(International Print/Online Journal)

SJIF IMPACT FACTOR: 5.565
PUBMED-National Library of Medicine ID-101739732

ISSN (Print): 2209-2870
ISSN (Online): 2209-2862

International Journal of Medical Science and Current Research (IJMSCR)
Available online at: www.ijmscr.com
Volume 6, Issue 2 , Page No: 548-551
March-April 2023

IJMSCR

Compound Heterozygosity Of Hemoglobin-S And Hemoglobin-D With Bone Crisis – Case Report

[1]Dr. Neelayadakshi.B, [2]Dr. Shobini Vishali V M*; [3]Dr. Yogalakshmi.E; [4]Dr. Padma Priya.B.S; [5]Dr. Nithin Diwagar

[1,2]Postgraduate-MD, [3,4]Tutor, [5]Assistant Professor,
Department of Pathology,
Saveetha Medical College, Thandalam, Chennai – 602105, Tamil Nadu, India

***Corresponding Author:**
Dr. Shobini Vishali V M
Saveetha Medical College, Thandalam, Chennai – 602105, Tamil Nadu, India

Type of Publication: Case Report
Conflicts of Interest: Nil

Abstract

Hemoglobin disorders affect over 330,000 newborn infants annually, and account for nearly 3.4% of deaths in children less than 5 years of age, and poses as a significant health problem worldwide.[1,2] Hemoglobinopathies include a diverse spectrum of inherited disorders of hemoglobin synthesis, ranging from thalassemia syndromes (quantitative defects) to structurally abnormal hemoglobin variants (qualitative defects).[3,4] Sickle cell disease (SCD) and hemoglobin-D hemoglobinopathy are inherited blood disorders. Patients with compound heterozygosity for hemoglobin-D (Hb-D) and hemoglobin-S(Hb-S) have a variable clinical course and it is difficult to differentiate these patients from those with homozygous SCD.[1] Only few cases of co-inheritance of structural hemoglobin variants like Hb-S, Hb-D, Hb-E have been described in the Indian population.[5] High performance liquid chromatography(HPLC) is an useful tool for the early identification of these disorders.[3]Here we present a case of 11 years old girl who presented to the pediatric department with history of pain and swelling and restriction of movement in the left hand and wrist since 1 month. She had complaints of fever for 1 day and no history of any prior trauma to the left hand. She had history of recurrent hospitalizations for bone pains, since she was about 8 years old. HPLC was done and she was diagnosed as a case of compound heterozygous for SCD and hemoglobinopathy-D. MRI left wrist showed early osteomyelitis with surrounding cellulitis changes in the wrist. We present this case due to its rare presentation- Compound heterozygosity of hemoglobin-S and hemoglobin-D, presenting as severe hemoglobinopathy with bone crisis.

Keywords: Bone crisis, Compound heterozygosity of Hb-S and Hb-D, Hemoglobinopathies, HPLC

Introduction

A Sickle cell disease (SCD) and hemoglobinopathy-D are inherited disorders of hemoglobin synthesis.[6]Hemoglobin-D occurs due to a mutation in codon 121, of the beta globin gene, thus leading to substitution of glutamic acid to glycine.[5] Sickle cell disease is a heterogeneous disorder that occurs due to a single point mutation in the sixth codon of the beta globin gene, which leads on to the substitution of glutamic acid to valine, thus leading to the formation of sickle hemoglobin.[5] As a result of this, the normally biconcave, pliable red blood cells assumes a sickle shape, which is rigid. Due to their shape, these erythrocytes can get trapped in small slow flowing vessels, leading to vaso-occlusion. The prevalence of sickle cell disease in India is approximately 2-34%, and the prevalence of hemoglobin-D in the Indo-Pak subcontinent is around 0.86%, which is relatively low.[5,6] In the heterozygous state, Hb-D is

hematologically silent, but when associated with other hemoglobinopathies like Hb-S, it can lead to a severe phenotype. Hence the detection of carriers is of extreme importance. We present this case due to its rare presentation - Compound heterozygosity of hemoglobin-S (Hb-S) and hemoglobin-D (Hb-D), presenting as severe hemoglobinopathy necessitating recurrent hospitalizations and now presenting with bone crisis.

