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Case Report

Wiskott Aldrich Syndrome: A First Case

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Abstract

Primary Immunodeficiencies are uncommon diseases revealed by early several infections. We made the diagnosis of our first Wiskott-Aldrich Syndrome case with several infections, eczema, microcytic thrombocytopenia, TCD4 and TCD8 lymphopenia, high level of IgA and IgG, mutation in exon 1 and duplication of cytosine in intron 2.

Keywords: *Wiskott Aldrich Syndrome; Cytosine; Intron 2*

Introduction

Primary Immunodeficiencies are uncommon diseases revealed by early several infections.

Case Presentation

An 8-month-old boy presented a severe and recurrent pruritic eczema producing ulcerated and hemorrhagic excoriations localized to the lower limbs, ankles, legs (Figure 1) and scalp (Figure 2). The skin was dry with hypo pigmented macules (Figure 3). All the ganglionic areas were free and there is no hepato-splenomegaly. His psychomotor development, weight and stature growth were normal. He had a history of hospitalization in the newborn, for neonatal infection, rectal bleeding and delayed umbilical cord healing. As an infant, he was hospitalized for pneumonia at 3 months and decapitated bacterial meningitis, with eczema, rhinitis and chronic diarrhea at 5 months. This boy is the only living child of a non-consanguineous couple. Two older siblings died of severe infections, eczema and bleeding, before two years of age. HIV test was negative. The CBC showed microcytic thrombocytopenia with moderate microcytic, hypochromic anemia. Lymphocytic immunophenotyping results showed lymphopenia with a slight increase of immunoglobulin (Table 1). Staphylococcus bacteria was isolated during bacteriological examinations. Molecular genetic studies showed a duplication of cytosine in the hemizygous state at intron 2: c.273 + 11dupC, referenced as a polymorphism with no effect on protein synthesis [2] and a hemizygous mutation at exon1: Exon1:c.37C>T(p.Arg13*) [3].

Discussion

Because of the physical examination and the medical history of this boy, we think about Wiskott-Aldrich syndrome. It is a rare immune deficiency that manifests by a classical triad combining recurrent and/or severe infections, eczema and microcytic thrombocytopenia [4].

