Chédiak-Higashi Syndrome: Case Report of Three Patients in an Iraqi Family in Tikrit City

Ahmed H. Al-anee and Ashoor R. Sarhat

Department of pediatric, Tikrit College of Medicine, University of Tikrit, Tikrit, Iraq

Abstract

Chediak-Higashi syndrome is a rare, inherited, multisystem disorder affecting the immune system, pigmentation, and neurologic functions, and characterized by recurrent infections, giant cytoplasmic granules, and oculocutaneous albinism. Here a case report of three patients in an Iraqi family treated in pediatric ward in Tikrit teaching hospital, Tikrit city. Three patients had oculocutaneous albinism, recurrent infections and giant cytoplasmic granules in the leukocytes. They are members of a poor consanguineous parents. They have different presentation regarding the onset, the clinical signs, and the subsequent coarse of the illness. Tow patients died of infectious complications during the accelerated phase and the other girl is still in the resting phase. Therapy included ascorbic acid and antibiotics. Chemotherapy was used for the accelerated phase in two patients. Early diagnosis and therapy of CHS is needed. Bone marrow transplantation should be indicated before the accelerated phase of the disease has developed.

Keywords: Chédiak-Higashi Syndrome, recurrent infections, and immnunodeficency.

Introduction

Chédiak-Higashi syndrome (CHS) is a rare childhood autosomal recessive disorder that affects multiple systems of the body[1]. CHS patients exhibit hypopigmentation of the skin, eyes, and hair; prolonged bleeding times; easy bruisability; recurrent infections; abnormal natural killer cell function; and peripheral neuropathy[2]. Onset in early childhood mostly leads to lymphohistiocytic infiltration into multiple organs and is presented with partial oculocutaneous albinism, recurrent bacterial infections and the development of an accelerated lymphocyte and macrophage activation syndrome in approximately 85% of patients, which is usually fatal[3,4], and death occur before age of 10 years[5]. The diagnosis is established by finding of large inclusions in all nucleated blood cells and this can be seen on wright-stained blood films and accentuated by peroxidase stain[6]. Specific therapy included ascorbic acid, antibiotics and cytostatic agents during the accelerated phase. Bone marrow transplantation was proposed, depending on clinical conditions and donor availability[7]. Morbidity results from patients succumbing to frequent bacterial infections or to an accelerated-phase lymphoproliferation into the major organs of the body. Most patients who do not undergo bone marrow transplantation die of a lymphoproliferative syndrome, although some patients with CHS have a relatively milder clinical course of the disease[8].

Case report

A. A. is a four- year-old female child of a poor family, present with history of recurrent chest infection during the last 3 yaers, and associated with failure to thrive and progressive pallor. Examination shows a girl with blue eyes and fair hair. Her weight and height are below 3rd percentile. Chest examination reveald scattered cripitations. Abdominal exam reveald only splenomegaly two centimeters below the left costal margin. The family had four other children two of them were affected and died because of CHS. The 1st one was a boy who presented at age of 8 months with fair hair, and blue eyes and poor feeding and diagnosed as CHS. The baby died four months after diagnosis. The second, was a female with same appearance of the affected boy but it is noticed by the family shortly after birth as shown in table 1. The baby is diagnosed as CHS after clinical assessment and blood film. This baby continue on conservative treatment with vitamin C, prednisone orally with heavy antibiotics during any sever illness. At the age of five years this child passed into a accelerated phase, with high fever, generalized lymphadenopathy, and hepatosplenomegaly and the patient died few months after that because of sever chest infection and sever nasal bleeding. The other two child in the family looks normal. The first one is a female 7 years age and new female baby 2 months age with black hair and eyes till now.

Discussion

CHS is a very rare disease internationally, and affects all races[9]. This poor family have three affected children (one boy and two girls) out of five children for this consanguineous marriage. This can be explained by that Familial consanguinity has been observed in 50% of the cases described in the literature[8]. All patients presented with phenotypic features of oculocutaneous albinism, including grey hair color. Recurrent infections were observed in all patients, with predominance of respiratory tract infections, and the clinical symptoms were easily controlled with antibiotics[7]. These infections became more frequent closer to the accelerated phase and, according to Bejaoui et al, they are associated with fever in this phase[10].

The diagnosis was established according to the following criteria: family history or consanguinity, occurrence of recurrent infections, partial albinism and detection of giant intracytoplasmic granules in leukocytes[7]. So the diagnosis of our cases was made by both complete blood picture which shows giant granules in the affected neutrophils and eosinophils and bome marrow examination which shows giant inclusion bodies in the leukocyte precursors.

