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INTERACTIVE CASE

A child with rash and arthritis: what is the diagnosis?

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THREE-YEAR-OLD FEMALE PATIENT

Chief complaint: red spots on the body

In September 2018, the patient suddenly developed red spots on the lower limbs. The following day, the number of lesions increased and edema and pain developed in the lower limbs, preventing ambulation. The mother denied fever and other symptoms but reported the occurrence of a cold 2 weeks prior. Hospitalization was indicated.

The physical examination indicated good overall health, absence of fever, weight of 14,400 g, height of 109.5 cm, and presence of bilateral posterior and anterior cervical polyadenopathy, painless and allowing movement, with a fibroelastic consistency and a diameter of <1 cm. No visceromegaly was observed.

The lower limbs presented many palpable purpuric lesions <1 cm with poorly defined margins (figure 1 and 2). The presence of soft, cold, and bilateral edema on the feet was observed. There was pain on passive movement, and edema in the right hand.

Complementary examinations (September 5, 2018)

Urea: 20; Creatinine: 0.3; Na: 139.2; K: 4.16; Ca: 11.8; Cl: 106



Figure 1. palpable purpura and bilateral foot edema.

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Figure 2. Palpable purpura and bilateral foot edema.

Glucose: 84; total serum bilirubin: 0.04; direct serum bilirubin: 0.0; indirect serum bilirubin: 0.0; GOT: 28; GPT: 6
Total proteins: 7.5
Albumin: 4.5
Red blood cells: 4.63 / Hb: 12.8 / HCT: 39%
Leukocytes: 12,700 (0, 2, 0, 2, 66, 21, 9)
Platelets: 429,000
SAE: pH: 6.0 / 2 to 3 pyocytes per field / Absence of proteinuria

Outcome

The pain and edema improved, and the patient started walking again. However, after the third day of hospitalization, abdominal pain developed after meals, which persisted until day 7, when the patient was examined in the Rheumatology Sector, and treatment was indicated, resulting in the remission of pain.

Questions

1- The triad including palpable purpura, particularly in the lower limbs, arthritis/arthralgia, and abdominal pain leads to the suspicion of:
   A) Idiopathic thrombocytopenic purpura
   B) Wegener's granulomatosis
   C) Henoch–Schönlein purpura (HSP)
   D) Churg–Strauss syndrome
   E) All of the above

The classification for HSP includes the following:[1]

- A mandatory criterion, which is palpable purpura or petechia, predominantly in the lower limbs, and one of the following four symptoms:
  - Abdominal pain
  - Arthritis or arthralgia
  - Renal impairment
  - Histopathology with IgA deposition

2- In the new classification of vasculitis, HSP is designated as:
   A) Granulomatosis with polyangiitis
   B) Eosinophilic granulomatosis with polyangiitis
   C) Microscopic micropolyangiitis
   D) Vasculitis by IgA
   E) Medium-vessel vasculitis

• Vasculitis is defined according to the size of the affected vessels (small, medium, and large). The Chapel Hill consensus nomenclature was updated in 2012. The adopted eponyms were replaced with descriptive names whenever possible:[2,3]

- Henoch–Schönlein purpura (HSP) → vasculitis by IgA (VIgA)
- Wegener's granulomatosis (WG) → granulomatosis with polyangiitis (GPA)
- Churg–Strauss syndrome (CSS) → eosinophilic granulomatosis with polyangiitis (EGPA)

• New subcategories have been added:[2,3]
• isolated vasculitis (e.g., vasculitis of the central nervous system)
• vasculitis associated with systemic diseases (e.g., systemic lupus erythematosus)
• vasculitis with probable etiology (e.g., vasculitis associated with hepatitis B virus)

3- What is true about HSP?
   A) Severe renal impairment is common in children.
   B) The main renal manifestation is proteinuria.
   C) The primary renal manifestation is arterial hypertension.
   D) HSP nephritis and IgA nephropathy are the same disease.
   E) The main gastrointestinal symptom in children is hematochezia.

