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Biermer's disease reveled by iron-deficiency anemia in a child: A case report and literature review

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ABSTRACT

We report the case of a 13-year-old girl with no particular medical history who presented with an anemic syndrome with weight stagnation associated with epigastralgia and transit disorders. The blood count confirmed the presence of a hypochromic microcytic anemia, and digestive exploration by oeso-gastroduodenal endoscopy revealed gastritis. The biopsy with an anatomo-pathological examination was in favor of a chronic atrophic gastritis in favor of Biermer's disease. The Helicobacter pylori test was negative. The immunological workup found a high level of anti-parietal cell antibodies confirming the diagnosis of Biermer's disease. Poorly described in children, Biermer's disease presents in our case a particular form due to the atypical clinical presentation different from the usual form described in the literature associating macrocytic anemia and vitamin B12 deficiency. Thus, Biermer's disease should be considered in the absence of a clear etiology for iron deficiency anemia.

Keywords: Biermer's disease, microcytic anemia, chronic gastritis, vitamin B12

INTRODUCTION

Biermer's disease is an autoimmune disease characterized by the presence of autoantibodies against parietal cells of the stomach and/or intrinsic factor inducing a deficiency in the latter leading to malabsorption of vitamin B12 or cobalamin [1,2]. This disease represents 20 to 50% of the etiologies of vitamin B12 deficiency in adults [3]. However, Biermer's disease remains rare in the pediatric population, only a few cases have been reported in the literature in pediatric patients [4-6]. The expressions of vitamin B12 deficiency are polymorphic and atypical, ranging from macrocytic anemia, hypersegmentation of neutrophils, neurological affection of the sensitive polyneuritis type to more advanced cases with marrow sclerosis and pancytopenia [7].

We report the case of a teenager who presented with a clinical picture of iron deficiency anemia that incidentally revealed a beginning Biermer's disease.

The study has been carried out in accordance with the Code of Ethics of the World Medical Association for experiments that involved humans. The aim of the study was clearly explained to the parents of the teenager and a written informed consent was obtained.

CASE PRESENTATION

Presenting concerns

A 13-year-old girl from eastern Algeria, with no particular pathological history, presented with chronic anemia (diagnosed since 2018) associated with asthenia, epigastralgia, transit disorders and weight loss. The clinical examination reveals a cutaneous-mucosal pallor and fragility of the phaneras.

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The questioning did not reveal any nutritional deficiencies or digestive or gynecological bleeding in this patient.

Clinical findings

The biological tests showed an aregenerative hypochromic microcytic anemia (hemoglobin: 7.5 g/dl, n: 11.1-14.7g/dl; mean corpuscular volume GMV: 67.1 fl, n: 75-95 fl; mean corpuscular hemoglobin concentration MCHC: 27.9 g/dl, n: 31-37 g/dl; reticulocytes: 51x10^3/mm^3, n: 80-120x10^3/mm^3), leukocyte and platelet levels are normal.

Hemoglobin (Hb) electrophoresis found a decrease in Hb A2 (1.8%, n: 2.2-3.2%), supplemented by a martial status test that came back in favor of an iron deficiency anemia (ferritinemia: 7 ng/ml, n: 8.8-184 ng/ml; serum iron: 0.12 mg/l, n: 0.4-1.5 mg/l).

A biological evaluation of the nutritional status (albuminemia: 38 g/l, n: 30-50 g/l; total protein: 77.44 g/l, n: 57-80 g/l), allowed to exclude an undernutrition at the origin of the iron deficiency anemia in this teenager.

The digestive signs associated with weight stagnation led us to perform an anti-transglutaminase antibody assay by ELISA, which was negative (anti-transglutaminase (tTG) IgG and IgA < 4 U/ml), and a weighted serum IgA assay also normal (serum IgA: 1.48 g/l, n: 0.58-3.58 g/l), eliminating celiac disease.

