Scholars Journal of Medical Case Reports
Abbreviated Key Title: Sch J Med Case Rep
ISSN 2347-9507 (Print) | ISSN 2347-6559 (Online)
Journal homepage: https://saspublishers.com

OPEN ACCESS

Internal Medicine

A Silent Hemoglobinopathy Revealed by Diffuse Osteosclerosis and Pseudo-Thrombotic Microangiopathy: Sickle Cell Disease

M. Zaizaa[1*], F. Ahallat[1], M. Biat[1], I. El Kassimi[1], N. Bahadi[1], S. Nawal[1], J. Khalil[1], A. Tahiri[1], Z. El Bougrini[1], O. Jamal, B. Talamoussa[1], A. Rkiouak[1], Y. Sekkach[1]

[1]Department of Internal Medicine A, Mohamed V Military Instruction Hospital, Rabat, Morocco

DOI: https://doi.org/10.36347/sjmcr.2025.v13i08.007 | **Received:** 03.06.2025 | **Accepted:** 25.07.2025 | **Published:** 06.08.2025

***Corresponding author:** M. Zaizaa
Department of Internal Medicine A, Mohamed V Military Instruction Hospital, Rabat, Morocco

Abstract **Case Report**

We report the case of a 50-year-old female patient, with no family history of sickle cell disease, presenting with an anemic syndrome associated with back pain. Biological and morphological examinations revealed a pseudo-thrombotic microangiopathy and diffuse osteosclerotic osteopathy. The diagnosis of composite heterozygous sickle cell disease S/C was confirmed by hemoglobin electrophoresis. This case highlights an atypical clinical presentation of sickle cell disease, emphasizing the importance of a thorough differential diagnosis.

Keywords: Sickle cell disease, Atypical presentation, Compound heterozygosity S/C, Thrombotic microangiopathy, Osteosclerotic osteopathy.

INTRODUCTION

Sickle cell disease is a common hemoglobinopathy characterized by the presence of hemoglobin S, which can present in different genetic forms. Diagnosis may be delayed in compound heterozygous forms, particularly S/C, due to sometimes atypical clinical manifestations. We report a clinical case illustrating this diagnostic difficulty.

CASE REPORT

We describe the case of a 50-year-old Moroccan patient, with no family history, who presented to the emergency department with abdominal pain accompanied by major asthenia and persistent spinal pain.

Upon arrival, the patient was hemodynamically stable and breathing normally. The Physical examination revealed a generalized pallor as well as a discreet subictery of the conjunctiva. Abdominal palpation revealed moderate splenomegaly, approximately two fingerbreadths in extent, without hepatomegaly. No other significant clinical signs were observed.

The initial biological assessment showed a bicytopenia, associating normochromic normocyte anemia with a regenerative response (Hb at 7 g/dL, VGM at 88 fL, reticulocytes at 175 000/mm 3), as well as a notable thrombopenia at 58 000/mm 3. Biological parameters indicated active haemolysis: marked elevation of lactate dehydrogenases (1100 U/L), moderate hyperbilirubinemia (total bilirubin at 18 µmol/L) and a fall in haptoglobin. The examination of the blood smear revealed the presence of schizocytes at 1.9%. The direct Coombs test was negative, and the viral serologies were all negative. The phosphocalcic assessment, as well as the electrophoresis of serum proteins with determination of urinary and serum light chains, were within the standards. The medullary cytological examination showed a rich bone marrow, without plasma-cell infiltration or morphological abnormalities.

Radiologically, the computed tomography confirmed the presence of splenomegaly (18.5 cm) and highlighted diffuse osteocondensation affecting the entire axial and peripheral skeleton. There were also biconcave settlements at the level of the lumbar vertebrae, initially suggesting a hematological process. In addition to the dorsolombarian MRI, we noted a heterogeneous medullary infiltration at hyposignal T1.

Bone mineral densitometry found a Z-score greater than +2.1 at the level of the spine and femur(figure1), thus confirming osteosclerosis. The PET scan detected bone deformities at the humerus, a rachis presenting a sinuous appearance with heterogeneous

fixation, as well as an asymmetry in the femoral head fixation (figure 2), without revealing suspected sign of malignancy.

Hemoglobin electrophoresis (figure 3) identified a heterozygous S/C composite hemoglobinopathy, confirmed by two successive analyses, leading to the diagnosis of heterozygous sickle cell disease.

