
Co-existence of sickle cell disease and hemidiaphragm paralysis

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ÖZET

Orak hücreli anemi ve hemidiyafagma paralizisi birlikteliği

Orak hücreli anemi, hücrenin rijid deformasyonuna yol açan anormal hemoglobin üretiminin neden olduğu bir hastalıktır. İnfeksiyonlar, akut splenik sekestrasyon krizleri, aplastik krizler, akut göğüs sendromu, inme, kolelitiazis, renal hastalıklar ve ağrı hastalığın majör komplikasyonlarıdır. Unilateral veya bilateral diyafagma paralizisi, frenik sinir zedelenmesini takiben veya miyopatiler, nöropatiler ve miyelopatiler gibi çeşitli motornöron hastalıklarıyla birlikte görülebilir. Hemidiyafagma paralizisi, bilateral paraliziden daha sık görülür ve genellikle göğüs radyografisinde diyafragmanın tek taraflı anormal yüksekliği ile teşhis edilir. Orak hücre hastalığı olan 14 yaşındaki kız hastanın rutin kontrolü sırasında çekilen göğüs radyografisinde belirgin sağ hemidiyafagma yüksekliği izlendi. Hastanın ne trauma ne de torasik cerrahi öyküsü vardı. Nörolojik muayenesinde duyu kusuru veya motor defisiti de yoktu. Toraksın bilgisayarlı tomografisi (BT)'nde belirgin derecede sağ hemidiyafagma elevasyonu saptandı. BT'sinde hiçbir patolojik bulgu yoktu. Spirometrik değerleri (beklenenin yüzdesi şeklinde) FEV₁= %53, FVC= %55, FEV₁/FVC= %97, PEF= %43 ve FEF_{%25-75}= %58 olarak orta-ağır derecede restriksiyon ile uyumluydu. Sağ hemidiyafagma paralizisi tanısı floroskopide Hitzenber Snif testin pozitif saptanmasıyla doğrulandı. Orak hücre hastalığında her ne kadar çeşitli patofizyolojik mekanizmaların santral nörolojik komplikasyonlara yol açtığı biliniyor olsa da, periferik sinir tutulumu bugüne kadar bildirilmemiştir. Burada, orak hücre hastalığı ve unilateral hemidiyafagma paralizisi olan 14 yaşındaki kız hastayı, aradaki ilişkinin kanıtlanması için daha çok sayıda olgu saptanması gerekmesine rağmen bugüne kadar bu birliktelik bildirilmediği için sunuyoruz.

Anahtar Kelimeler: Orak hücreli anemi, diyafagma paralizisi, komplikasyon, birliktelik.

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SUMMARY

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Sickle cell anemia is a disease caused by production of abnormal hemoglobin. Infection, acute splenic sequestration crisis, aplastic crises, acute chest syndrome, stroke, cholelithiasis, renal disease and pain are the major complications. Unilateral or bilateral diaphragm paralysis maybe seen following phrenic nerve injury and with a variety of motor-neuron diseases, myelopathies, neuropathies, and myopathies. Prominent right hemi-diaphragma elevation was observed on chest radiograph of a 14 years' old female patient with sickle cell disease. Her medical history yielded neither trauma nor intra-thoracic surgery. She didn't have either motor deficit or sensation disorder on any region of her body. Thorax CT yielded no lesion except the significantly elevated right diaphragma. Her cranial CT showed no lesion, too. Diagnosis of right hemidiaphragm paralysis was confirmed by positive Hitzenberg Sniff test on fluoroscopy. Although several pathophysiologic mechanisms are known to be involved and lead to central neurologic complications in sickle cell disease, involvement of peripheral nerves have not been reported. Here we present a 14 years' old female patient with sickle cell anemia and unilateral diaphragm paralysis, co-existence of which have not been reported so far.

Key Words: Sickle cell anemia, diaphragm paralysis, complication, co-existence.

Sickle cell (SC) anemia is a disease caused by production of abnormal hemoglobin, which binds to other abnormal hemoglobin molecules within the red blood cell to cause rigid deformation of the cell (1). The obstruction of small vessels by sickle cells results in repeated infarctions, leading to gradual involvement of all organ systems, most notably spleen, lungs, kidney and brain (2). Infection, acute splenic sequestration crisis, aplastic crises, acute chest syndrome, stroke, cholelithiasis, renal disease and pain are the major complications of this disease (3). Many neurologic complications other than stroke have also been described in SC disease including drowsiness, coma, convulsions, headache, temporary or permanent blindness, cranial nerve palsies and paresthesias of the extremities (3). The lungs are also commonly affected, with infarcts, emboli (from marrow infarcts and fat necrosis), and a markedly increased propensity for pneumonia (3).