Diagnostic focus and assessment

An esophageal endoscopy with biopsy was also performed showing a congestive gastric mucosa and an oedematous duodenal mucosa, lined with a whitish staining in favor of bulbo-duodenitis.

The anatomical-pathological examination of the biopsy fragments was in favor of a chronic gastritis with moderate intensity and atrophy without signs of *Helicobacter pylori* (HP) infection, nor of metaplasia or dysplasia with the presence of two lymphoid clusters compatible with a Biermer disease (Fig. 1). In the duodenum, lymphocytic infiltration was estimated to be 10-20% locally.

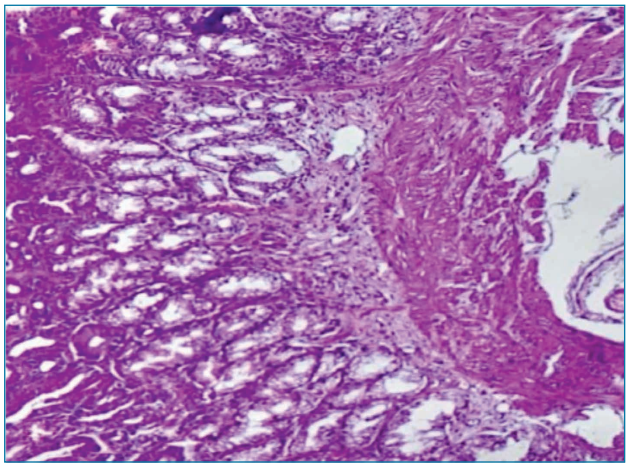

FIGURE 1. Chronic antral gastritis with moderate intensity and atrophy without signs of HP infection

The research of autoantibodies against gastric parietal cells came back strongly positive (equal to 1/80th) on triple substrate (liver, kidney and rat stomach). Nevertheless, the vitamin B12 dosage was normal with a serum level of 376 pg/ml.

The diagnosis of Biermer's disease in this adolescent girl was retained in view of the presence of anatomopathological criteria of chronic atrophic gastritis with lymphocytic inflammatory infiltrate and absence of HP infection. And criteria of autoimmunity marked by the presence of autoantibodies against gastric parietal cells.

Therapeutic focus and assessment

The management of our patient was based on iron supplementation and dietary education to correct the anemia.

Iron was prescribed in the form of ferrous iron (sodium feredetate), at a dose of 10 mg/kg/d, divided into three doses at mealtimes for 6 months. The parents and the child were informed of the potential side effects of the treatment, namely black stools, digestive disorders, headaches and dizziness.

This treatment is associated with a vitamin C supplementation of 500 mg twice a day in order to promote iron absorption.

Vitamin B12 supplementation is not indicated in our patient because serum levels remain normal; supplementation will be indicated as soon as hepatic reserves are exhausted.

Follow-up and monitoring

The response to treatment is rapid, with the occurrence of a reticulocyte crisis around D10.

The monitoring elements of our management are based on the appearance of the reticulocytic crisis between D8 and D10 of the iron-based treatment.

During the treatment period, monitoring by a blood count formula and a ferritin level allows to determine the effectiveness of the treatment, the progressive correction of the anemia was observed after 2 months of treatment, but it is the delayed normalization of the ferritin that allows putting an end to the treatment.

Concerning Biermer's disease, a clinical and biological monitoring of this patient in required with periodic measurements of vitamin B12, intrinsic factor, a blood count formula and annual endoscopy control's in order to follow the evolution of the disease and to control possible complications.

DISCUSSION

Biermer's disease is an autoimmune disorder characterized by atrophic gastritis which is responsible for a defect in the secretion of intrinsic factor by the gastric parietal cells leading to malabsorption of vitamin B12 which is the cause of the hematological manifestations [8]. Vitamin B12 or cobalamin is a hydrosoluble vitamin that plays an important role in hematopoiesis and the development of the nervous system [9]. It is provided exclusively by the food supply and is mainly found in animal products such as meat, fish, eggs and dairy products. In the duodenum and jejunum this vitamin is linked to the intrinsic factor produced by the fundus parietal cells and the body of the stomach, which also promotes the absorption of vitamin B12 in the terminal ileum [10].

