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GIANOTTI-CROSTI SYNDROME

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ABSTRACT

We present a case of a 3 years and 8 months old female child with a generalized maculoerythematous rash associated with positive serologies for Epstein Barr virus, Echovirus and Coxsackie that raise suspicion of Gianotti-Crosti syndrome. The extremely low prevalence of this syndrome and the very long duration of the disease are highlighted, the rash can persist for up to 4 months.
We discuss this case both in order to make health professionals aware of the existence of this rare condition, which should be considered in the differential diagnosis of a viral rash, and to educate the community (school, kindergarten) that tends to isolate affected children during persistence of the rash, which is considered contagious.

Keywords: Gianotti-Crosti syndrome, papulous acrodermatitis, child

INTRODUCTION

Gianotti-Crosti syndrome, also known as childhood papular acrodermatitis, is a rare dermatological pathology that occurs in children aged between 9 months and 9 years. The representative symptoms are petechial eruptions on the skin of the upper, lower limbs and buttocks [1,2,3]. The pathology is generally preceded by a viral, bacterial infection or post-immunization [4,5]. Pathophysiological, Gianotti-Crosti syndrome occurs as a result of a type IV hypersensitivity reaction in the derm caused by a viral or bacterial antigen. Immunohistochemical studies reveal inflammatory skin infiltrate as a characteristic feature. The more common occurrence in children with atopic dermatitis also suggests an immune mechanism [2,5,6]. Skin biopsies are nonspecific and reveal local spongiosis, parakeratosis, moderate acanthosis, and psoriatic hyperplasia. Lymphocyte and perivascular histiocytic infiltrates are observed in the papillary dermis. Erythrocyte extravasations can be observed in the papillary dermis [2,7]. There is no racial predisposition for the development of Gianotti-Crosti syndrome. In pediatric age, both sexes are affected equally. It occurs most frequently between 9 months and 9 years (minimum incidence is reported at 3 months and the peak incidence at the age of 15 years), but more than 90% of patients are under 4 years of age. Morbidity is particularly significant in Gianotti-Crosti syndrome caused by hepatitis B virus infection. The rash lasts on average 2-4 weeks, but can last up to 4 months [1,2,3]. The differential diagnosis is made with: polymorphic erythema, insect bite, urticaria, atopic dermatitis, pediatric follicular keratosis, Langerhans cell histiocytosis [2,6]. Gianotti-Crosti syndrome is gen-

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erally a benign pathology, which, in the absence of complications, does not require specific treatment [2,7].

The informed consent of the child's mother whose case is presented was obtained, as well as the Opinion of the Ethics Commission of Poderas Academic Hospital no. 174, dated 19.05.2021.

CASE PRESENTATION

Presenting concerns

We present the case of a 3 years and 8 months old female, hospitalized in the Pediatrics department of the Ponderas Academic Hospital for maculoerythematous rash in placards with a tendency to confluence and a slight swelling of the knees.

Clinical findings

The girl comes from an urban environment, from parents with atopic background, the mother is being known to be allergic to penicillins. It is the first child from pregnancy with physiological evolution, born at term (41 weeks) in maternity, with birth weight 3,200 g, Apgar 9 and a good postnatal evolution. It is fed with breast milk from birth to the age of two, diversified starting with the age of 6 months. She is vaccinated up to date according to the national scheme and performed the prophylaxis of rickets with vitamin D3.

From birth until present, the girl has been diagnosed with atopic dermatitis, acute pharyngitis, upper way infection and an episode of acute bronchiolitis.

