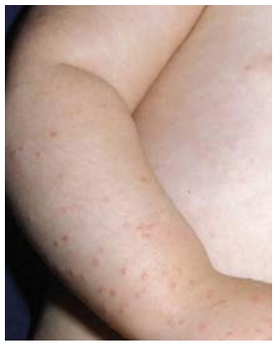

Figure 1. Papular rash on hand and arm, formed by same size elements and without presence in the thorax.

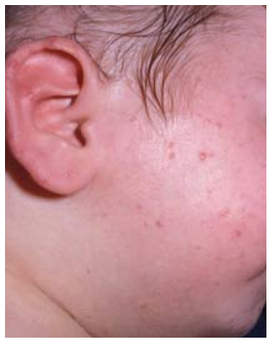

Figure 2. Papular rash on the face and the ear.

with HBV. This low incidence is an important factor for the pediatrician. It could be said that the evolution to chronic HBV disappears and consequently a possible wrong prognosis.

With the implementation of HBV vaccine, hence the low incidence of HBV, PA has no longer been a kind of disease for which it is important to establish the etiologic agent. The associated features of PA will be those who will show the necessity of an etiologic study. The present situation of low incidence with PA caused by HBV helps not to study the etiology. The possibility of chronic infections by HBV with minimal clinical manifestations conditioned the fact of knowing the etiological agent.

Pediatrician has to establish the clinical diagnosis of cutaneous lesions and, if it is possible, associate them to any type of viral or bacterial infection or any immunization. Its clinical manifestations are quite clear, with monomorphic lentil-sized, dense, normally nonconfluent, flat-topped papular elements and sometimes with some microvesiculars, in the face, symmetric in upper and lower extremities, without reaching the buttocks, and persist for 3-5 weeks (Fig 1,2). Clinical diagnosis is quite easy for the pediatrician (17).

In these countries, we suggest guidelines of actuation (Fig 3) in order to avoid unnecessary complementary exploration of the child. After establishing the clinical diagnosis of PA, doing a correct anamnesis of the immunization history and the existence of fever syndrome, or prodromic features; it will be necessary to set a difference between those who are HBV immunized and those who are not.

In the case of non-immunized patients, hepatic function and other viral serologic studies including HBV are required. In the other case, it is necessary to do a clinical evaluation of the existence of lymphadenopaties and/or splenomegaly. In immunocompetent children without these clinical features, only symptomatic control is required. Although the etiology for EBV or CMV is possible, the lack of splenomegaly excludes the destruction of the spleen. The inexistence of splenomegaly makes the splenic rupture difficult, which is one of the serious complications in these infections. The absence of lymphadenopathies, splenomegaly, hepatomegaly and prolonged fever excludes clinically the existence of a severe haematological disease (18).

When there is splenomegaly and/or lymphadenopaties, it is necessary to do blood cell counts and study aminotransferases, and selectively serological studies of EBV and CMV.

To summarize, the pediatrician that visits a child with acrolocated eruption has to be able to identify the exanthemes that will be used to establish the differential diagnosis, at the same time that has to know the immunization history. In the case of a child immunized of HBV with PA, the complementary exploration will only be done with the presence of splenomegaly and/or lymphadenopathies. The fact of saving pain in explorations in children will be a benefit if the physician has experience in the clinical diagnosis.

Before ending, we would like to warn that in high-rate countries, it is not infrequent the adoption of children from China and Russia, where the incidence of HVB is high. With these children, it is necessary to know from the very arrival their serological situation against the HVB virus (19, 20).