- Renal impairment, which determines the long-term prognosis, is reported in 20%–55% of children and 49%–83% of adults.[4]
- In children, renal impairment tends to be mild and may manifest as isolated hematuria. Hematuria is the most common symptom. Severe manifestations such as nephrotic syndrome and renal failure are more common in adults.[4]
- HSP nephritis and IgA nephropathy are glomerulopathies characterized by mesangial deposits of abnormally glycosylated IgA1 immune complexes and may sometimes be indistinguishable. In IgA nephropathy, immune complexes are deposited exclusively in the kidneys.

There is plenty of indirect evidence suggesting a close relationship between the two conditions. For example, cases of monozygotic twins in which one developed HSP while the other developed IgA nephropathy have been reported. Despite similar histopathological results, the presentation and course of the two diseases are distinct.[5,6,7]

- The primary symptom in the gastrointestinal tract is abdominal pain. Other symptoms include nausea, vomiting, and melena/hematochezia. The occurrence of pancreatitis is also possible.[4]

Involvement of the lungs and nervous system is rare.[1]

4- What is the complementary test that may be important for diagnosing HSP?
   A) Antineutrophilic antibody screening
   B) Histopathological examination showing granulomatous inflammation.
   C) Fixed nodules, cavities, or infiltrates on chest CT
   D) Histopathological examination showing a predominance of IgA
   E) None of the above

- In practice, the diagnosis of HSP is clinical[3]. There are no specific laboratory tests. However, one of the diagnostic criteria is the presence of immune complexes in a renal biopsy with the predominance of IgA.[5]
- Leukocytosis, thrombocytosis, and elevated C-reactive protein and serum IgA may occur.[5]
- ANCA positivity is a characteristic of ANCA-associated vasculitis, which involves granulomatosis with polyangiitis (GPA), eosinophilic GPA (EGPA), and microscopic polyangiitis (MPA).[8]
- Pulmonary involvement is rare in HSP but common in other forms of vasculitis.[9]
- All patients with EGPA develop asthma, and 25%–55% of patients with MPA present with alveolar hemorrhage syndrome.[10]
- Bilateral parenchymal nodules, including cavitary nodules, or alveolar hemorrhage syndrome may occur in 52%–94% of GPA cases.[10]
- In Takayasu arteritis, there may be involvement of the pulmonary artery, and subsequent pulmonary hypertension may occur in up to 86% of patients.[10]

5- The two most common vasculitides in children are:
   A) Henoch–Schönlein purpura and Takayasu arteritis
   B) Kawasaki disease and Wegener's granulomatosis
   C) Henoch–Schönlein purpura and Kawasaki disease
   D) Churg–Strauss syndrome and Wegener's granulomatosis
   E) Henoch–Schönlein purpura and Kawasaki disease

- Data from national registries indicate that the most common vasculitides in children are HSP and Kawasaki disease (KD).[3]
- HSP is the most frequent vasculitis in most countries, with an incidence of 13–20 per 100,000 in patients younger than 17 years and a peak incidence of 70 per 100,000 in children aged 4–6 years.[3]
- The incidence of KD ranges from 3.7 to 239 per 100,000 in patients younger than 5 years, depending on the evaluated population. The incidence of KD is the highest in Japanese patients.

6- With regard to the treatment of HSP, it can be stated that:
   A) The early use of corticosteroids prevents kidney disease.
   B) Treatment is usually supportive.
   C) Treatment with intravenous gamma globulin should be early.
   D) Anti-inflammatory drugs and fish oil are the treatment of choice for abdominal pain.
   E) Immunosuppressants without corticosteroid therapy are indicated for nephritis.

HSP treatment is supportive.[1,3]

Patients with arthritis respond well to anti-inflammatory drugs. Corticosteroids are indicated for abdominal pain and severe cutaneous involvement.[3]

No studies to date have demonstrated that the early use of corticosteroids prevents kidney disease.[3]

The treatment for HSP nephritis and IgA nephropathy is the same and depends on the level of proteinuria and the glomerular filtration rate. In addition to supportive treatment, corticosteroid therapy, either alone or associated with immunosuppressants, is indicated.[7]

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