The current disease begins about 14 days before presentation in our clinic with fever (maxim 39°C) accompanied by diffuse abdominal pain, diarrhea (2-3 stools/day) and arthralgias of the knees. The parents decide to perform a test RT-PCR (reverse transcription polymerase chain reaction) for SARS-CoV-2 (severe acute respiratory syndrome coronsvirus 2), the results being negative for the parents, but positive for the child. Home treatment with Azithromycin is initiated on the recommendation of the family doctor, but the patient becomes apathetic, fever increase (maxim 38-39°C), which is why parents request an ambulance and she is hospitalized for three days at an infectious diseases hospital. Because the results are negative for two consecutive RT-PCT COVID-19 tests, she is transferred to a public hospital for children with the diagnosis of interstitial pneumonia, Epstein Barr virus, Echovirus and Coxsackie infection (positive IgM serologies) for which oral Clarithromycin treatment is instituted.

At the children's hospital, hepatocytolysis syndrome is detected (alanine transaminase = 190 U/l, aspartate transaminase = 122 U/l, lactate dehydrogenase = 768 U/l) with negative serology for hepatitis B virus and treatment with Clarithromycin and antipyretics is given. She was discharged after two days with the diagnosis of acute pharyngitis, infectious mononucleosis, for which she received treatment at home with Clarithromycin (5 days completed), hepatoprotectors and antipyretics.

After two days from discharge, the patient presented a pruritic micropapuloerythematous rash, initially on the face, later extended on the limbs and trunk. The next day was reassessed by the pediatrician and received treatment with antiviral and antihistaminic at home. The fever disappeared, but the eruption become more and more severe in evolution, which is why she came to emergency room of Ponderas Academic Hospital; here she received a dose of corticosteroid intravenous and hospitalized for further investigations and treatment.

On physical examination, her weight was 16 kg, with satisfactory general condition, without fever. Systems examination revealed a generalized non-pruritic micromaculo-erythematous rash (Fig. 1). The mucous membranes are discreetly hyperemic, the lips were dry and the jugal mucosa had lesions (Fig. 2). The child also had lymphadenopathies (retroauricular, latero-cervical, inguinal and axillary), knee swelling, depapillated tongue, discrete hyperemic pharynx and discrete hepatomegaly.

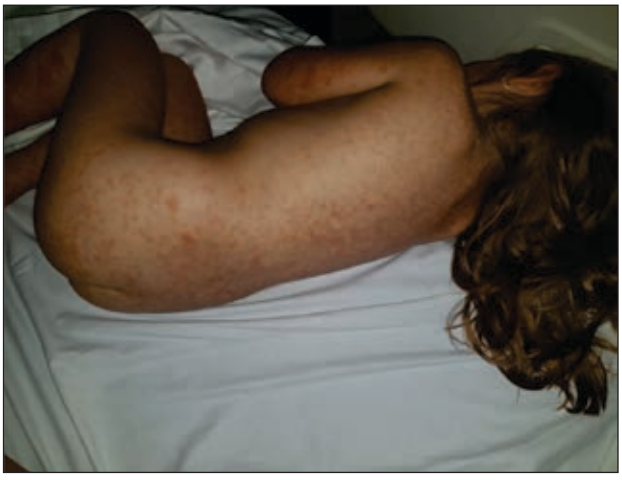

FIGURE 1. *Generalized micromaculoerythematous rash*

Diagnostic focus and assessment

Investigations revealed the following results: lymphocytosis, hepatocytolysis syndrome, slightly increased ferritin, the absence of biological inflammatory syndrome and IgG for Epstein-Barr, cytomegalovirus and enterovirus and IgM for Epstein Barr virus.

Abdominal ultrasound revealed modarately fluid content in the intestines and accentuated peristalsis

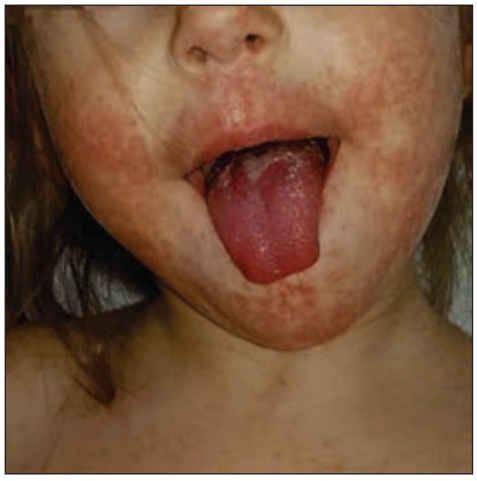

FIGURE 2. *Papular lesions affecting the face*

with minimal amount of homogeneous transonic fluid in Douglas (4 ml). Pediatric surgery examination infirm acute surgical abdomen as a cause of abdominal pain.