The clinical presentation of the disease usually appears at birth or shortly after birth (the baby might be born with normal appearance and then develop later the appearance of blue eyes and fair hair)[13]. Different clinical presentations occur in these patients, the first affected boy was normal at birth and then start to develop the clinical picture of the disease, while the other two affected girls have clinical appearance of the disease at birth. Even these two girls have some degree of darkening of their fair color of hair and eyes with time as noticed by the family. The notification of the family about some degree of darkening in the color of their children hair color (the two girl) can be explained by the fact that there is some degree of improvement in the granular function with time as noticed by some articles[14]. The bleeding time was prolnged in the three patients. These findings are typical findings in patient with Chediak-Higashi syndrome[11]. Before the accelerated phase, specific antibiotics control the infection without prolonged administration, as observed in non-immunodeficient patients, but in contrast to what occurs in patients with phagocyte disorders such as chronic granulomatous disease and severe neutropenia[12].

Although our last two patients have some degree of developmental delay in regard to speech , hearing, vision ,and gross motor as compared with their peers, the brain MRI of both was normal. This finding dose not go with the typical finding in patient with CHS in which it shows diffuse brain atrophy[15]. This might be due to that this developemental delay may be due to the repeated infection with multiple admission and poor feeding which may leads to nutritional deficiency of major nutrients and vitamins (for gross motor delay) and repeated otitis media because of immune defeciency (for delay in hearing ans speech) and for photophobia and vitamin deficiency (for delay in vision) [15,16].

The clinical course of the three patients were typical with partial oculocutaneous albinism, recurrent bacterial skin and chest infection with attacks of bleeding nose or upper GIT bleeding followed by prolifrative phase with hepatosplenomegaly and lymphadenopathy (seen only in the 2nd affected baby)[13]. This due to the fact that the first affected boy died at early life because of repeated infections and dose not reach to the prolifrative phase, and the last girl is still in the resting phase although she is now 5 years age the age at which the first girl was died because of the prolifrative phase which explain the difference in the clinical coarse and severity between the three affected patients.

The patients treated with the classical supportive treatment of CHS with oral vitamin C (which correct the micrtubular defect invetro) [2] and antibiotic and antiviral treatment for repeated infections[11] in addition to the help of surgeon and dental therapist for associated surgical (like skin and perianal abscess in the last two girls) and dental problems (as dental cares in the last affected girl). Bone marrow transplant which is the only solution to the disesease[15]. Genetic counseling was done regarding education the family about the disease and the recurrence risk in the subsequent pregnancy.

Clinical featuers	Case 1	Case 2	Case 3
Sex	Male	Female	Female
Age of onset	8 months	Birth	Birth
Time of death	12 months	5 years	Still alive
FTT	Yes	Yes	Yes
Pallor	Yes	Yes	Yes
Spleen	Yes	Yes	Yes
Liver	Yes	Yes	No
Bleeding	Yes	Yes	No
Resp. infections	Yes	Yes	No
OM	Yes	Yes	Yes
Skin infection	Yes	Yes	Yes
UTI	No	No	No
Other infections	Yes	Yes	Yes
Speech delay	No	Yes	Yes
hearing	No	Yes	Yes
Visual	No	No	Yes
Gross motor	No	Yes	Yes
Skin abscess	Yes	Yes	No
Perineal abscess	No	Yes	Yes
Mouth ulceration	Yes	Yes	Yes
Dental caries	No	No	Yes
partial oculocutaneous albinism	Yes	Yes	Yes
Accelerated phase	No	Yes	No

Table 1: Clinical featuers of three chediak-higashi syndrome patients.

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متلازمة تشيدياق–هيغاشي، تقرير حالة لثلاثة مرضى من عائلة عراقية في مدينة تكريت

احمد العاني و عاشور رفعت سرحت

فرع طب الأطفال ، كلية الطب ، جامعة تكريت ، تكريت ، العراق

الخلاصة

متلازمة تشيدياق– هيغاشي هي اعتلال نادر، متوارث، يصيب أجهزة جسمية متعددة، الجهاز المناعي، الاصطباغ، الوظائف العصبية، ويتميز بالالتهابات المتكررة، حُبَيبات السائل الخلوي العملاقة، برص الجلد والعينين. وهذا تقرير حالة لثلاثة مرضى من عائلة عراقية. عولجوا في مستشفى تكريت التعليمي في مدينة تكريت.المرضى الثلاثة كان لديهم التهابات متكررة، حُبَيبات السائل الخلوي العملاقة في كريات الدم البيضاء، برص الجلد والعينين. وهم من عائلة فقيرة من أبوين قريبين. كانت عندهم اختلافات في تجليات المرض والعلامات السريرية والمساق اللاحق للمرض. توفي اثنان منهم بسبب المضاعفات الانتانية خلال المرحلة المعجلة والبنت الأخرى لازالت في المرحلة الساكنة. تَضمّنَ العلاجُ حامضَ أسكوربيك ومضادات حيوية. العلاج الكيمياوي إستعملَ للمرحلةِ المُعَجَّلةِ في مريضين. وهناك حاجة للتشخيص والعلاج المبكّر. زرع نُخاعِ العظم يَجِبُ أَنْ يُشارَ إليه قبل تطوّرْ المرض إلى المرحلةِ المُعَجَّلةِ .

لكلمات الدليلية: متلازمة تشيدياق– هيغاشي، تقرير حالة لثلاثة مرضى من عائلة عراقية.