After ruling out common causes of osteosclerosis, the diagnosis was that of a thrombotic pseudomicroangiopathy associated with diffuse osteocondensing osteopathy, secondary to S/C sickle cell disease.

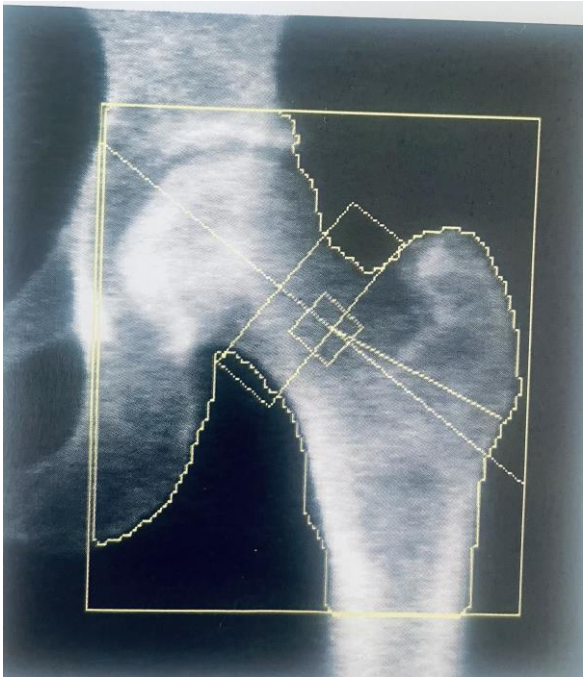

Fig. 1: Bone densitometry with increase in bone mineral density

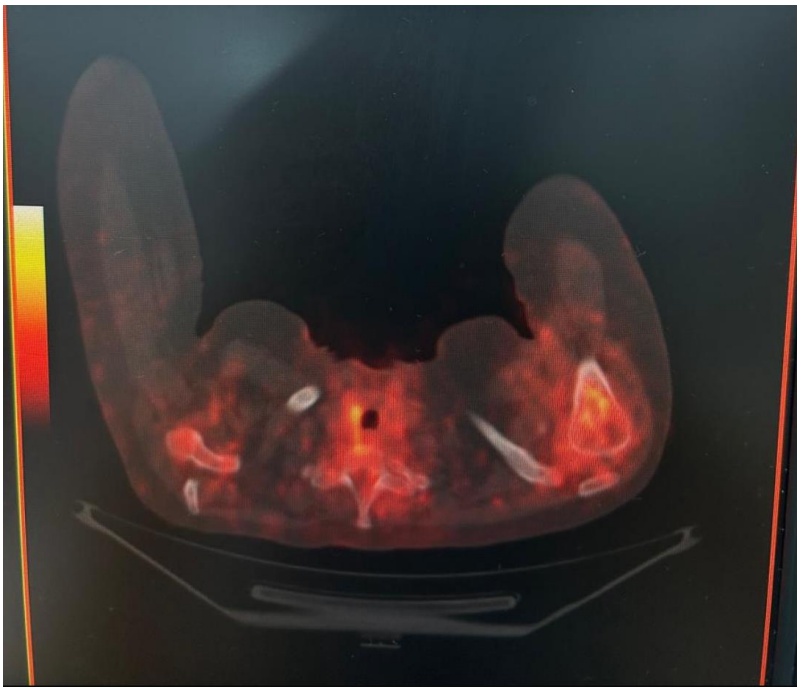

Fig. 2: axial section of the TEP scan au18-DFG showing intense focal hyperfixation at the level of the iliac bone