Therapeutic focus and assessment

Under the treatment performed in the hospital with intravenous corticotherapy, antihistamines and local emollient, the evolution of the disease was favorable. After the introduction of intravenous cortisone treatment, a slight improvement was observed compared to the day she came. Second day, at the clinical examination, the pacient had a generalized papuloerythematous rash with a tendency to confluence on the face and limbs (Fig. 3), some elements having a petechial appearance, including palms and soles (Fig. 4), associated with prurit in the lower limbs. The lesions on the face became rough, with a tendency to exfoliate and the elements on the lower abdomen were paler. Bilateral subangulo-mandibular and latero-cervical adenopathy were also observed.

It was dermatologically evaluated and the suspicion of sindrome Gianotti-Crosti was discussed; it was recommended to introduce in the treatment plan an anti-H1 antihistamine, topical corticosteroids and local emollients.

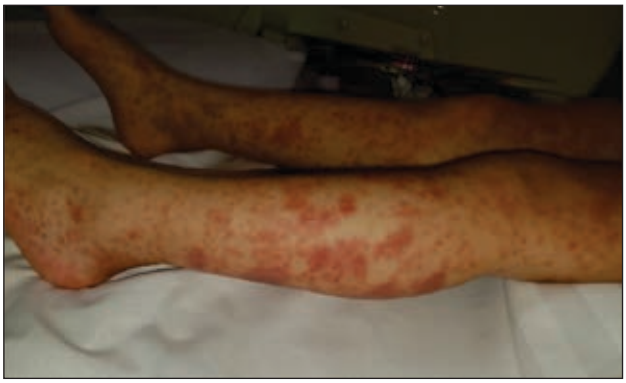

FIGURE 3. *Papular lesions affecting the legs*

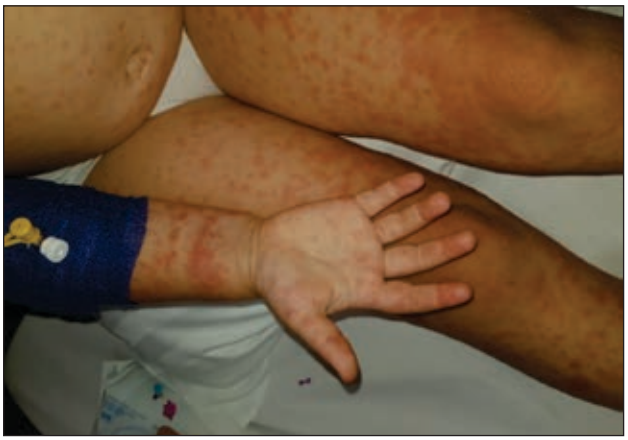

FIGURE 4. *Papuloerythematous lesions on the palms and legs*

On the third day of treatment, the clinical examination showed a rash with decreased intensity on the trunk and the absence of pruritus with an accentuation of the rash on the face.

The patient was discharged after another four days of cortizon treatment (seven days of hospitalization) with a relatively good general condition, without fever, with improved lesions, but persistent and much paler on the face, arms and legs. At home it was recommended to continue the treatment with an antiH1 antihistamine and local with emollients and topical corticosteroid (Fig. 5).