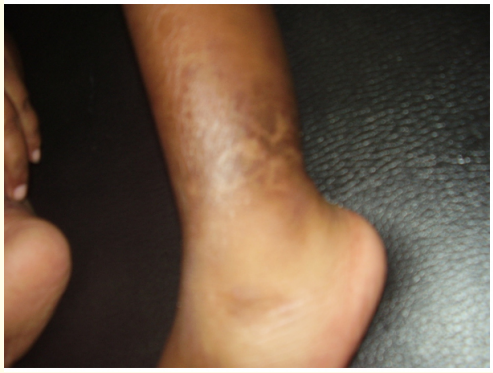

Figure 1: *Ulcerated and hemorrhagic excoriations in legs.*

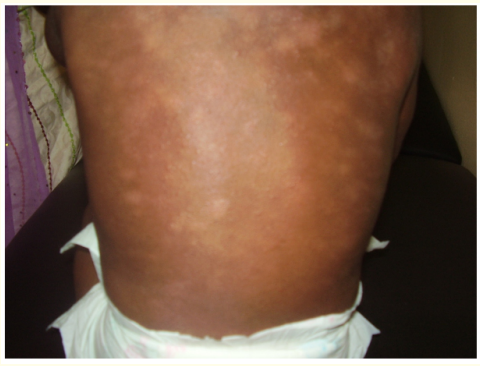

Figure 2: *Ulcerated and hemorrhagic excoriations in scalp.*

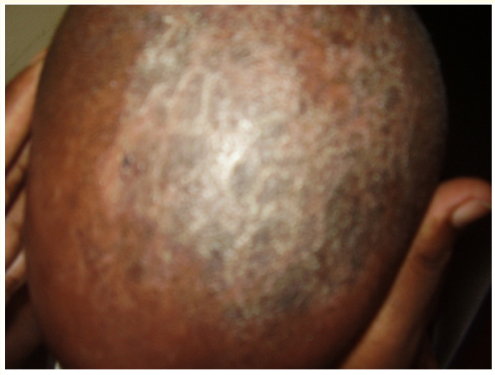

Figure 3: *Hypo pigmented skin macules.*

Exams	Results
CBC	Platelets count: 43,000/µL (43 x 10^9/L)
	Mean Platelet Volume (MPV): 5.47Fl
	Hemoglobin (Hb): 8.6 g/Dl
	Mean Corpuscular Volume (MCV): 59.4Fl
	Mean Corpuscular Hemoglobin (MCH): 18.8 pg/cell
Immunoglobulin	IgA: 1.68 g/l (1,680 mg/L)
	IgG: 10.55 g/l (10,550 mg/L)
	IgM: 1.25 g/l (1,250 mg/L)
Lymphocytes	Total Lymphocytes: 2,760/µL (2.760 x 10^9/L)
	TCD3: 2,213/µL (2.213 x 10^9/L)
	TCD4: 729/µL (0.729 x 10^9/L)
	TCD8: 295/µL (0.295 x 10^9/L)

Table 1: *Laboratory exams.*

It is a rare genetic disease, linked to the X chromosome (Xp11.22-23), with recessive gonosomal transmission. The diagnosis is confirmed by the presence of the WASP gene mutation which regulates the actin cytoskeleton [5].

Condition

This boy is the only living child of his mother. His Two older siblings died of severe infections, eczema and bleeding, before two years old. He presents early severe infection, since neonatal period. His CBC showed microcytic thrombocytopenia.

Diagnosis

The first symptoms of our patient appeared during the neonatal period, at two weeks of life with a neonatal infection, rectal bleeding and delayed umbilical cord healing. In fact, bacterial, viral or fungal infections may be early, recurrent, and sometimes particularly severe. HIV test was negative. The main causative bacteria are encapsulated since patients are unable to produce anti-polysaccharide antibodies. There is also an alteration of phagocytic functions and antigen presentation functions. The response to protein antigens is often inadequate. Eczema is one of the characteristic manifestations of the disease. It is described in 71% of patients in a large cohort of WAS [6] and may be mild or severe, transient or permanent with current dermatological investigations. In the most severe form, the persistence of eczema, its resistance to treatment and the pruritus-induced excoriations increase the risk of bacterial surinfections. Thrombocytopenia is usually microcytic in patients with WASP gene mutations, except in missense mutations [5]. The presence of micro platelets is considered pathognomonic [5]. In our patient, the Mean Platelet Volume (MPV) was 5.47fl.

T lymphocyte abnormalities and B lymphocyte functions are constant and present early in the classical form. In our patient, we found lymphopenia, predominant on CD4+ and CD8+ T lymphocytes an increase level of IgA and IgG. Although some authors reported decreased level of IgM and increased level of IgA and IgE [5]. According to other studies, serum levels of IgG are generally normal and IgM levels are moderately decreased, although they may all be normal or elevated. Antibody responses are sufficient for some antigens and insufficient for others [5].

Confirmation of the diagnosis requires demonstration of the WAS gene mutation by genomic sequencing. With paternal consent, our patient was tested and results showed a duplication of a hemizygous cytosine in intron 2, referenced as a polymorphism without effect of

the protein synthesis [2] and another hemizygous mutation in exon 1, referred as Wiskott Aldrich Syndrome in the literature [3]. Other mutations have been reported in the literature [7].

According to some authors, the lack of expression of the WASP is the cause of a severe phenotype, with the risk of premature death if treatment is not available [8].

Management

The patient received symptomatic treatments such as corticosteroids but unsuccessfully. He is receiving a treatment to ensure a better quality of life such as anti-infectious prophylaxis and symptomatic management of eczema and thrombocytopenia.

The curative treatment is bone marrow transplantation [9] or gene therapy [10], but there are unavailable. However, extracorporeal circulation is a new modality recently described [8].

Lessons for the clinician

- Recurrent eczema with early severe infections must be investigated;
- Microcytic thrombocytopenia is a biological uncommon symptom;
- The patients' history must be considered, even if there are death or similar cases;
- The diagnosis should be evocated while a child presents early severe infections, eczema and microcytic thrombocytopenia;
- This case is the first Wiskott-Aldrich Syndrome (WAS) confirmed in Senegal.

Conclusion

Wiskott Aldrich Syndrome should be considered if infections, eczema, microcytic thrombocytopenia.

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