Brain MRI and CT findings in sickle cell disease patients from Western Saudi Arabia

Mamdooh M. Kotb, MSc, PhD, Wahid H. Tantawi, MSc, PhD, Ayman A. Elsayed, MSc, PhD, Ghazi A. Damanhouri, MRCP, Hussein M. Malibary, PhD.

ABSTRACT

Objective: To report the clinical and imaging findings in patients living in the Western Province of the Kingdom of Saudi Arabia where the Benin b-globin gene haplotype is prevalent.

Methods: Our study population consists of 36 sickle cell disease patients (17 males, 19 females; age range, 1.6-35.6 years; mean age, 19.4 years) with suspected cerebrovascular complications. Major clinical presentations were as follows: stroke symptoms or history of stroke in 13 (36%) patients, severe headache in 16 (44.4%), and seizures in 9 (25%). All patients underwent brain CT, or MRI study, or both, including diffusion imaging and magnetic resonance angiography. We conducted the study between August 2001 and June 2004 at King Abdul-Aziz University Hospital, Jeddah, Kingdom of Saudi Arabia.

Results: Based on MRI, or CT, or both, we found cortical infarction in 30.6% (11/36) of patients. The frontoparietal temporal region was the most commonly involved part and occurred in 4 patients. We diagnosed small vessel disease in 38.9% (14/36) of patients, and involvement was bilateral in 9 patients. Small vessel disease involved deep white matter more than basal ganglia, and the caudate nucleus was the most commonly involved site in basal ganglia. We detected cerebral atrophy in 52.8% (19/36) of patients. An unusual finding was an epidural hematoma associated with skull bone infarctions and scalp edema that we successfully managed conservatively. We observed a widening of the diploe space of the skull in 10 patients. We saw adenoid hypertrophy in a significant number of patients (72% [26 of 36]).

Conclusions: Sickle cell disease cerebrovascular complications are of major concern to the physician. Cerebral atrophy is the most common imaging finding followed by small vessel disease and then by cortical infarction. There was an increased incidence of adenoid hypertrophy.

Neurosciences 2006; Vol. 11 (1): 28-36

Sickle cell disease (SCD) is the most common inherited hemoglobinopathy, and is an extremely important and serious health care issue in Saudi Arabia, some other Middle East countries, certain regions in Africa, USA, and India. Estimates state that 20% of the population in some parts of Saudi Arabia have the sickle cell trait. The first report of the sickle cell gene in the eastern province of Saudi Arabia was by Lehman et al, in 1963. An interesting aspect of SCD in Saudis is the extremely variable clinical and hematological presentation seen in patients from different regions of the Kingdom, thus classifying SCD as a heterogeneous disease. Two well-defined forms of SCD are seen in Saudis. In the eastern province, the disease is milder, where in the western province the disease is severe and similar to that reported in Africans or those whose ancestors come from Africa. We can explain the
variability in the clinical presentation of SCD on the basis of various genetic and environmental factors.

Patients from the eastern part of Saudi Arabia carry the Saudi-Indian β-globin gene haplotype, while the Benin haplotype is the major one in the western areas of Saudi Arabia, Egypt, Jordan, and Syria. So, SCD in Saudi Arabia is unique. Stroke, brain atrophy, and cognitive impairment are major neurological consequences of SCD. Approximately 25% of all patients will have a neurological complication over their lifetime, and stroke occurs by the age of 20 in 11% of the patients. Both CT and MR imaging are the initial tests of choice for stroke assessment in SCD while transcranial Doppler (TCD) is the imaging tool of choice for stroke prevention. There are several reports describing brain MRI and CT findings in SCD patients from the western hemisphere. The purpose of this study is to report the clinical and brain-imaging findings using MRI, or CT, or both in 36 SCD patients, living in Saudi Arabia, with suspected neurological complications. All patients are from the western province of Saudi Arabia where the disease has rather a severe course.

