OLGU SUNUMU **CASE REPORT**

LEG ULCER, PULMONARY HYPERTENSION AND SILENT CEREBRAL INFARCT IN TWO PATIENTS WITH SICKLE CELL DISEASE

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ABSTRACT

Sickle cell disease is an inherited hemoglobinopathy and polymerization of deoxygenated HbS lead to clinical manifestations of the disease. The stroke rate in sickle cell disease patients with silent cerebral infarct is 14-fold higher than in those with normal MRI. We present two patients of sickle cell disease with leg ulcer, pulmonary hypertension and silent cerebral infarct and the only symptom was the leg ulcer.
Key Words: Sickle cell disease, leg ulcer, silent cerebral infarct, pulmonary hypertension

ORAK HÜCRE HASTALIĞI OLAN İKİ HASTADA BACAK ÜLSERİ, PULMONER HİPERTANSİYON VE SESSİZ SEREBRAL İNFARKT

Orak hücre hastalığı kalıtsal bir hemoglobinopatidir ve deoksijene olan HbS'in polimerizasyonu hastalığın klinik bulgularına neden olur. Sessiz serebral infarktı olan orak hücre hastalarında, beyin MR bulguları normal olan hastalara göre inme riski 14 kat daha fazladır. Bacak ülseri, pulmoner hipertansiyon ve sessiz serebral infarktı olan ve tek semptomun bacak ülseri olduğu orak hücre hastalığı olan iki hastayı sunmaktayız.
Anahtar Kelimeler: Orak hücre hastalığı, bacak ülseri, sessiz serebral infarkt, pulmoner hipertansiyon

INTRODUCTION

Sickle cell disease (SCD), is an inherited blood disease and the gene for sickle hemoglobin (HbS) results in the substitution of valine for glutamic acid normally present at the sixth position from the amino terminus of the β chain of hemoglobin (1). This change allows HbS to polymerize when deoxygenated, since valine can dock with complementary sites on adjacent globin chains.

The polymerization of deoxygenated HbS is the primary indispensable event in the molecular pathogenesis of SCD and lead to clinical manifestations of the disease (2).

We report here two cases of SCD with leg ulcer, silent cerebral infarct (SCI) and pulmonary hypertension (PH) that the only symptom was leg ulcer.

CASE REPORT 1

An 18-year-old male presented with a 1-year history of an ulcer on his right leg. Three years ago, the patient has experienced an ulcer on his left leg. The patient had 6 siblings and none of them had similar disease. His parents were second degree relatives. There was no history of blood transfusion or pain crises in his personal and family history.

Physical examination revealed an ulcer in 7x6 cm in diameter on the right pretibial area (Fig 1). A scar was also present in 3 cm in diameter on his left lower leg.

Neurological examination was normal. There was no history of seizure. Magnetic Resonance Image (MRI) revealed three cerebral infarctions localized in caput caudat nucleus in 1x1 cm, parietal lobe in 4x1.5 cm and frontal lobe in 3x1 cm in diameter (Fig 2).

Electrocardiogram was normal. Transthoracic echocardiography revealed an enlarged left atrium of 40 mm (normal 24-38 mm), left ventricular end-diastolic diameter of 57 mm (normal 46 mm +/- 4), left ventricular end-systolic diameter of 35 mm (normal 30 mm +/- 4), right ventricular diastolic diameter of 34 mm (normal 11-25 mm) and normal left ventricular systolic function. Pulmonary arterial systolic pressure was estimated as 48 mmHg using tricuspid regurgitation jet.

Hemoglobin electrophoresis revealed homozygous sickle cell anemia. Laboratory tests revealed a hemoglobin 7.2g/dl, hematocrit of 19.4%, white blood cell count of 14.5x10^3/µL, platelet count of 568x10^3/µL.

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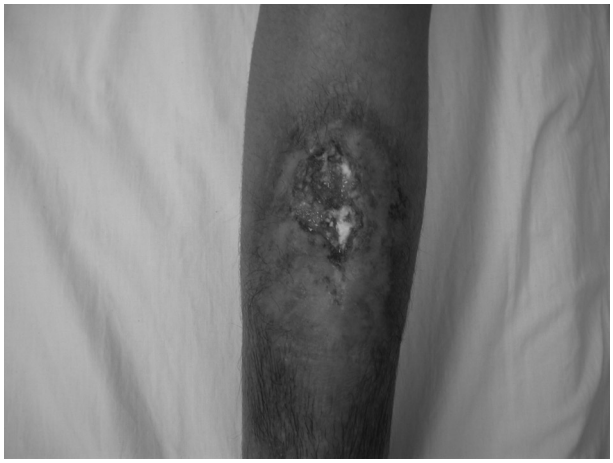

Figure 1- Leg ulceration over the right anterior tibia.

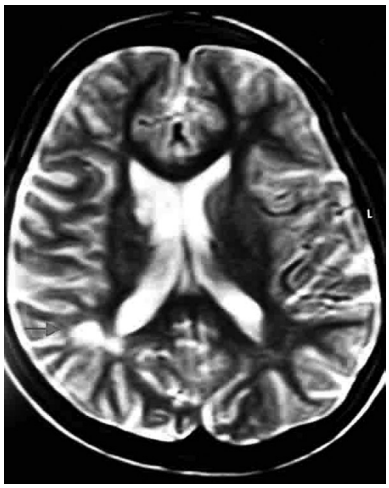

Figure 2- T2-weighted axial MRI showing a hyperintense lesion in right parietal lobe.