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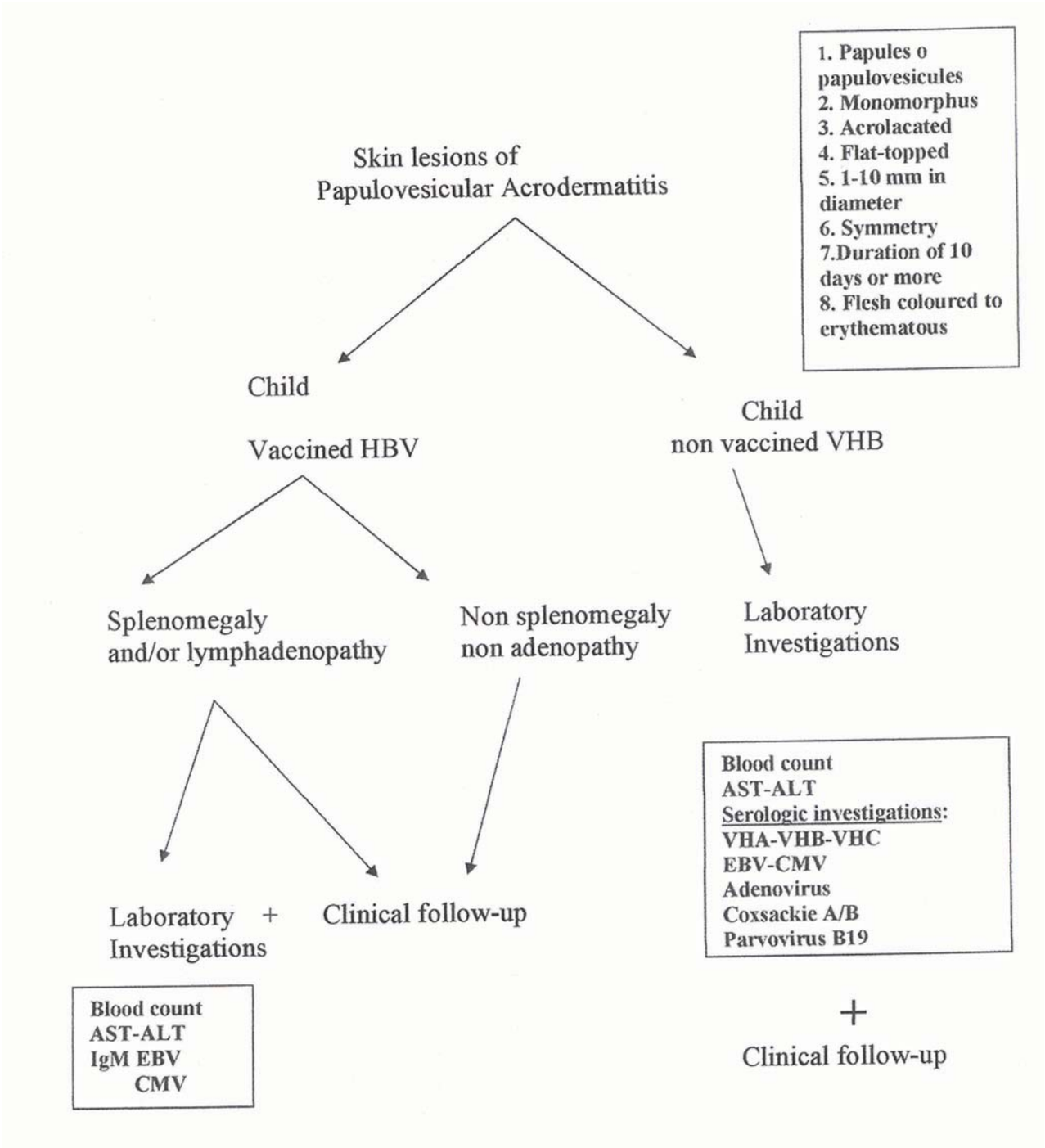

Figure 3. Protocol for the evaluation and diagnostic etiologic of papulovesicular acrodermatitis.

Papular Acrodermatitis in Children

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Twenty-one Cases of Papular Acrodermatitis During the Time of the Systematic VHB Immunization: Suggested Guidelines and Management to Determine the Etiology
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Martínez-Roig A, Sánchez-Sánchez X, López N, Seidel V, Bonet M. *Int Pediatr* 2007;22(2) 77-82.

QUESTIONS

1. Which of the following is usually not associated to the clinical presentation as Papular Acrodermatitis?
a. Epstein-Barr virus infection
b. Scarlet fever
c. Parvovirus B19 infection
d. Hepatitis B virus infection
e. Enterovirus infection

2. Which of the following features is not typical of Papular Acrodermatitis?
a. Polymorphic skin eruption
b. Similar size (lentil-sized)
c. Non-confluent
d. Papular
e. Symmetrical distribution

3. In the case of a child with PA, who is immunized against HBV, complementary tests such as serological, hematological and liver function studies should be performed
a. Always
b. Never
c. At lymph node enlargement
d. At lymph node and spleen enlargement
e. Both c and d

4. Which of the following studies is not necessary to find out the etiology of PA in a child not immunized against HBV?
a. Hepatitis A virus serology
b. Hepatitis B virus serology
c. Epstein-Barr virus serology
d. Tuberculin test
e. Parvovirus B19 serology

5. Why has the prognosis of PA improved now that the association to HBV infection is lower?
a. Because of the shortening of the disease
b. Because the evolution to chronic hepatitis has disappeared
c. Because local symptoms are less
d. Because the risk of spleen rupture is lower
e. Because skin biopsy is not always necessary

Papular Acrodermatitis in Children

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