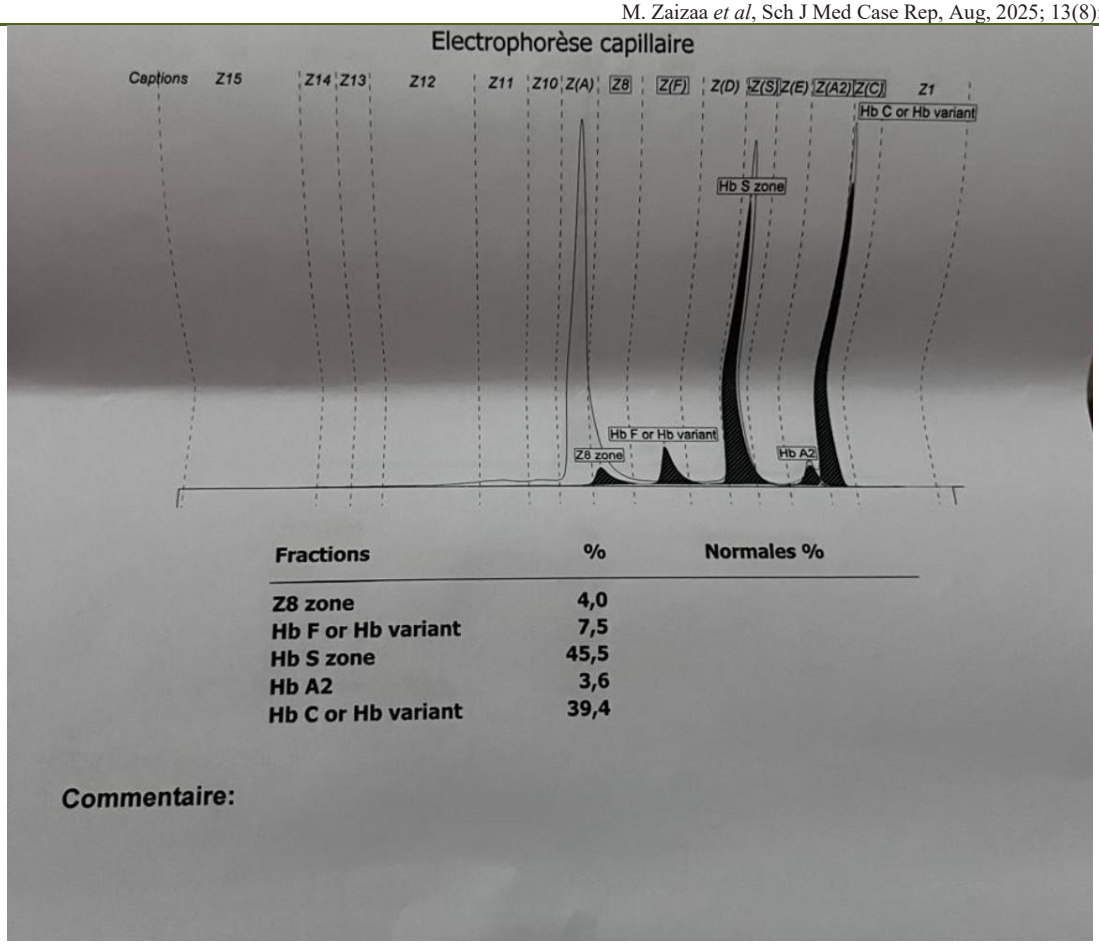

Fig. 3: Hemoglobin electrophoresis: Sickle disease

DISCUSSION

Sickle cell disease is an autosomal recessive hemoglobinopathy characterized by the presence of abnormal hemoglobin S, which causes sickle-shaped deformation of red blood cells, including their flexibility, leading to chronic hemolysis as well as vaso-occlusive phenomena [1]. The S/C form, less frequent than the homozygous SS form, usually presents a more moderate clinical picture, but can nevertheless be accompanied by serious complications, as illustrated by our observation.

Our patient presented with a thrombotic pseudo- microangiopathy (pseudo-TMA), characterized by microangiopathic hemolytic anemia with the presence of schistocytes, thrombocytopenia and signs of biological hemolysis, but without other classic criteria of typical microangiopathic hemolytic syndrome. This clinical picture is rare in Sickle cell disease but has been described in the literature as an"atypical microangiopathic hemolysis syndrome" or pseudo-TMA [2,3]. Pseudo-MAT in sickle cell disease results mainly from the increased fragility of sickle cell red blood cells subjected to mechanical and oxidative stress, as well as chronic intravascular hemolysis exacerbated by vaso-occlusive phenomena. The latter lead to local and systemic endothelial activation, thus mimicking a thrombotic microangiopathy picture [4]. The distinction between pseudo-TMA and true TMA is essential because treatments diverge: plasmapheresis, for example, which is the key to treatment in thrombotic thrombocytopenic purpura [5] has no place in pseudo-TMA linked to sickle cell disease.

