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A child with Chediak-Higashi syndrome-A case study

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Abstract

Master "A", 7 years old male child with a rare genetic disorder called Chediak-Higashi syndrome is presented here. The child was initially diagnosed to have Chediak-Higashi syndrome with Hemophagocytic lymphohistiocytosis(HLH). The child was on treatment since 2010. Recently in 2016, the child was admitted with febrile neutropenia, pseudomonas septicemia, pneumonia, marked edema and deep jaundice. He received treatment with Tazocin and was discharged in a good condition. After one week, the child was readmitted with hyperthermia, poor oral intake and respiratory distress. In the evening he was noticed to have encephalopathy with staring gaze and lapses of disorientation and frequent nystagmus. The child also developed septic shock and multi organ failure. The child progressed into severe hypotension with blood pressure 58/26 mm Hg, heart rate 40 beats/ minute and saturation 82% on 15 Liters' of O_2 via non-rebreathing mask, and developed asystole. Death was confirmed by fixed and dilated pupils, no pulse and no heart beats.

Keywords: Chediak-Higashi syndrome, Genetic disorder, Children.

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Introduction

Chediak-Higashi Syndrome (CHS) is a very rare autosomal recessive disorder that affects multiple systems of the body in childhood. Patients with CHS presents with hypopigmentation of the eyes, skin, hair, easy bruisability, prolonged bleeding time, recurrent infection, abnormal natural killer cell function, and peripheral neuropathy. The patients develop frequent bacterial infections in the major organs of the body. CHS was first described by Dr. Beguez-Cesar in 1943. He identified neutropenia and abnormal granules in leukocytes in three children. Chédiak, a hematologist of Cuba reported another case in 1952. Higashi, a Japanese pediatrician, described a series of cases in 1954 [1-3]**.**

The Chediak-Higashi syndrome gene was identified in 1996 as the LYST or CHS1 gene and is localized to bands 1q42-43. The CHS protein is seen in the cytoplasm of cells of a variety of tissues and represented an abnormality of organellar protein trafficking [4]**.** CHS is rare, with less than 500 cases described and published worldwide over the last 20 years [5,6]. CHS affects all races. It is suggested by Al-Khenaizan that CHS may be underreported in persons of darker-skinned races [7]**.** The symptoms of CHS usually appear soon after birth or in children younger than 5 years. The mean age of onset is 5.85 years; however, most patients die before the age of 10 years [3].

Specific therapy includes ascorbic acid, antibiotics and cytostatic agents during the accelerated phase. Bone marrow transplantation is proposed, depending on clinical conditions and donor availability [9]. 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 [10].

CHS syndrome leads to early death from infection or hemorrhage. Intractable respiratory and cutaneous infections usually prove fatal before a child with CHS reaches age 10 years. Longer survival is possible, but the lymph nodes, spleen, and liver become enlarged and a malignant lymphoma develops. A few patients have survived to age 20 years [3].

The most important measures to prevent routine infections include education of the child and caregivers regarding effective hygiene and careful attention to oral and dental care. Skin protection and sunglasses should be used to prevent sunburn and to protect sensitive eyes from ultraviolet light. The live vaccines are contraindicated in these children [8].

Case Report

Master "A", 7 years old, one of the twin male children**,** born to parents who had consanguineous marriage was admitted in Sultan Qaboos University Hospital in 2010. He presented with multiple massive cervical lymphadenopathies, hepatosplenomegaly, and retroperitoneal lymph nodes enlargement with sepsis, seizures and otitis media. On assessment, the abdomen was soft, non-tender with hepatosplenomegaly 6 cm each, hypo pigmented skin with blond hair and spiking high temperature. The child also had complaints of recurrent episodes of right ear discharge which was sticky, copious and foul smelling for 1 year. The septic work up and ferritin, triglycerides, coagulation profile, TORCH and Epstein Barr serology was done. The results were positive for Epstein Barr infection. The child was initially diagnosed to have Chediak-Higashi syndrome with Hemophagocytic lymphohistiocytosis (HLH). The child was treated with steroids, chemotherapy, anti-epileptics and antibiotics.

The child continued to get admitted in the hospital in 2011, 2012, 2013, and 2014. The reasons for repeated admission were seizures, otitis media, febrile neutropenia, sepsis, bronchiectasis, and spikes of temperature. The child was treated with HLH protocol, antibiotics and antiepileptic medications.

The child was referred for bone marrow transplantation in Sultanate of Oman. Matched donors were unavailable for the child to have bone marrow transplantation. Hence bone marrow transplantation was not done for the child. Another twin of the child died at the age of 4 years with Chediak-Higashi syndrome. The cause for the death of the child was sepsis.

In the beginning of 2015, the child was admitted and treated for chronic otitis media with recurrent infections with pseudomonas aeruginosa, bronchopneumonia and severe peripheral neuropathy. The child was pale, had continuous spikes of temperature, nystagmus, marked hepatosplenomegaly, and pitting edema.

In the end of 2015, the child was again admitted and treated for febrile neutropenia and pneumonia. The child developed anemia, deep jaundice and hepatosplenomegaly, deranged Liver Function Test, and coagulopathy.

In the beginning of 2016, the child was admitted with 2 days history of persistent fever, poor oral intake and lethargy. On admission, the child was sick, highly febrile, more markedly jaundiced with multiple wasem scars (steel or an iron rod about the size of a pencil heated until red and then pressed into the flesh for two-to-three seconds at the appropriate place for healing on the patient's body) and respiratory distress. On examination, bronchial breathing was found over the right infra-scapular area, crepitus over the right base with reduced air entry, 8 cm palpable spleen, palpable 10 cm liver, reduced Hb of 6.4, and increased Bilirubin of 492 mg/dL. The child was treated with antibiotics.

