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Sickle Cell Thalassemia: A Case Report and Review of Literature

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Author's contribution

The sole author designed, analyzed and interpreted and prepared the manuscript.

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Case Study

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ABSTRACT

Sickle cell disease is a single gene disorder causing a debilitating systemic syndrome characterized by chronic anaemia, acute painful episodes, organ infarction and chronic organ damage and by a significant reduction in life expectancy. Combined sickle cell beta thalassemia disease is the most common form of sickle cell disease in people of Mediterranean descent, including people of Italian, Greek or Turkish heritage. We experienced a three years old girl who was admitted with bronchopneumonia and found to have anaemia which was proved to be sickle cell thalassemia.
Conclusion: Sickle cell disease should be considered in pneumonic child with severe anemia.

Keywords: Sickle; cell; thalassemia; anaemia; hemoglobin S; vaso-occlusion; sickling; globin; mutation; inheritance; crisis; pulmonary; reticulocyte.

ABBREVIATIONS

HSCT: Hemopoietic stem cell transplant; Hb-S: Hemoglobin S; RBC: Red blood cells; SCA: Sickle cell anaemia; SCD: Sickle cell disease.

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1. INTRODUCTION

Sickle cell disease (SCD) is an autosomal recessive disorder of red blood cells (RBC) in which RBC contains hemoglobin S (Hb-S). The basic problem of Hb-S is that in deoxygenated state RBC become deformed and rigid taking the crescent or sickle shape (sickling phenomenon) which decreases the cell's flexibility and consequently exposing the patient to the risk of vaso-occlusive complications [1]. The severity of the disease varies because the beta thalassemia gene may still produce a small amount of normal hemoglobin. Vasoocclusive phenomena and hemolytic anemia are the clinical hallmarks of SCD. Vasoocclusion results in recurrent painful episodes and a variety of serious complications that can lead to life-long disabilities and even death.

2. CASE SUMMARY

A 3 years old Kuwaiti girl 4th issue of her non consanguineous parents, was admitted on 1st March 2015 with 10 days history of fever and cough not responded to oral antibiotic. There was no history of bone aches, abdominal pain, weight loss or previous hospital admission. She was fully vaccinated with normal perinatal and developmental history. On further inquiry, her mother told that there is a positive family history of thalassemia trait.

On examination the girl was looking lethargic, pale, febrile, temperature was 38.5℃, Respiratory rate 36 breaths/minute, Pulse 110 /minute, BP 95 /60, Her weight and height were on 25th Centile. There was no bleeding, bone aches or lymphadenopathy. Her systemic examination was unremarkable with no hepatosplenomegaly.

Laboratory investigations showed hemoglobin 5.6 gm/dl, MCV 54, Reticulocytic count 2.16%, Total leucocytic count 16.9x10^{9}/L and platelets 401x109/L. Septic work up was positive with C-reactive protein was 135 mg/L, erythrocyte sedimentation rate was 98 mm/hr and blood culture was positive for Streptococcus pneumonia. Peripheral blood film revealed microcytic hypochromic anaemia with neutrophilic leucocytosis. Renal function and liver function tests were normal. Sickling test was positive and coombs' test was negative. Hemoglobin electrophoresis revealed HbA2: 5%, HbS: 67% and HbF 28%. Chest X ray showed right sided pneumonia. The patient received filtered packed RBCs once and intravenous antibiotic for seven days and discharged in a good general condition and normal hemoglobin with further follow up.

3. DISCUSSION

Sickle cell disease (SCD) and its variants are genetic disorders result from the presence of a mutated hemoglobin, HbS. It is an autosomal recessive disorder which was first described by Herrick in 1910. SCD causes significant morbidity and mortality. Morbidity, frequency of crisis, degree of anemia, and the organ systems involved vary considerably from person to person [2].

HbS results from substitution of amino acid valine for glutamic as the 6th amino acid of the beta-globin chain, which produces a hemoglobin tetramer (alpha2/betaS2) that is poorly soluble if deoxygenated [3].

In SCD, the production of HbS causes pathophysiological consequences. The commonest form (>70% of SCD worldwide) [4] results from homozygous inheritance of the β^{S}-mutation and is known as either 'SCD SS' or as 'sickle cell anaemia' (SCA). SCD can also result from the inheritance of β^{S} in combination with a wide range of other HBB mutations, the two most common being a second structural β-globin variant β^{C} (SCD SC) and one of many β-thalassaemia mutations that leads to decreased production of normal β-globin (SCD S/β-thalassaemia) [4].

The world health organization estimates that 2.3% of people are carrier of SCD. Many countries have an unknown distribution of carriers because their populations include different ethnic groups due to migration [5]. Hb electrophoresis can differentiate Sickle Cell Syndromes [6].