Methods. Our study population consists of 36 patients (17 males, 19 females) recruited from a pool of SCD patients attending King Abdul-Aziz University Hospital during the study period. Inclusion criteria included only patients with suspected cerebrovascular complications, and there were no patient exclusion criteria. The average patient age was 19.4 years, with an age range of 1.6-35.6 years. All patients were Saudi except one Chadian. Thirteen (36%) presented with, or had history of stroke symptoms, 16 (44.4%) had severe headache, 9 (25%) had seizures. Meningitis-like symptoms (fever and neck stiffness) were seen in only one patient (2.8%). One patient presented with shock and another one with fainting attack. The prevalence of other clinical findings was as follows: hyperreflexia 2.8% (1/36), diminished vision in the left eye 2.8% (1/36), focal numbness 2.8% (1/36), and dizziness 2.8% (1/36). Some patients had a combination of the above presentations. The study was conducted between August 2001 and June 2004 at King Abdul-Aziz University Hospital, Jeddah, Kingdom of Saudi Arabia. A typical head CT examination (Light Speed QX/i; GE Medical Systems, Waukesha, Wis.) was performed with 5-mm contiguous transverse sections, 140 kVp, 340 mAs, and 2-second scanning time. The MR imaging was performed with a 1.5-T system (Symphony; Siemens Medical Systems, Erlangen, Germany) using a standard head coil. A typical MR imaging examination consisted of sagittal T1-weighted imaging (500/14 [repetition time msec/echo time msec]; field of view, 23 cm; acquisition matrix, 256 x 192 pixels; 5-mm section thickness with a 1-mm gap; and one signal acquired). Fast spin-echo T2 and intermediate-weighted MR images were obtained with 2,900/18, field of view of 23 cm, acquisition matrix of 256 x 256 pixels, 5-mm section thickness with 1-mm gap, and one signal acquired. Transverse fluid-attenuated inversion recovery MR images were obtained with 7,900/114/2,500 (inversion time msec), field of view of 23 cm, acquisition matrix of 256 x 192 pixels, 5-mm section thickness with 1-mm gap, and one signal acquired. Diffusion weighted (DW) MR images were obtained with single-shot echo-planar imaging with 4,200/139, field of view of 23 cm, matrix of 256 x 128 pixels, 5-mm section thickness with 1-mm gap, and 20 transverse sections. The maximum gradient amplitude was 30 mT/m, and b values were 1,000 and 500 sec/mm² with 6 gradient directions and 3 signals acquired, with an image acquisition time of 126 seconds. Trace DW MR images and apparent diffusion coefficient (ADC) maps were computed by taking the geometric mean of the 6 gradient-direction DW MR images. Two or more radiologists reviewed all cases. Infarctions, small vessel disease, and atrophy were diagnosed based on criteria described by Runge. The MR angiographic examination was performed using a 3-dimensional time of flight sequence, to obtain spoiled gradient-echo images in the transverse plane at 64-section levels. The following parameters were used: 43/7.15; field of view, 23 cm; flip angle 25; matrix, 192x256; effective thickness 1 mm; and acquisitions, one in 7 minutes. The MR angiograms were centered at the sella turcica so that major arteries from the circle of Willis could be seen. The 64 sections were reconstructed into a transverse slab by using standard maximum intensity projection algorithm. Sagittal T1-weighted MR images and the CT lateral scout view of the skull were evaluated for the presence or absence of widening of diploic space of the skull. Measurements of the adenoid pads were based on the method of Vogler et al. Using the midline T1-weighted MR image or the CT scout view, the thickness of the adenoid pad was measured along a line constructed perpendicular to the anterior clival surface.

Results. Table 1 shows the prevalence of infarction, small vessel disease, atrophy, and diploic thickening in brain MRI, or CT, or both based on the clinical picture, while Table 2 shows the prevalence of cortical infarction, small vessel disease, and atrophy in our 36 SCD patients based on brain MRI, or CT findings, or both. Cortical infarction was diagnosed in 11 (30.6%) of our 36 patients based on MRI or CT findings. The frontoparietal temporal region was the most commonly involved part and occurred in 4 patients. Bilateral affection of both cerebral hemispheres occurred in 6 patients while unilateral affection was seen in the remaining 5 patients. Based on combined MRI and CT findings, small vessel disease tends to be bilateral, as this was the case in 9 patients and unilateral in 5 patients only. Parenchymal abnormalities consistent with cortical infarction were seen on MR images of 33% (6/18)
Table 1 - Prevalence of infarction, small vessel disease, atrophy, and diploic thickening in brain MRI, CT, or both in SCD patients based on the clinical picture.