The most important respiratory muscle is the dome-shaped diaphragm, which is innervated by cervical motor neurons C3-5 via the phrenic nerves. Diaphragm paralysis can involve either the whole diaphragm (bilateral) or only one leaflet (unilateral). Unilateral or bilateral diaphragm paralysis maybe seen following phrenic nerve injury and with a variety of motor-neuron diseases, myelopathies, neuropathies, and myopathies (4). Hemidiaphragm paralysis is more common than bilateral paralysis and is usually diagnosed from unilateral elevation of the hemidiaphragm on chest radiograph (4).

Here we present a 14 years' old female patient with sickle cell anemia and unilateral diaphragm paralysis, co-existence of which have not been reported so far.

CASE REPORT

A 14 years' old female patient known to have sickle cell anemia and being periodically followed up since she was six months' old, admitted

to pediatry clinic for her routine control visit. She did not have any complaints other than fatigue and dyspnea on exertion. She had suffered from 5-6 painful vaso-occlusive crisis per year until she was 10 years' old and only five in total since then. A pale skin was observed on inspection. Increased dullness and decreased intensity of pulmonary sounds on posterior wall of right hemi-thorax were detected. Physical examination of her cardio-vascular and other systems were entirely normal. She had neither motor deficit nor sensation disorder on any region of her body including dermatomes of cervical 3-5 from which phrenic nerves originates. Her complete blood count (CBC) results were as follows WBC: 10.32, RBC: 2.62, HGB: 8.6, MCH: 32.8, MCV: 96.1 fL, MCHC: 33.9 pg, PLT: 337, MPV: 10.1. Hemoglobin electrophoresis yielded HbS: 86.4, HbF: 5.1, and HbA2: 5.4. Prominent right hemidiaphragm elevation was observed on her routine postero-anterior (PA) chest radiograph. The apex of the right hemi-diaphragm was significantly (> 4 cm) higher than that of the left (Figure 1). Any other radiological abnormality was not observed. Spirometry showed moderate to severe restriction in respiratory function with her $FEV_1 = 53\%$, $FVC = 55\%$, $FEV_1/FVC = 97\%$, $PEF = 43\%$ and $FEF_{25-75\%} = 58\%$ of predicted. Her medical history yielded neither trauma nor intra-thoracic surgery, as possible causes of



Figure 1. PA chest radiograph of the patient shows the elevated right diaphragm with its apex significantly (> 4 cm) higher than that of the left.

diaphragm paralysis. So computerized tomography (CT) of thorax and upper abdominal ultrasonography (USG) were performed in order to rule out any possible reason for phrenic nerve paralysis such as a mediastinal mass and for right diaphragm elevation such as a hepatic tumor, respectively. Thorax CT yielded no lesion except the significantly elevated right diaphragm (Figure 2). Upper abdominal USG was normal with absence of any hepatic tumor and subpulmonary effusion. Her cranial CT showed no lesion, too. Diagnosis of right hemidiaphragm paralysis was confirmed by positive Hitzenberg Sniff test on fluoroscopy.

DISCUSSION

Pulmonary complications lead to mortality and morbidity in patients with SC disease (5). In addition lung function abnormalities are present in young children with SC disease and restrictive abnormalities become more prominent with increasing age (6). This patient has moderate to severe restrictive type pulmonary dysfunction but this situation is probably due to unilateral diaphragm paralysis in major part rather than the SC disease itself.

Diaphragm paralysis maybe seen following phrenic nerve injury and with a variety of motor-neuron diseases, myelopathies, neuropathies, and myopathies (4). None of these possible reasons could be identified in our case. She didn't have any motor deficit or sensation disorder on any part of her body, either. She had exposed neither to trauma nor to intra-thoracic surgery. Besides CT of thorax did not show any mediastinal mass or any lesions such as pneumonia, pleurisy, aortic aneurysm, substernal goiter, neoplasm adjacent to a phrenic nerve all of which may lead to phrenic nerve injury or compression. Thorax CT revealed the significantly elevated right diaphragm (Figure 2).