Case Report:

A 11years old girl presented to the paediatric department with history of left hand and wrist swelling and pain since about 1 month, associated with restriction of movement in her left wrist. She had complaints of fever for 1 day and no history of any prior trauma to the left hand. Patient also had a history of recurrent hospitalizations for bone pains, since she was about 8 years old. HPLC was done and she was diagnosed as a case of compound heterozygous for SCD and hemoglobinopathy-D. USG abdomen showed splenomegaly. X-RAY of both wrists [Figure 1] was done and MRI left wrist was done - showed early osteomyelitis with surrounding cellulitis changes in the wrist.

Patients Hb was 11.3g/dl, RDW- 19.5%, platelet- 2.32 lakhs/cu mm, TC- 5,340, DC- N- 58.2% L- 32.4% M- 4.3% E-4.9% B- 0.2%, Retic count- 1.8%, CRP- 24.5, PT- 12.8, INR- 1.11, APTT- 35.3. Peripheral smear showed sickle cells. Wound swab showed no growth, sickling test done (with Sodium Metabisulphite method) was positive [Figure 2]. HPLC test was done, which showed features suggestive of compound heterozygous for HbS and HbD (S window- 28.3% and unknown- 42.2%), HbF- 19.6%, HbA2- 1.1%. Patient was taken up for surgery. Bone culture sent from the operation theatre also showed no growth.

Figure 1- X-RAY both wrists

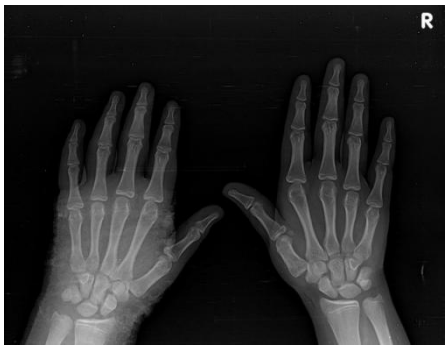
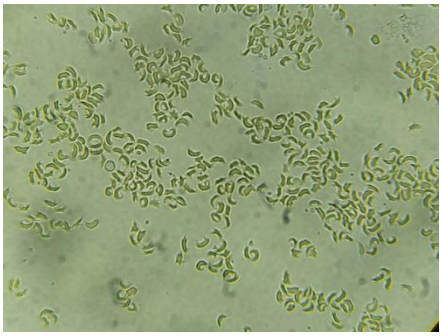


Figure 2- Sickling test positive



Discussion:

Hemoglobinopathies are a group of inherited disorders with diverse presentations ranging from thalassemia syndromes to hemoglobin variants with abnormal structure.[3,6] They usually occur due to single gene disorders leading to abnormalities in hemoglobin production and function.[6] It is extremely important to identify these disorders from an epidemiological point of view, for the prevention

Volume 6, Issue 2; March-April 2023; Page No 548-551

of more serious hemoglobin disorders.[3] Sickle cell disease (SCD) is the most common hemoglobinopathy that is seen globally.[6] Under conditions of low oxygen tension, the abnormal Hb-S in SCD undergoes polymerization leading to the formation of fragile sickle shaped cells. This in turn leads to hemolytic anemia and vaso-occlusion of blood vessels.[6]

Hemoglobin D is usually hematologically silent when present in the heterozygous state.[7] Sickle cell trait is also generally benign since the concentration of Hb-A is more than 50% in these patients, which in turn prevents the polymerization of the remaining Hb-S under physiologic conditions.[8] However, when it is associated with other hemoglobinopathies as a compound heterozygous, it can lead to a severe clinical phenotype, the most serious of these being hemoglobin-S.[7] Hemoglobin-D in heterozygous state may combine with hemoglobin-S, which can manifest as moderate to severe (HbSD) hemoglobinopathy as seen with our case.[6,7] HPLC aids in the rapid and accurate detection of hemoglobinopathies and its variants, and hence serves as an useful tool for the early detection and management of hemoglobinopathies and its complications.[3]

The most common complication in patients with sickle cell disease, which requires hospital admission includes vaso-occlusive crises and osteomyelitis.[9]

Declaration Of Patient Consent

The authors certify that they have obtained all appropriate patient consent forms. They have given their written informed consent for publication .