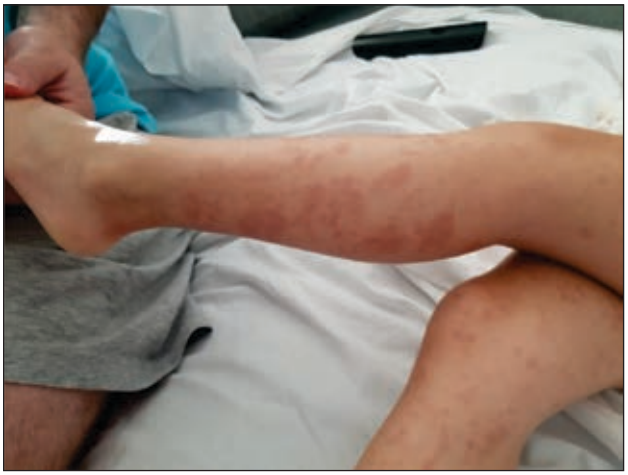

FIGURE 5. *Papular lesions in remision*

Follow-up and monitoring

After 7 days she returned to control: the skin lesions were remitted on the cephalic extremity, trunk and abdomen, improved on the arms and forearms and accentuated on the lower limbs. Treatment with antiH1 antihistamines and is still recommended and a dermatological control was suggested. At the following dermatological examinations, within twenty-one days, the lesions were present on the legs, but gradually begun to remit.

Follow-up at 3 months: the girl is afebrile, with a relatively good general condition and the rash has completely cleared.

DISCUSSION

Gianotti-Crosti syndrome is currently considered, according to several published studies, such as those of Brandt et al. and Pedreira et al., a standard-reaction dermatosis associated with viral and bacterial infections or post-immunization [6,8]. The most common causative agent is considered hepatitis B virus, other pathogens involved being hepatitis A, C, Epstein Barr virus, influenza virus, parainfluenza, cytomegalovirus and respiratory syncytial virus. Although rare, in studies by Snowden et al., Brandt et al. and Al Dhaheri et al., cases with bacterial etiology have also been reported such as: group A beta-hemolytic Streptococcus, intracellular *Mycobacterium avium*, *Mycoplasma pneumoniae*, *Bartonella henselae*, *Borrelia burgdorferi*, Meningococcus, as well as cases of post-immunization anti-polio, anti-diphtheria, anti-influenza, anti-pertussis, anti-rubella, anti-hepatitis A and B, anti-H1N1 [5,7,8]. In our case, we assume that the trigger of the syndrome was multiple, the patient having antibodies for both Epstein Barr virus and cytomegalovirus, Echovirus and Coxsackie.

The main clinical feature of Gianotti-Crosti syndrome is the presence of an exanthema, which may be preceded by upper respiratory tract infections, diarrhea or pharyngitis. The rash in this case is characterized by a papular or vesiculopapular erythematous rash with acral spread, frequently starting from the buttocks. Other areas of the body (torso, elbows, knees, palms and soles) are not usually affected; however, their involvement does not exclude the diagnosis, according to the study of Al Dhaheri HS et al. [5]. In our case, the patient has an atypical appearence of the rash, which begins on the face and then spreads throughout the body, including the palms and soles.

The systemic manifestation associated with Gianotti-Crosti syndrome includes fever, malaise, diarrhea and lymphadenopathy (25-35% of patients) which are also evident in patients in the studies of Al Dhaheri et al. and Llanora et al. [5,9]. Hepatic changes are rare and are observed mainly in hepatitis B virus, Epstein Barr and cytomegalovirus infection as evidenced in studies of Craig-Müller et al., Al Dhaheri et al. and Pedreira et al. [2,5,6]. Of all the systemic manifestations associated with Gianotti-Crosti syndrome, our patient presented only fever and lymphadenopathy. In particular, the patient had arthralgias and joint swelling. The liver changes found in our patient could be explained by the presence of antibodies to Epstein Barr virus and cytomegalovirus, which means that the patient has recently been infected with these viruses.