Sickle cell-beta thalassemia is divided into sickle cell-beta^{0} thalassemia and sickle cell-beta^{+} thalassemia, based on complete absence of beta globin or presence of reduced amounts of beta globin, respectively, which in turn determines the level of HbA [3]. The percentage of HbA produced in individuals with beta^{+} thalassemia ranges from 5 to 30 percent, depending on the molecular defect of the mutation [3]. The clinical and hematologic severity of sickle cell-beta thalassemia is an inverse function of HbA quantity [7]. Patients with

sickle cell-beta^{o} thalassemia (ie, no HbA production) have a clinical course as severe as homozygous SCD; ie, HbSS, sickle cell anemia [7].

The clinical features of SCD are defined by chronic anaemia, sepsis, haemolysis and recurrent acute vaso-occlusive crises. The last feature is characterized by pain and a systemic inflammatory response that may be severe, episodic and unpredictable. Some of the most common features of SCD along with descriptions of current management are summarized in Table 1.

Acute chest syndrome is the second most common cause of hospitalization and is characterized by intrapulmonary ischaemia and infarction, systemic hypoxia and pulmonary infiltrates on chest X ray as seen in our case [4]. Community-acquired pneumonias and fat embolism from bone marrow necrosis have been implicated in its pathogenesis. In a recent study, 50% of paediatric and adolescent patients with SCD had acute pulmonary events during a median follow-up of 21 months [4].

The diagnosis of SCD relies on the analysis of haemoglobin, most commonly using either protein electrophoresis or high performance liquid chromatography. Subjects with the most common form of SCD, SCD SS, produce no HbA, but predominantly produce HbS with variable amounts of haemoglobin F (HbF) and haemoglobin A2 (HbA2), while those with SCD SC produce mainly HbS and HbC. DNA-based methods are commonly used to confirm the diagnosis of SCD in complicated cases [4]. Peripheral blood film for target cells with elongated and characteristic sickle erythrocytes. Other investigations may be needed e.g urinalysis, Renal function tests, Blood gases analysis, secretory phospholipase A2 (predictor for acute chest syndrome), X ray chest and long bones, MRI for affected bones (to differentiate osteomyelitis from bone infarction), US abdomen (spleen, gall bladder, kidney), Echocardiography for pulmonary hypertension may be done [2].

The treatment of SCD aims to control the symptoms and treatment of complications. It includes management of vaso-occlusive crisis (hydration and blood transfusion), chronic hemolytic anaemia (blood transfusion, iron chelating agents, folic acid, vitamins), chronic pain (NSAID, Morphia, Amitryptyline), prevention and treatment of infections (pneumococcal, Hib & meningococcal vaccine, Penicillin prophylaxis, antibiotic mainly Macrolides and 3rd generation cephalosporin) [2,8]. Hydroxyurea 10-15 mg/kg/day increases HbF and thus reducing the frequency of vaso-occlusive crisis. Prevention of organ damage by preventing tissue ischemia (blood transfusion, Aspirin) and treatment of pulmonary hypertension with Sildenafil may be needed [9].

Transfusion therapy is mainly reserved for specific indications such as stroke risk reduction, renal failure or recurrent painful crises that are not responsing to treatment with hydroxycarbamide. Allogeneic haemopoietic stem cell transplant (HSCT) is the only curative treatment for SCD and is successful in 85%–90% of patients [4]. The Eligibility criteria for HSCT for SCD includes the availability of a fully HLA-matched sibling donor, Sickle cell disease (SCD-SS or SCD-Sβ0-thalassemia) and if complicated with Stroke or CNS event lasting longer than 24 hours, Recurrent ACS (at least 2 episodes in the last 2 years, Recurrent severe debilitating vaso-occlusive crisis (three or more severe pain events per year for the past 2 years), Sickle nephropathy or avascular necrosis of multiple joints [6].

Table 1. Common clinical presentations of SCD

Problem	Presenting symptoms	Management
Vaso-occlusive pain	fever, erythema, swelling and focal bone pain	Analgesia, Fluid.
Acute chest syndrome	fever, chest pain, tachypnea, cough, hypoxemia and wheezing	Antibiotic, oxygen, fluid, transfusion.
Stroke	- Focal motor deficits (e.g., hemiparesis, gait dysfunction) - Speech defects - Altered mental status	Transfusion.
Splenic sequestration	Rapid onset of pallor and fatigue. Abdominal pain is often present	Fluid, Transfusion.

(*Summarized from Lanzkowsky (2011) [6] Manual of pediatric hematology and oncology)*

Gene therapy is still in development and aims to abrogate SCD-related symptoms by manipulation of haemopoietic stem cells, either by viral vector-mediated insertion of a functional β globin gene or by gene-editing techniques aiming at reducing intracellular sickling by increasing production of HbF [4].

In France, a Phase I/II clinical trial of gene therapy for SCD and thalassemia with lentiviral vectors is in its early phases, but no reports have been published [10]. Prognosis is variable and life expectancy is usually shortened to 42 years for males and 48 years for females [2].

4. CONCLUSION

Peripheral blood film should be checked and sickle cell disease should be kept in mind in any child with pneumonia and severe anemia.

CONSENT

It is not applicable.

ETHICAL APPROVAL

It is not applicable.

COMPETING INTERESTS

Author has declared that no competing interests exist.

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