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Case Report

IgA-associated Vasculitis in a child: case report

Vasculite associada à IgA em criança: relato de caso

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ABSTRACT: Vasculitis associated with immunoglobulin A (VIgA), also known as Henoch-Schonlein purpura, anaphylactoid purpura or rheumatic purpura is a small vessel vasculitis associated with deposition of IgA immune complexes, of unknown etiology and affecting mainly children. In most pediatric cases, it is a self-limited disease with cutaneous, joint, gastrointestinal and renal manifestations. The differential diagnosis includes other vasculitis, such as systemic lupus erythematosus, meningococcemia, disseminated intravascular coagulation and uremic hemolytic syndrome. In this article, the main aspects of HSP in children are addressed, highlighting the importance of early differential diagnosis. The clinical case of a 5-year-old female patient with purpuric lesions treated in a first approach as a severe bacterial infection is presented. After medical re-evaluation, there was a therapeutic change with the use of glucocorticoids resulting in a significant improvement of symptoms.

Keywords: Children; IgA vasculitis; Henoch Schonlein purpura; Small vessel vasculitis.

RESUMO: A Vasculite associada à imunoglobulina A (VIgA), também conhecida como púrpura de Henoch-Schonlein, púrpura anafilactóide ou púrpura reumática é uma vasculite de pequenos vasos associada a deposição de imunocomplexos IgA,de etiologia ainda desconhecida e que acomete principalmente crianças. Em grande parte dos casos pediátricos, é uma doença autolimitada com manifestações cutâneas, articulares, gastrintestinais e renais. O diagnóstico diferencial inclui outras vasculites, como lúpus eritematoso sistêmico, meningococcemia, coagulação intravascular disseminada e síndrome hemolítica urêmica. Neste artigo abordam-se os principais aspectos da VIgA nas crianças, salientando-se a importância do diagnóstico diferencial precoce. É apresentado o caso clínico de uma paciente do sexo feminino de 5 anos com lesões purpúricas tratada numa primeira abordagem como infecção bacteriana grave. Após reavaliação médica houve alteração terapêutica com uso de glicocorticóides resultando em melhora expressiva dos sintomas.

Palavras-chave: Crianças; Vasculite por IgA; Púrpura de Henoch Schonlein; Vasculite de pequenos vasos.

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INTRODUCTION

Immunoglobulin A-associated vasculitis, also known as Henoch-Scholein purpura, is a non-thrombocytopenic leukocytoclastic vasculitis characterized by deposits of Immunoglobulin A in small vessels, especially those of the skin, joints, gastrointestinal tract, and kidneys. Affecting principally the pediatric age group, male and Caucasian, with a peak incidence at 6 years of age[1]. Although the etiology remains unknown, several triggering factors are related to the onset of the disease: food, insect bites, vaccines, medications, exposure to cold and mainly bacterial infections of the upper airways by streptococci[1]. The differential diagnosis includes other primary immune vasculitides, such as systemic lupus erythematosus and vasculitis secondary to serious bacterial diseases such as meningococcemia, hemolytic uremic syndrome and disseminated intravascular coagulation[1,2]. In this sense, it is necessary the early diagnosis and timely appropriate intervention, given the possible serious gastrointestinal and renal complications, resulting from a prolonged clinical course[2].

CASE REPORT

The case below was described with the consent and authorization of the parents to publish the data.

This is a VFT infant, 3 years and 4 months old, female, born on November 22, 2011, city of Uberlândia. The parents sought an emergency care in the city on May 05, 2015, the patient presented with abdominal pain, vomiting and red spots on the body (Figures 1, 2 and 3). On this occasion, the diagnostic hypothesis of meningococcemia was made, and she was hospitalized and intravenous therapy with a third-generation cephalosporin (ceftriaxone) was started for 6 days.