Bone complications are among the most frequent and disabling manifestations of sickle cell disease. They are generally linked to repeated of bone tissue ischemia secondary to vaso-occlusive phenomena [6]. Our case illustrates an uncommon form of diffuse osteocondensing osteopathy, characterized by extensive osteosclerosis in the axial and peripheral skeleton.

The pathophysiology of osteosclerosis in sickle cell disease is multifactorial: bone marrow hyperplasia in response to chronic anemia can lead to an increase in local bone density, while repetitive bone infarcts lead to anarchic bone repair and an increase in trabecular density. [7]

Osteosclerosis may also reflect impaired bone remodeling induced by disease-related pro-inflammatory cytokines and oxidative stress [8]. Radiologically, diffuse osteosclerosis can be confused with malignant (myelofibrosis, metastases, lymphoma) or infectious pathologies (osteomyelities) [9]. In our case, the use of advanced imaging tests (CT, MRI, PET scan) as well as

a bone biopsy made it possible to eliminate these diagnoses, confirming a sickle cell etiology.

Early diagnosis allows for adapting treatment, particularly by avoiding unnecessary or potentially dangerous treatments, including surgery, which should be avoided due to an increased risk of perioperative complications [10]. And by implementing specific strategies such as pain management associated with functional rehabilitation methods, appropriate transfusions, and the use of hydroxyurea [11].

This case highlights the importance of a rigorous diagnostic approach in the face of an atypical presentation of thrombotic microangiopathy associated with diffuse bone abnormalities. The absence of a family history of sickle cell disease should not exclude the diagnosis, particularly in geographical areas with a high prevalence of the disease or in patients from at-risk populations [12]. Hemoglobin electrophoresis is a key tool to confirm the diagnosis.

CONCLUSION

Our observation illustrates an atypical and rare form of S/C sickle cell disease revealed by a picture of thrombotic pseudo-microangiopathy and diffuse osteocondensing osteopathy. It enriches the literature on the clinical diversity of the disease and underlines the need for increased clinical and diagnostic vigilance, in order to improve patient management and prognosis.

REFERENCES

1. Connes P, Renoux C, Joly P, Abi Nader El . Vascular pathophysiology of sickle cell disease.Presse médicale 2023 ;52 (4) :104202. doi.org/10.1016/j.lpm.2023.104202
2. Chatterjee T, Uba A, Toth PP. Pseudo-thrombotic microangiopathy in sickle cell disease: pathophysiology and clinical implications. Hematology. 2018;23(7):435-441.
3. Sahu KK, Siddiqui AD, Cerny J. Hemolytic anemia with features of thrombotic microangiopathy in sickle cell disease: a diagnostic challenge. Blood Cells Mol Dis. 2020;85:102447.
4. Kato GJ, Steinberg MH, Gladwin MT. Intravascular hemolysis and the pathophysiology of sickle cell disease. J Clin Invest. 2017;127(3):750-760.
5. Moake JL. Thrombotic microangiopathies. N Engl J Med. 2002;347(8):589-600.
6. Hernigou P et al. Manifestations ostéo-articulaires de la drépanocytose. Gazeta Médica da Bahia 2010;80(3):74-9.
7. Bolarinwa RA, Eze JC, Bakare AA. Skeletal manifestations of sickle cell disease: a review. Afr Health Sci. 2016;16(3):731-740.
8. P.Giordano , F. Urbano, G. Lassandro, M. Felicia . Mechanisms of Bone Impairment in Sickle Bone Disease. Int. J. Environ. Res. Public Health 2021, 18, 1832 .doi.org/10.3390/ijerph18041832
9. F. cloran, K. Banks. *AJR* Teaching File: Diffuse Osteosclerosis with Hepatosplenomegaly. AJR Am J Roentgenol, 2007,188(3) :18-20 doi: 10.2214/AJR.05.2141.
10. Rudy HL et al. Review of sickle cell disease and spinal pathology. Global Spine J 2019;9(7):761-6.
11. Ware RE, de Montalembert M, Tshilolo L, Abboud MR. Sickle cell disease. Lancet. 2017;390(10091):311-323.
12. Gene Reviews Editorial Team. Sickle Cell Disease. In: Adam MP, Mirzaa GM, pagon RA et al : university of washington, Seattle ,1993-2025 chapter: Diagnosis and Clinical Management. April 4, 2025