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Original Research Paper

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COELIAC DISEASE AND FANCONI ANEMIA: RARE ASSOCIATION IN PEDIATRIC AGE GROUP

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ABSTRACT

Introduction: The association of coeliac disease (CD) and aplastic anemia (AA) had been rarely described specially in pediatric group. This is the fifth report in the literature to date that suggests an association of AA with CD in the pediatric population.

Case presentation: We report first case in Marrakesh, of a 11-year-old girl, followed for celiac disease since the age of 2 years. She was under a gluten free diet. She presented a persistent anemia, which revealed Fanconi disease with presence of chromosomal abnormalities on the karyotype. After a while, bone marrow aspiration showed acute myeloid leukemia type 0. Chemotherapy was done according to the AML-MA-2011 protocol. The patient died by overwhelming hemorrhagic syndrome after induction II.

Discussion- Conclusion: All four pediatric cases reported with this potential association are from South East Asia but our case is the first from Africa. This association may be more frequent than previously. More studies are needed on this particular association, which has been largely under- estimated until now.

KEYWORDS : child; coeliac disease; fanconi disease; leukemia

INTRODUCTION

Celiac disease (CD), an autoimmune disease once thought to be uncommon, is now being increasingly identified, as an immunemediated disorder elicited by gluten and related prolamines in genetically susceptible individuals 1]. Many hematological manifestations, mostly due to nutritional deficiencies, have been associated with CD [2]. Anemia remains the most common hematological manifestation in childhood CD 3 due to many mechanisms, and can be the sole presenting symptom. Both aplastic anemia and celiac disease have a similar underlying autoimmune process but an association between the two is seldom reported. There have only been four pediatric cases reporting this association and this case is the first reported in Moroccan pediatric patient.

We report the fifth case of CD and aplastic anemia a rare association in pediatric age group

CASE PRESENTATION

A 11 years old female child, born out of consanguineous marriage, with history of CD diagnosed at age of two revealed by malabsorption syndrome characterized by diarrhea, steatorrhea, weight loss, and failure to thrive. Both duodenal biopsy and tissue transglutaminase antibodies confirmed diagnosis. Free gluten diet was not respected.

After lost of follow up, patient presented at age of 7 with intense palor, and diffuses petechiae. CBC showed pancytopenia (hemoglobin 6,7 g/dl, platelet count of 29 × 109/L, mean corpuscular volume (MCV) and mean corpuscular hemoglobin (MCH) of 100 fl and 34 pg, respectively with no atypical cells, total leucocyte count of 2 109/l, absolute neutrophils count of 0,4 109/l). Bone marrow aspiration and bone marrow biopsy showed dysmeilopoeisis and hypoplasia; the patient was transferred to pediatric hematology. Assessment of hypoplasia showed hypersensitivity to chromosomal breakage induced by mitomycin C (MMC) and no other congenital abnormalities were found. The little girl was transfusion-dependent for years.

At age of 11, she was admitted for pallor, abdominal pain. Physical exam showed: splenomegaly, lumb oedema and petechial. Laboratory investigation revealed a hemoglobin of 63 g/L, total leucocyte count of 30 ×109/L, platelet count of 6×109/L and MCV of 83 fl. Blood smear showed presence of blasts cells. Bone marrow aspiration confirms the diagnosis of leukemia and immunophenotypic analysis concluded on myeloid leukemia type 0. Patient was in bad performance status with total protein at 5.1 g/l and albumin of 1.9 g/l. So, treatment was reporting until nutrition conditioning. Chemotherapy was done according to Moroccan protocol (AML-MA- 11) but patient died after Induction II because of sever hemorrhagic syndroma.

DISCUSSION

Celiac disease is a frequent cause of hematologic disorders. Anemia and hyposplenism may be the most common hematologic complications [2]. There are some case reports of anaemia with severe thrombocytopenia [3], and pancytopenia in CD. Cause of pancytopenia in CD is multifactorial. Severe deficiency of Iron, folic acid, vitamin B12, and other nutriments can lead to pancytopenia. Leucopenia may be due to deficiency of folate and copper whereas thrombocytopenia may be autoimmune in nature. CD is associated with other organ- specific autoimmune disorders.

Very few cases of association of CD with AA have been reported worldwide. First three cases of CD associated with AA were reported by Grey-Davies and al. [4]. Mahishewari and al reported the first pediatric case report, which suggests an association of CD with aplastic anemia in children, in 2012 [5]. Until today, total of 12 cases with CD–AA association have been reported in the literature, out of which four are pediatric cases. In three of these four pediatric cases, both diseases were diagnosed simultaneously [5-7]. In one case AA is developed after a previous diagnosis of CD [8]. In our case, diagnosis of CD was made before AA. All the adults cases reported were female while 1 of the four pediatric cases were female [7;9]. We report the second female case in the pediatric population. All four pediatric cases reported are from India or Pakistan in where the incidence of CD is very high [10]. Our case is the first one reported from Africa and in whom the etiology of AA is being related to Fanconi.

The link between AA and CD is still unclear, but these two diseases share an underlying immune pathological mechanism, with auto-reactive T-cells mediating tissue- specific destruction. CD is a unique autoimmune disorder in which the environmental precipitant, gluten, is involved and it may involve many organs in body including bone marrow. On the other hand, micronutrient deficiency in CD like iron, folic acid, vitamin B12, copper and others, as a result of malabsorption, may be instrumental in bone marrow hypoplasia [5;7].

In our case, association between Fanconi anemia and CD might be explained by a genetic disorder that is not identified yet.

Gluten free diet, micronutrient supplement along with immunosuppressant therapy like cyclosporine and glucocorticoid may help recovery of bone marrow in AA–CD association, particularly in economically poor patients in developing countries who cannot afford bone marrow transplantation or Anti-Thymoglobine therapy. A gluten-free diet decreases the exposure to antigenic stimuli that lead to bone marrow suppression and reverts the process [5]. Cyclosporin therapy in AA may also modulate the course of CD, particularly in typical symptomatic gastrointestinal cases [11]. There is a report of stabilization of CD in a pediatric patient after allogeneic hematopoietic stem cell transplantation [12] which further strengthens our decision to advise transplantation. It is likely that bone marrow transplant was the cure.

For our patient unfortunately she developed an acute myeloid leukemia (AML) which are not easy to manage because the sensitivity to DNA-damaging agents limits the therapy they can tolerate. The chemotherapy suggested for this patient is sequential [13,14]. Overall, Allogeneic hematopoietic stem cell transplantation is the only definitive treatment of Fanconi patients with AML, and currently offers a 30% to 40% long-term overall survival rate [15].

CONCLUSION

This is the first case report suggesting an association between celiac disease and Fanconi anemia in the pediatric population. An association between CD and AA is now well described, especially in adult patient. We urge clinicians as they search Fanconi anemia in AA, to be vigilant for signs of CD in child with AA.

Conflict of interest

The authors declare that there is no conflict of interest regarding the publication of this paper.

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