<table>
<thead>
<tr>
<th>Clinical picture</th>
<th>Patient number</th>
<th>Infarction</th>
<th>Small vessel disease</th>
<th>Cerebral atrophy</th>
<th>Diploic space thickening</th>
</tr>
</thead>
<tbody>
<tr>
<td>Only CVA</td>
<td>9</td>
<td>6</td>
<td>7</td>
<td>8</td>
<td>5</td>
</tr>
<tr>
<td>CVA and seizures or headaches</td>
<td>4</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>2</td>
</tr>
<tr>
<td>Only headache</td>
<td>11</td>
<td>1</td>
<td>3</td>
<td>5</td>
<td>2</td>
</tr>
<tr>
<td>Headache and eye symptoms</td>
<td>2</td>
<td>1</td>
<td>0</td>
<td>1</td>
<td>0</td>
</tr>
<tr>
<td>Headache, fever, hyperreflexia*</td>
<td>1</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>1</td>
</tr>
<tr>
<td>Only seizures</td>
<td>5</td>
<td>1</td>
<td>2</td>
<td>1</td>
<td>0</td>
</tr>
<tr>
<td>Meningitis-like symptoms</td>
<td>1</td>
<td>0</td>
<td>0</td>
<td>1</td>
<td>0</td>
</tr>
<tr>
<td>Shock</td>
<td>1</td>
<td>1</td>
<td>0</td>
<td>1</td>
<td>0</td>
</tr>
<tr>
<td>Fainting</td>
<td>1</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Focal numbness</td>
<td>1</td>
<td>0</td>
<td>1</td>
<td>1</td>
<td>0</td>
</tr>
<tr>
<td>Total</td>
<td>36</td>
<td>11</td>
<td>14</td>
<td>19</td>
<td>10</td>
</tr>
</tbody>
</table>

*MRI revealed frontal epidural hematoma, skull bony infarctions, and scalp edema
SCD - sickle cell disease, CVA - cerebrovascular accident

Table 2 - Prevalence of cortical infarction, small vessel disease, and atrophy in 36 SCD patients based on brain MRI, CT findings, or both.

<table>
<thead>
<tr>
<th>Imaging findings</th>
<th>N (%)</th>
<th>Male:female ratio</th>
<th>Mean age and range in years</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cortical infarction</td>
<td>11 (30.6)</td>
<td>7:4</td>
<td>20.7 (9.4-30.03)</td>
</tr>
<tr>
<td>Small vessel disease</td>
<td>14 (38.9)</td>
<td>8:6</td>
<td>18.4 (1.6-30.5)</td>
</tr>
<tr>
<td>Atrophy</td>
<td>19 (52.8)</td>
<td>11:8</td>
<td>20 (5.3-30.5)</td>
</tr>
<tr>
<td>Total</td>
<td>36 (100)</td>
<td>17:19</td>
<td>19.4 (1.6-35.6)</td>
</tr>
</tbody>
</table>
**Figure 1** - A 20-year-old male sickler with chronic right middle cerebral artery infarction. **a)** Fluid-attenuated inversion recovery image shows right subcortical gliosis (straight arrow) with widening of Sylvian fissure, cortical sulci, and dilatation of right lateral ventricle. There is associated decrease in the size of right cerebral hemisphere. **b)** Maximum intensity projection MR angiography image shows occlusion of right internal carotid artery. Small right anterior cerebral artery is noted (straight arrow) with M1 segment of the middle cerebral artery (curved arrow) reconstituted via the posterior communicating artery.

**Figure 2** - A 25.4-year-old female sickler presented with epilepsy. The MR showed cerebral atrophy and bilateral deep white matter small vessel disease. Axial FLAIR MR image shows bilateral deep white matter high signal intensity foci (curved arrow).

**Figure 3** - A 19.6-year-old male with right-sided cerebrovascular accident and hemorrhagic infarction. The CT brain study (not shown) revealed low attenuation area at left lentiform nucleus with associated effacement of cortical sulci. Follow-up axial T1-weighted MR image shows high signal intensity at both lentiform nuclei, more on the left side, due to methemoglobin (curved or sickled arrows). There are also bilateral temporoparietal thin gyriform lines of high signal intensity, more on the left side. There is widening of sylvian fissures and cortical sulci for patient age denting cerebral atrophy. Also noted thickening and decrease signal intensity of skull bone marrow.