Part of the vitamin B12 is stored in the liver (2 to 3 mg), these stocks allow to cover the needs in vitamin B12 during the deficits of contribution for a 2 to 4 years duration [11]. The hematological manifestations are classically characterized by an aregenative macrocytic anemia with medullary megaloblastosis, pancytopenia, morphological abnormalities of platelets, and neutrophilic polynuclei [12], however, these manifestations remain mostly atypical both clinically and biologically with a usually insidious beginning [13].

Biermer's disease manifests mainly in adults over 60 years of age [14], it remains rare in young people and children and is exceptional in infants [15]. Its main mechanism is based on the presence of autoantibodies against parietal cells leading to an alteration in the functioning of the cells responsible for acid secretion (alteration of the proton pump) and gastric atrophy leading to a deficit in the synthesis of intrinsic factor and to achlorhydria. These two consequences are the causes of vitamin B12 deficiency by malabsorption and iron deficiency because the latter requires gastric acidity to be converted into soluble ferrous iron that is easily absorbed by the intestinal mucosa. In the rare cases of Biermer's disease in the pediatric population reported in the literature, the clinical presentation of this pathology was atypical and in rare cases Biermer's disease presented with the usual forms of macrocytosis and neurological impairment. A female predominance has been found in children with this condition in the various cases reported in the literature [16].

Thus, Serraj et al. reported the case of a 15-year-old girl who presented a severe hematological disorde revealing a vitamin B12 deficiency with an acute hemolytic anemia associated with ascites; the clinical presentation associated a vitamin B12 deficiency, a hemolytic anemia, thrombocytopenia, fever and a renal failure giving the aspect of a thrombotic microangiopathy [6]. In another study, Cariou et al. reported the case of a five-month-old exclusively breastfed infant who presented a vitamin B12 deficiency associated with methylmalonic aciduria, as well as weight and psychomotor retardation; this vitamin deficiency was the consequence of an unrecognized maternal Biermer disease [4]. Biermer's disease in children can present in several clinical and biological forms, it can be normocytic or macrocytic, as well as isolated or associated with pancytopenia, as in the case reported by Amrani et al. in an adolescent girl where Biermer's disease was revealed by repeated epistaxis and a pronounced anaemic syndrome associated with a growth delay and digestive symptoms; The haemogram showed pancytopenia, severe hypochromic macrocytic anaemia and leuko-neutropenia with thrombocytopenia [17].

One of the complications of achlorhydria in Biermer's disease is martial deficiency; the association of Biermer's disease with iron deficiency anemia has been described in adults in several studies, but remains uncommon in children. The study by Zulfiqar et al. which found a martial deficiency in 29% of subjects with Biermer disease (42 subjects), this deficiency affected essentially young female subjects [18]. This association with a female predominance was also found in other studies, notably by Lagarde et al. and Marignani et al. [19,20].

Although presenting a disease of Biermer, our patient did not have a deficiency in vitamin B12 nor neurological signs, that can be explained by the early diagnosis of this disease and the persistence of stock of vitamin B12 still covering the needs of the organism.

CONCLUSIONS

Biermer's disease is a rare pathology in children and can present in many atypical forms. In the absence of a clear etiology, chronic iron deficiency anemia in children associated with digestive signs should require specialized investigations in order to detect a possible gastric disorder caused by a dysfunction of the parietal cells responsible for both Biermer's disease and a defect in iron absorption leading to associated iron deficiency anemia.

Biermer's disease is poorly described in pediatrics, in our study we noted microcytic iron deficiency anemia associated with atrophic gastritis, which is probably underdiagnosed in adolescent iron deficiency anemias. Thus, Biermer's disease should be considered in the absence of a clear etiology for iron deficiency anemia.

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