Patients with SC disease have an approximately 25% chance of developing some type of neurological complication in their lifetime (7). The neurological complications result from one point mutation that causes vasculopathy of both large and small vessels. Anemia and the resultant cerebral hyperemia produce conditions of hemody-

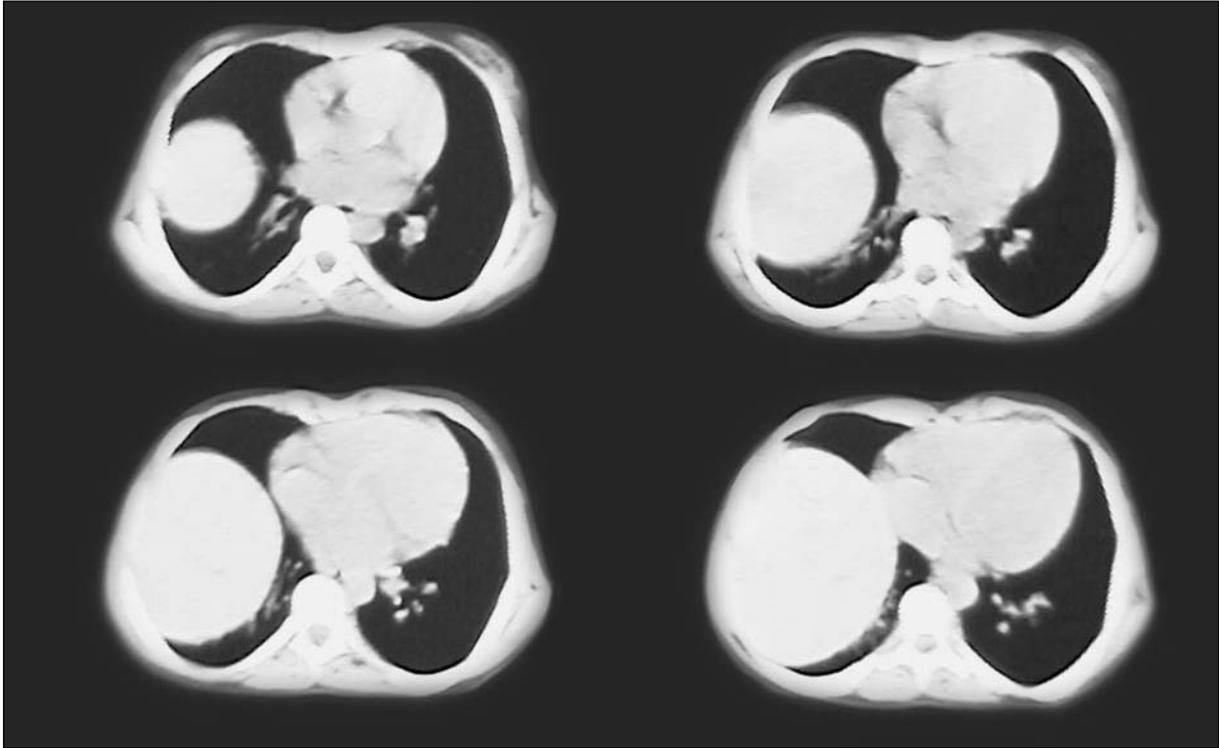


Figure 2. CT slices of her thorax shows only the elevated right diaphragm without any mediastinal mass or parenchymal lesions.

namic insufficiency. Sickled cells adhere to the endothelium, contributing to a cascade of activated inflammatory cells and clotting factors, which result in a nidus for thrombus formation. Because the cerebrovascular reserve becomes exhausted, the capacity for compensatory cerebral mechanisms is severely limited. There is evidence of small-vessel sludging, and a relative deficiency of nitric oxide in these vessels further reduces compensatory vasodilatation. Both clinical strokes and silent infarcts occur, affecting motor and cognitive function (7). Nevertheless these may explain only central neurological complications in SC patients. In our case cranial CT was normal as well as her motor and cognitive functions. We suspect, if similar mechanisms which are involved in the repeated vaso-occlusive crises may also lead to peripheral nerve dysfunction which has not been reported so far.

Therefore, we present this case as a co-existence of sickle cell disease and hemidiaphragm paralysis.

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