References:

1. Al-Barazanchi ZA, Abdulateef SS, Hassan MK, Jaber RZ. Double heterozygosity for hemoglobin S and D Punjab in Basra, Iraq: A clinical and hematological study of 42 patients. Journal of Applied Hematology. 2019 Oct 1;10(4):134.
2. Modell B, Darlison M. Global epidemiology of haemoglobin disorders and derived service indicators. Bulletin of the World Health Organization. 2008 Jun;86(6):480-7.
3. Sachdev R, Dam AR, Tyagi G. Detection of Hb variants and hemoglobinopathies in Indian population using HPLC: report of 2600 cases. Indian journal of pathology and microbiology. 2010 Jan 1;53(1):57.
4. Kutlar F. Diagnostic approach to hemoglobinopathies. Hemoglobin. 2007 Jan 1;31(2):243-50.
5. Italia K, Upadhye D, Dabke P, Kangane H, Colaco S, Sawant P, Nadkarni A, Gorakshakar A, Jain D, Italia Y, Ghosh K. Clinical and hematological presentation among Indian patients with common hemoglobin variants. Clinica Chimica Acta. 2014 Apr 20;431:46-51.
6. Rohilla M, Malhotra P, Das R, Jain V, Prasad GR, Kalra J. Compound Heterozygous Hemoglobin SD Disease Presenting As Sickle Cell Crisis in Pregnancy. Journal of Woman's Reproductive Health. 2016 May 17;1(2):25.

Vaso-occlusive crisis can occur in any organ, but it commonly involves the bone, in which case, the patient presents with intense bone pain localized to one or more areas of their skeleton, as seen in our case.[9] MRI is a very sensitive imaging technique for detecting bone involvement.[9] However, MRI is not helpful in distinguishing between infarction/infection and infarction/increased marrow haemopoiesis in sickle cell disease.[9]

Sickle cell patients also have increased susceptibility to infections- osteomyelitis.[9] Salmonella being the most common cause of osteomyelitis in patients with SCD, followed by staphylococcus aureus and gram-negative enteric bacilli.[9,10] However, in our case, bone culture showed no growth.

Conclusion:

In our case study patient had developed bone crises due to her inherited disorder - Compound heterozygous of hemoglobin-S (Hb-S) and hemoglobin-D (Hb-D), presenting as severe hemoglobinopathy. If the diagnosis of compound heterozygosity of hemoglobin-S (Hb-S) and hemoglobin-D (Hb-D) is missed, it results in long lasting functional sequalae. So early identification, creating awareness, and educating the maternal and paternal blood relatives of patients with hemoglobinopathy for screening, molecular analysis, genetic counselling is necessary, so as to stop the disease before it passes on to the next generation.

Volume 6, Issue 2; March-April 2023; Page No 548-551

7. Aslan D. Is hemoglobin D trait hematologically silent: comparison with healthy controls and β-thalassemia carriers. Journal of Pediatric Hematology/Oncology. 2020 Oct 26;42(7):e698-701.
8. Witkowska HE, Lubin BH, Beuzard Y, Baruchel S, Esseltine DW, Vichinsky EP, Kleman KM, Bardakdjian-Michau J, Pinkoski L, Cahn S, Roitman E. Sickle cell disease in a patient with sickle cell trait and compound heterozygosity for hemoglobin S and hemoglobin Quebec–Chori. New England Journal of Medicine. 1991 Oct 17;325(16):1150-4.
9. Almeida A, Roberts I. Bone involvement in sickle cell disease. British journal of haematology. 2005 May;129(4):482-90.
10. Bennett OM, Namnyak SS. Bone and joint manifestations of sickle cell anaemia. The Journal of bone and joint surgery. British volume. 1990 May;72(3):494-9.

Volume 6, Issue 2; March-April 2023; Page No 548-551