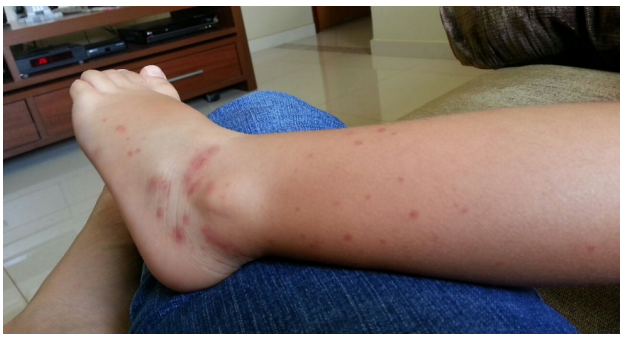

Figure 1. Purpuric lesion on the left foot and ankle

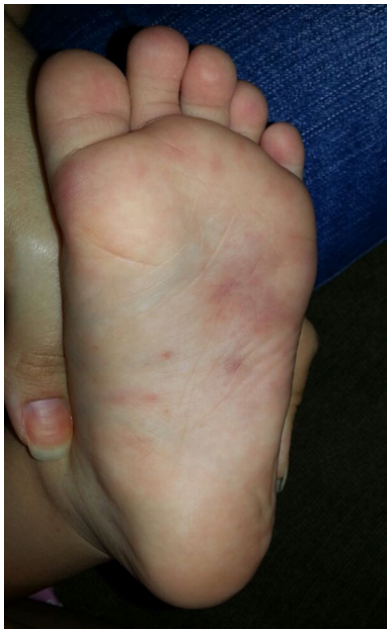

Figure 2. Purpuric lesion on the lower part of the left foot

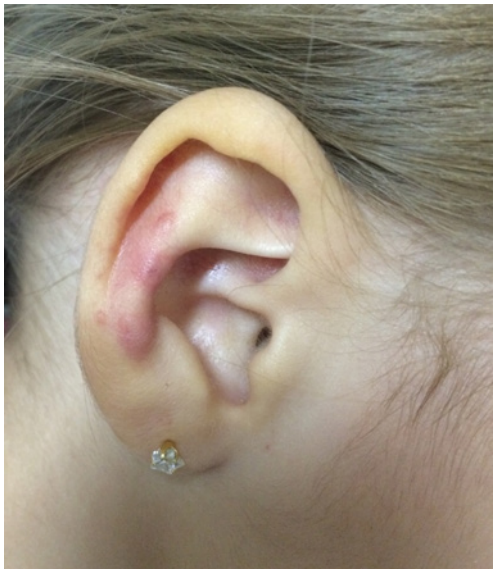

Figure 3. Purpuric lesion in the external ear

With no improvement in the clinical picture, on the 7th day of the disease, the parents sought pediatric medical care in a private office. At the time, the child presented with worsening abdominal pain, bloody vomiting when trying to feed, oliguria with dark colored urine and blackened stools. On examination, attention was drawn to the compromised general condition with skin pallor and signs of dehydration, associated with erythematous skin lesions, with petechiae and ecchymosis predominant in the lower limbs (Figures 4 and 5), gluteal region (Figure 6), extending to the hands (Figures 4 and 5). Figure 7), feet and ears.