CASE REPORT 2

A 30-year-old woman presented with a one month history of a painful ulcer. She has had recurrent leg ulcer history up to 4 years ago. Hydroxyurea therapy has been started 4 years ago and the ulceration has not been recurred until one month ago. Her brother (26 years old) has also SCD; but there was no history of leg ulcer. Her parents were second degree relatives.

On physical examination, there was an ulcer covered with crust on her left medial malleolus 2cm in diameter and a scar adjacent to the ulcer. There were also two scars on the right medial malleolus.

Neurological examination was normal. There was no history of seizure. MRI revealed an infarction localized bilaterally in occipital region (Fig 3).

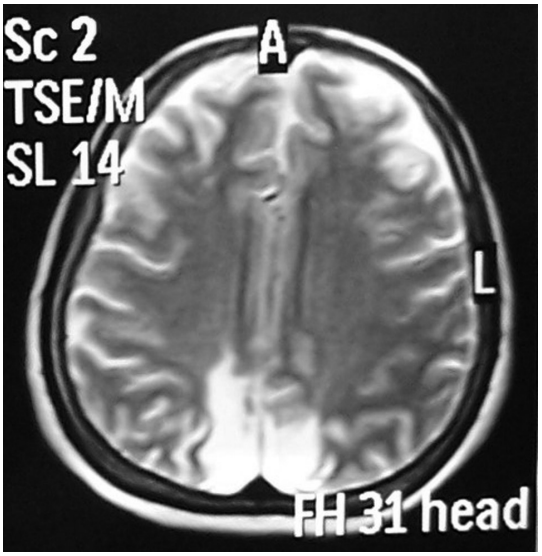

Figure 3- T2-weighted axial MRI showing a hyperintense lesion in both occipital lobes.

Electrocardiogram showed normal sinus rhythm. Transthoracic echocardiography revealed an enlarged left atrium of 39 mm (normal 24-38 mm), left ventricular end-diastolic diameter of 56 mm (normal 46 mm +/- 4), left ventricular end-systolic diameter of 35 mm (normal 30 mm +/- 4), right ventricular diastolic diameter of 36 mm (normal 11-25 mm) and normal left ventricular systolic function. Pulmonary arterial systolic pressure was estimated as 47 mmHg using tricuspid regurgitation jet.

Hemoglobin electrophoresis revealed homozygous sickle cell anemia. Laboratory tests revealed a hemoglobin 7.8g/dl, hematocrit of 20.7%, white blood cell count of 8.9x10^3/µL, platelet count of 758x10^3/µL.

DISCUSSION

SCD is most common hemoglobinopathy in equatorial Africa. The gene is also found in northern Greece, Sicily, Turkey, Saudi Arabia, and India (3). SCD is frequent especially in South-east part of Turkey (4).

Patients with the disease with homozygous expression of hemoglobin SS have a high incidence of leg ulcers. Although the exact cause of leg ulceration in SCD is not known, trauma, venous incompetence, anemia, poor circulation, local tissue hypoxia and increased adhesion of sickle cells to vascular endothelial cells are suggested

factors in ulcer formation (5,6). Medial malleoli is the most common site of leg ulceration in SCD, however anterior tibial area, dorsum of the foot, Achilles tendon area, and ankles may also be affected (7).

PH is a common complication of adult patients with SCD and the prevalence differs from 30-63% (8-11). It is believed that PH develop in these patients as secondary to anemia and vaso-occlusive events (9,12-14). Although, the early symptoms of PH in SCD patients do not differ from the symptoms of SCD patients without PH, those patients with PH have a high mortality, compared with SCD patients without PH (14,15). In our patients left and right heart chambers were dilated. However, the LV systolic performance was normal. Those findings were in agreement with those in previous reports (12,13).

SCI is defined as an MRI of the brain without history or physical findings of a focal neurological deficit. SCI is prominent in infants and toddlers younger than 4 years of age with SCD, and cumulative prevalence continues to increase until at least 14 years of age. Low pain event rate, history of seizure, leukocyte count >11.8.109/L, and the SEN globin gene haplotype were associated with an increased incidence of SCI (16). The stroke rate in patients with SCI is 14-fold higher than in those with normal MRI (17). SCI is likely accounted for by chronic hypoxia in the microvasculature ensuing from progressive cerebrovascular disease in the major cerebral arteries (18). In a multicenter study of 173 patients 15% had an abnormality on MRI without a history of clinical stroke (19). Frontal and parietal lobes are the most affected areas (20). There were three SCI in parietal, frontal and caput caudat nucleus in the first patient. Bilateral occipital infarction was detected in the second patient.

In conclusion, clinician should be aware that SCI and/or PH can present in a patient with leg ulcer in SCD and the only symptom may be leg ulceration. However, large series are required in order to determine whether leg ulcer is a risk factor for SCI and PH.

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