The diagnosis in this case was a clinical one, as the parents refused to perform the skin biopsy. Due to its rare occurrence, Gianotti-Crosti syndrome should be included in the differential diagnosis for molluscum contagiosum, papular urticaria, polymorphic erythema, insect bite, atopic dermatitis, pediatric follicular keratosis, Langerhans cell histiocytosis, according to Craig-Müller et al. and Pedreira et al. studies [2,6]. The course of the disease is benign and self-limiting, and its resolution lasts up to 4 months, without leaving scars, according to the same studies [2,6] have been reported recurrences, but are less common. In the case of our patient, the lesions began to heal gradually after about 30 days, disappearing completely after about 3 months.

Most cases do not require treatment. Lesions appear to resolve more quickly with the use of medium-potency topical corticosteroids. Antihistamines may be prescribed to control pruritus, and systemic corticosteroids are recommended in acute cases. The treatment in this case respected the data from the literature. Being an extended form of the disease, the treatment with a systemic corticosteroid was started for 7 days, completing the treatment scheme with a local corticosteroid to speed up the healing of the lesions. The patient also received local emollients and an H1 antihistamine to control the itching.

CONCLUSIONS

Reporting this case we encourage pediatricians working in both outpatient pediatric clinics and hospital emergency rooms to consider the Gianotti-Crosti syndrome in the differential diagnosis of viral rash.

Health professionals should be advised that the child's papular acrodermatitis is a benign condition often confused with other skin infections that occur in childhood, leading to the isolation of the affected child.

If there is any doubt about the diagnosis, the patient should be referred to a dermatologist.

We point out that it is not a contagious disease and therefore does not require isolation or restriction of the child's participation in school or other activities in the presence of other people. However, if the associated infection proves to be contagious, isolation should be considered in relation to the symptoms of the associated condition.

The families of patients should also be educated on the evolution of the disease and its duration.

REFERENCES

1. Metelitsa AI, Fiorillo L. Recurrent Gianotti-Crosti syndrome. *J Am Acad Dermatol.* 2011 Oct;65(4):876-877.
2. Craig-Müller SA, Elston DM. Gianotti-Crosti syndrome. Available at: https://emedicine.medscape.com/article/911275.
3. Chuh A, Zawar V, Sciallis GF, Kempf W, Lee A. Pityriasis Rosea, Gianotti-Crosti Syndrome, Asymmetric Periflexural Exanthem, Papular-Purpuric Gloves and Socks Syndrome, Eruptive Pseudoangiomatosis, and Eruptive Hypomelanosis: Do Their Epidemiological Data Substantiate Infectious Etiologies? *Infect Dis Rep.* 2016 Mar 21;8(1):6418.
4. Zawar V, Chuh A. Efficacy of ribavirin in a case of long lasting and disabling Gianotti-Crosti syndrome. *J Dermatol Case Rep.* 2008 Dec 27;2(4):63-6.
5. Al Dhaheri HS, Al Kaabi A, Kara Hamo Y, Al Kaabi A, Al Kaabi S, Al Tatari H. Unusual Presentation of Gianotti-Crosti Syndrome due to Epstein-Barr Virus Infection. *Case Rep Dermatol Med.* 2016;2016:1017524.
6. Pedreira RL, Leal JM, Silvestre KJ, Lisboa AP, Gripp AC. Gianotti-Crosti syndrome: a case report of a teenager. *An Bras Dermatol.* 2016 Sep-Oct;91(5 suppl 1):163-165.
7. Snowden J, Rice AS, O'Shea NE. Papular Acrodermatitis. 2021 Jan 5. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2021 Jan.
8. Brandt O, Abeck D, Gianotti R, Burgdorf W. Gianotti-Crosti syndrome. *J Am Acad Dermatol.* 2006 Jan;54(1):136-4.
9. Llanora GV, Tay CM, van Bever HP. Gianotti-Crosti syndrome: case report of a pruritic acral exanthema in a child. *Asia Pac Allergy.* 2012 Jul;2(3):223-6.