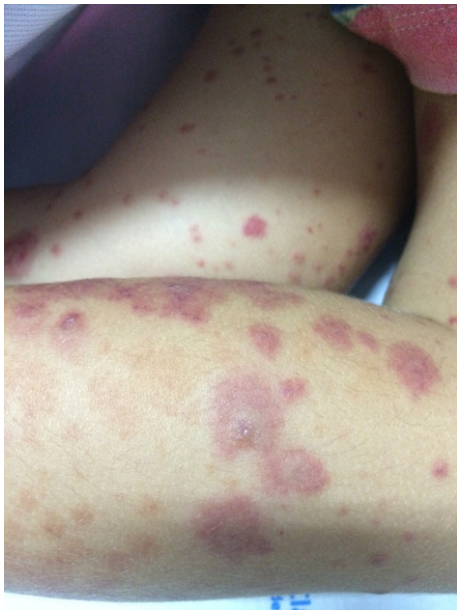

Figure 4. Palpable purpura in the lower limbs region

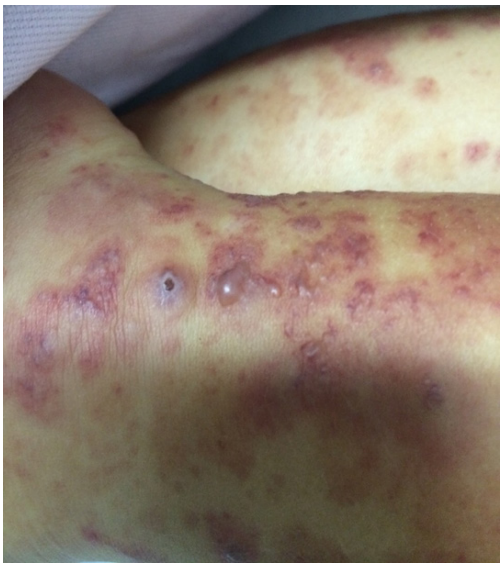

Figure 5. Palpable purpura and blisters on the right ankle

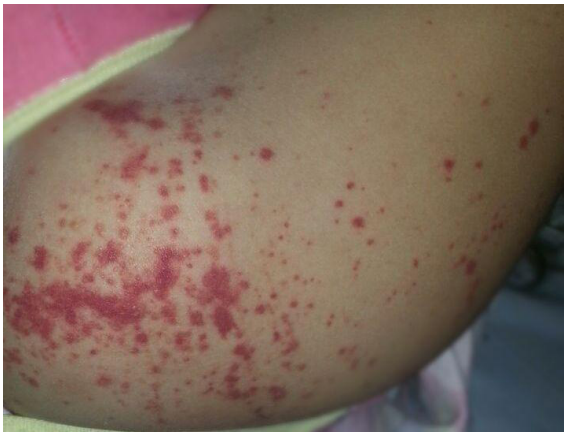

Figure 6. Palpable purpura in the gluteal and lumbar regions

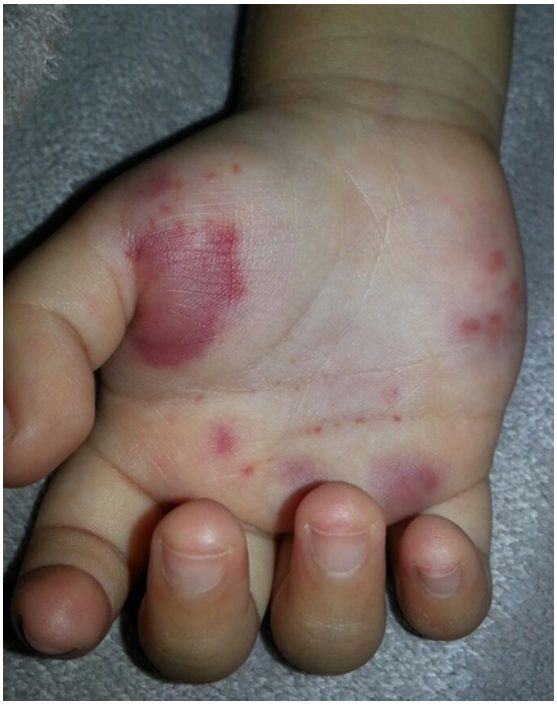

Figure 7: Purple lesion on the right hand

The suspicion of IgA vasculitis was then raised. The patient was readmitted for fluid replacement and complementary tests, when a complete blood count, serum IgA, type I urinalysis and erythrocyte sedimentation rate were requested.

The exams on May 11, 2015 showed an elevated serum IgA dosage of 276.0 mg/dl (vr: 20.0 to 100 mg/dl), as well as an erythrocyte sedimentation rate of 21 mm (vr women: up to 20 mm). The type I urinalysis showed the presence of ketone bodies, amorphous phosphate crystals, mucus filaments, traces of hemoglobin and a small amount of red blood cells: 10,500/mL (vr: up to 10,000/mL). The blood count showed leukocytosis as the only alteration, with total leukocytes of 12,800 per mm^3 (vr: 4,000 to 12,000 per mm^3). Confirming, in association with the clinical picture, the diagnostic suspicion.

The following day, May 12, 2015, treatment with prednisolone 2mg/kg/day was started, followed by dose reduction to 1.5mg/kg/day, 1mg/kg/day and 0.5mg/kg/day. every three days at home. On return, after two weeks of evolution, the patient presented clinical improvement of pain and lesions. Notably, no new lesions appeared and the old ones involuted (Figure 8); Laboratory tests with normalization of urinary sediment. Clinical and laboratory monitoring was maintained for a few months to detect complications, especially the presence of nephritis. Patient evolved without complications.