The child's condition deteriorated and the child was sicker with persistent high spikes of fever and respiratory distress. The child was prepared for palliative care since curative treatment was unavailable. The DNR code status was discussed with the parents and approved with treating physician.

In the evening, the child was noticed to have encephalopathy with staring gaze and lapses of disorientation and frequent nystagmus. Father was counselled about the terminal status of the child. The assessment showed high urea and creatinine 14 mg/dl & 52 mg/dl respectively. The child also had severe metabolic acidosis with hypokalemia, hyperphosphatemia, hypocalcemia, increasing conjugated hyperbilirubinemia, deranged LFT, severe thrombocytopenia with drop of platelet count, and deranged coagulation.

The impression was that the child was going into liver failure and renal impairment with gram negative septicemia. Pediatric nephrology, gastroenterology and endocrine teams were involved to give their expert input for treating the child's condition. The child received a bolus of KCL over 4 h and planned to give HCO_3 correction over the next 4 h. However, the child suddenly deteriorated at around 2:40 am and started bleeding from cannula site. He had progressively dropping heart rate and B.P along with gasping. The child was started a bolus of N/S 20 ml/kg. The child progressed into severe hypotension with B.P, 58/26 mmHg, HR 40 beats/ minute and saturation 82% on 15 L of O_2 via non-rebreathing mask. Then he developed asystole. Death was confirmed by fixed and dilated pupils, no pulse and no heart beat sounds. The child was declared dead at 03:08 am. The immediate cause of death was Septic shock with multi organ failure.

Discussion

Chédiak-Higashi syndrome is a rare autosomal recessive disorder that arises from a mutation of a lysosomal trafficking regulator protein, which leads to a decrease in phagocytosis [11,12]. The decrease in phagocytosis results in recurrent pyogenic infections, albinism and peripheral neuropathy. The child presented in this case analysis also had recurrent episodes of infection which is the result of decrease in phagocytosis.

Chédiak-Higashi syndrome is rare, with fewer than 500 cases published worldwide over the last 20 years [5,6]. CHS is the fifth reported case in Sultanate of Oman. Chédiak-Higashi syndrome (CHS) affects all races [7].

The affected child was an Omani. Symptoms of Chédiak-Higashi syndrome (CHS) usually appear soon after birth or in children younger than 5 years. The mean age of onset is 5.85 years; however, most patients die before age 10 years [3]. This child developed symptoms soon after birth. The twin brother of this child also died of the same condition.

Patients with CHS exhibit hypopigmentation of the skin, eyes, and hair; prolonged bleeding times; easy bruisability; recurrent infections; abnormal natural killer cell function; and peripheral neuropathy [1-3]. Master "A"'s skin was hypo pigmented and pale, hair was blond and the child also had complaints of severe peripheral neuropathy. The child had febrile neutropenia with spikes of temperature. Recurrent infections were noticed in the child in the form of multiple cervical lymphadenopathies, retroperitoneal lymph nodes enlargement with sepsis, otitis media, positive Epstein Bar infection, and infections with pseudomonas aeruginosa. As mentioned in the literature that patients with CHS will have prolonged bleeding times and easy bruisability, Master. "A" had severe thrombocytopenia with drop in platelet count and deranged coagulation.

Most patients undergo an accelerated phase, which is a nonmalignant lymphohistiocytic lymphomalike infiltration of multiple organs that occurs in more than 80% of patients. This lymphoma like stage is precipitated by viruses, particularly by infection by the Epstein-Barr virus [3]. The case reported here also had accelerated infiltration which is diagnosed as Hemophagocytic lymphohistiocytosis (HLH). The child also had cervical lymphadenopathies, hepatosplenomegaly and retro peritoneal lymph nodes enlargement with sepsis. The child was positive for Epstein-Barr virus infection.

It is associated with anemia, bleeding episodes, and overwhelming infections leading to death. Infections most commonly involve the skin, the lungs, and the respiratory tract and are usually due to Staphylococcus aureus, Streptococcus pyogenes, and Pneumococcus species [4]. Master. "A" reported to have anemia, deranged coagulation and recurrent infections. The child suffered with infections of lungs in two different occasions with bronchiectasis and bronchopneumonia. The cause of death in this child was septic shock with multi organ failure as rightly said in the literature.

Most patients who do not undergo bone marrow transplantation die of a lymphoproliferative syndrome [1-3]. The child was referred for bone marrow transplantation. However, the child could not have bone marrow transplantation as the child could not get matched donors.

The disease is often fatal in childhood as a result of infection or an accelerated lymphomalike phase; therefore, few patients live to adulthood. In these patients, a progressive neurologic dysfunction may be the dominant feature [4]. Approximately 50-85% of patients develop a fatal accelerated phase, namely hemophagocytic lymphohistiocytosis (HLH), characterized by pancytopenia, high fever, hemophagocytosis, and marked infiltration of organs by lymphocytes, leading to multiorgan dysfunction [3]. As cited in the afore mentioned references, the child died at the age of 7 years. The child could not have a transition to the adulthood as his condition was deteriorating with sepsis, neurological dysfunction and multi organ failure and finally to death.

Recommendations

The nursing measures to prevent routine infections include education of the child and caregivers regarding effective hygiene and meticulous attention to oral and dental care. Skin protection and sunglasses should be used to prevent sunburn and to protect sensitive eyes from ultraviolet light. While these patients can safely receive all killed or inactivated vaccines, live vaccines are contraindicated.

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