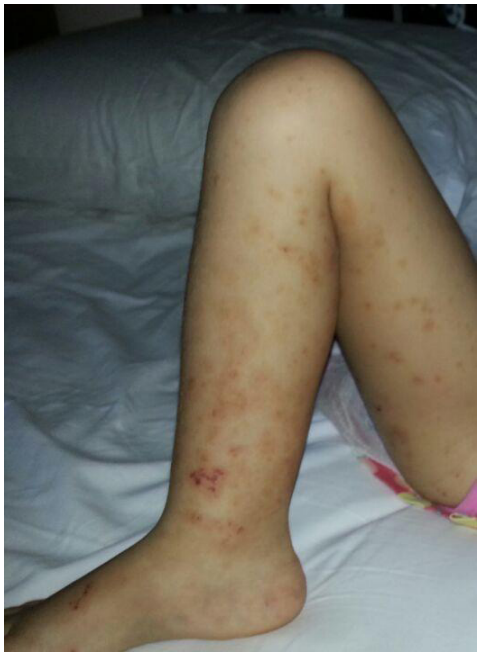

Figure 8. Involution of maculopapular lesions in the right lower limb

DISCUSSION

IgA vasculitis is a leukocytoclastic, non-thrombocytopenic, small vessel vasculitis characterized by the deposition of IgA, which causes increased vascular permeability and blood leakage to adjacent tissues[3].

It occurs more frequently in childhood, with a higher incidence among children aged 2 to 6 years, with seasonal peaks (fall and spring)[2,4]. Males are more affected, as well as Caucasians[4]. An increase in the incidence in siblings and family members points to the possibility of a genetic predisposition, with a possible role in increasing susceptibility to one or more manifestations such as nephritis[5].

The exact triggering mechanisms of VIgA are still unknown. However, adenovirus, hepatitis A and B, rubella, chickenpox, parvovirus B19, Epstein-Barr virus, group A beta-hemolytic streptococcus, Mycoplasma pneumoniae, enterobacteria and Toxocara canis stand out, as the main triggering viruses and bacteria[4,6]. Most cases (40 to 50%) of VIgA are preceded by upper airway respiratory infections[4,7].

In addition to these, dyes, preservatives, insect bites and some drugs have already been described in the literature, such as all types of vaccines, main antibiotics and immunomodulatory agents, mainly TNF-α[7] blockers. It is postulated that the inflammatory process results from a deposition of immune complexes in the walls of blood vessels, with activation of the complement system[2].

Clinically, IgA vasculitis is manifested by skin lesions (petechiae, palpable purpura), subcutaneous edema, arthritis and abdominal pain[4,6]. The clinical picture is usually acute, with maculopapular, urticarial and petechial lesions, evolving for larger purpura, which does not disappear with digital pressure[1,4,6]. The purpuric lesion is usually palpable, with a preferential distribution in the lower limbs and buttocks, but other areas can be affected, such as the arms, face and trunk[1,4,6]. They can converge, forming large ecchymoses, and evolve with vesicles, hemorrhagic blisters and ulcerations[1,4]. When the purpura regresses, it turns brownish and gradually disappears, it usually does not evolve with a scar.[1] Subcutaneous edema is common[1,3]. As Lesions appear in outbreaks, lasting from 3 to 10 days in younger children and are preferentially located on the hands and feet[1]. Symptoms usually last from 2 to 6 weeks[1].

Renal impairment occurs in approximately 1/3 of children, but in only a small percentage it is a life-threatening complication[1,4,6]. Symptoms range from mild conditions, such as microscopic hematuria and mild proteinuria, to hypertension. and renal failure[4,6].

CNS involvement occurs occasionally, with manifestations ranging from headache and behavioral changes to seizures, peripheral neuropathies, intracerebral hemorrhage, and encephalopathy[6,7].

The case described in the article follows the same classic characteristics in the literature: age range, involvement during autumn, characteristic symptoms of the lesions and associated symptoms, such as significant abdominal pain, hematemesis with any attempt at oral ingestion; smaller and darker urine as well as darkened stools. Changes in urinary sediment and elevation in serum IgA were confirmed. The diagnosis was based on the evolution and the clinic since there are no specific laboratory alterations of this disease. The platelet count was normal, as well as the red and white series showed mild leukocytosis in the hemogram. These results rule out the differential diagnosis of lesions secondary to vasculitis due to more serious bacterial diseases such as menigococcemia[1]. Urine Type I may show hematuria and cylindruria, as well as altered renal function,[4] which was not evidenced in the case described.

Skin biopsy is only indicated in cases of atypical evolution and evidence of leukocytoclastic vasculitis with deposits of IgA and C3 on immunofluorescence. There is evidence that IgA deposition is not pathognomonic of VIgA[6], and can be found in other vasculitis such as cryoglobulinemia and in secondary hypersensitivity to drugs. On the other hand, the literature describes cases of VIgA without IgA deposition, possibly due to a false negative, which reinforces the need for collection to be performed in a recent lesion (in the last 24 hours) to increase the possibility of detecting the presence of IgA[6].

The diagnosis is currently based on the mandatory presence of palpable purpura plus 1 of the other 4 criteria proposed by the European League Against Rheumatism (EULAR), Pediatric Rheumatology European Society (PRES) and Pediatric Rheumatology International Trials Organization (PRINTO) (Table 1)[8].

Table 1. Diagnostic criteria for VIgA according to EULAR/PRINTO/PRES

Criteria	Glossary
Purple (required) and at least one of the following:	Purpura (usually palpable) or petechiae, predominantly in limbs without thrombocytopenia If purpura with atypical distribution is required histological demonstration of IgA deposits
1- Abdominal pain	Diffuse colicky pain of sudden onset. Invagination or bleeding may occur
2- Histopathology	Leukocytoclastic vasculitis with IgA deposits or proliferative glomerulonephritis with IgA deposits
3- Arthritis or arthralgia	Sudden-onset arthritis (edema, pain, functional limitation) Sudden-onset arthralgia (pain)
4- Kidney involvement	Proteinuria > 0.3g/24h or urinary albumin/creatinine ratio > 30 mmol/mg in urine sample. Hematuria or > 5 RBCs/field high resolution or RBC casts in urine sediment or > 2+ on test strips

Source: Table adapted from Ozen S, 2010[8]

The literature demonstrates that, when there is renal involvement, follow-up of up to 5 years may be necessary, considering that up to a third of cases may present recurrence of the disease for up to two years.[1,5] The case described was monitored with annual assessments of renal functions and no complications were identified. Complications related to scrotal involvement may also occur: orchitis, epididymitis or testicular torsion also correspond to emergency situations in VIgA and occur in a minority of cases[1,4,5].

The treatment of VIgA should be unique according to the clinical condition of each patient and should be directed towards the identification and removal of the possible agents involved: infections, food, drugs, vaccines, etc[9]. Purpura usually improves without the need for treatment, do not respond to non-steroidal anti-inflammatory and antiallergic drugs[1,6,9]. Generally, analgesics (paracetamol) are indicated for arthralgia; non-steroidal anti-inflammatory drugs (such as naproxen) to control arthritis; corticosteroids (prednisone, prednisolone, and/or pulse therapy with methylprednisolone) for severe abdominal pain, severe nephritis, inflammation of the testicles (orchitis), as well as other serious and rare conditions (neurological involvement and bleeding from the lungs)[9]. Ranitidine is commonly used. in all cases with abdominal pain, which may be associated with corticosteroids[9].

Immunosuppressants (such as: cyclophosphamide, cyclosporine A, azathioprine, among others), intravenous gammaglobulin or plasmapheresis are rarely used and usually in patients with nephritis or other severe manifestations that have not improved with corticosteroids[4,6,9].

FINAL CONSIDERATIONS

A constant update in the literature of pathologies such as VIgA, Henoch-Schonlein purpura, associated with illustrative cases like this one with a focus on diagnosis are of extreme importance in the scientific community.

It is necessary to emphasize that the diagnosis of HSP is eminently clinical, made from the association of signs and symptoms with the patient's age group, and that due to the sudden onset of symptoms and clinical presentation of an acutely ill child, the attending physician may present difficulty in analyzing possible differential diagnoses.

The case described illustrates the importance of knowing the clinical criteria for the proper diagnosis of this entity. Mismanagement of the disease, in addition to possible adverse events due to inadequate treatment of the disease, prolongs the clinical picture and potentiates the appearance of possible complications with a risk of negative impact on the child's quality of life.

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