**Figure 4** - A 10.4-year-old boy with severe headache and left sided hyperreflexia. Imaging revealed epidural hematoma, bony skull infarctions, and subcutaneous collections. Coronal T2-weighted MR image shows that the epidural collection is of mixed signal intensity with low signal intensity foci inside (curved arrow).
patients (Figure 1). Cortical infarction was seen in bilateral hemispheres in 4 patients, but involvement was asymmetric, with one side more involved than the other, in all patients. The frontotemporoparietal region was the most commonly involved part of the cerebral hemisphere (4 patients). Small vessel disease was identified in 44% (8/18) of patients. Small vessel disease was bilateral in 6 patients (Figure 2). Small vessel disease involved deep white matter in 7 patients with or without involvement of the basal ganglia. Isolated affection of the caudate nucleus was seen in one patient. The caudate nucleus was the most commonly involved part of basal ganglia (5 patients) followed by lentiform nucleus (2 patients). Atrophy for patient age was seen in 61% (11/18) of patients. Therefore, cerebral atrophy was the most common findings followed by small vessel disease. Abnormal vascular findings seen at MR angiography included focal narrowing of vessel lumen seen in one patient, while vessel occlusion was seen in 2 patients. All abnormal findings on MRA had evidence of infarction on MR images. Hemorrhagic infarction occurred in one patient in whom earlier CT showed only infarction (Figure 3). No evidence of subarachnoid hemorrhage was detected in any patient. All patients, including those with severe headache, showed no MR evidence of sinus thrombosis. The MR venography was negative in 2 patients suspected clinically to have sinus thrombosis. Unusual MRI findings were observed in a 10 year-old-boy who presented with headache, left hyperreflexia, and fever (Figure 4). The MRI revealed a well-defined extra-axial abnormal signal intensity area that was of intermediate signal on T1-weighted images and of heterogeneous high signal intensity with low signal intensity foci on T2-weighted images. That lesion showed no significant enhancement on post contrast study. The lesion was diagnosed as an epidural hematoma. Subgaleal collections were also observed. In addition, there was thickening of the skull diploic space that showed multiple non-enhancing low signal intensity areas. A subsequent bone scan was diagnostic of multiple skull bone infarctions. Parenchymal abnormalities consistent with cortical infarction were seen on CT images of 28% (9/32) of patients. Infarction was hemorrhagic in only one patient, for whom MR was not performed. Cortical infarctions were seen in bilateral hemispheres in only 2 patients. The most commonly involved region was frontotemporoparietal, which was affected in 3 patients followed by frontoparietal, and temporal lobe involved each in 2 patients. Small vessel disease or lacunar infarctions were identified in 31% (10/32) of patients. Small vessel disease or lacunar infarctions were multiple and bilateral in 6 patients. Deep white matter was the most commonly involved site (8 patients) followed by caudate nucleus (7 patients). Atrophy for patient age was seen in 46.9% (15/32) of patients. Therefore, atrophy was the most common imaging findings followed by small vessel disease. The most common presentation in cases of atrophy was stroke or history of stroke in 8 patients followed by headache in 5 patients. Widening of the diploic space of the skull was observed on either or both CT and MRI images in 10 patients. Marked low signal intensity of the calvarial bone marrow compared to gray matter on T1-weighted images was observed in 6 patients (Figure 3). Incidental notice of adenoid hypertrophy on sagittal images of brain, or scout lateral view of CT exams was seen in a very significant number of patients (72% [26 of 36]).

**Discussion.** The first worldwide reported case of SCD was described in a dental student named Walter Clement, originally from the Eastern Caribbean, while he was studying in Chicago. However, the first reported neurological complication of SCD was a left hemiparesis that occurred in a 3-year-old baby. In SCD, repeated adherence of sickled red blood cells to the endothelium followed by forcible removal results in endothelial injury with subsequent cell proliferation (intimal hyperplasia) and luminal narrowing of large cerebral vessels. This is considered a macrovascular scenario for cerebral ischemia in SCD. Approximately 75% of ischemic strokes in SCD are the result of occlusion of large arteries. The major clinical features of stroke in SCD include the young age of involvement (median age 6 years), the predominance of infarction in children, and of hemorrhage in adults, and a 50-70% tendency to recurrence within 3 years of the attack. Subtle motor changes and transient attacks of weakness or numbness are likely to be missed in young children. Early detection of cerebral pathology, as well as prevention of overt stroke are important goals in the management of SCD. Acute infarction in SCD is treated differently from that in other patients. Initial treatment includes stabilization of vital signs, careful hydration, and red cell transfusion. The most effective way to prevent recurrence of infarctive stroke is through chronic transfusion therapy (CTT). The standard recommendation is to maintain the HbS percentage at less than 30% for the initial 3 years. This goal typically needs transfusion every 3-4 weeks.

We diagnosed cortical infarction in 11 (30.6%) of our 36 patients based on MRI or CT findings. The frontoparietal temporal region was the most commonly involved part, and occurred in 4 patients. Bilateral affection of both cerebral hemispheres occurred in 6 patients while we saw unilateral affection in the remaining 5 patients. Moritani et al reported the usual and unusual MRI findings, including diffusion and perfusion images, in 30 patients all with sickle cell cerebrovascular disease and concluded that MRI and MRA are useful in defining the basis and etiology for stroke and evaluating the effects of transfusion therapy. In 28 patients with white matter infarction, bilateral affection was more than unilateral
involvement (25 of 28) while in 19 patients with cortical infarction, unilateral affection was more often seen (11 of 19). Infarction of basal ganglia and thalamus was seen in 12 patients. On the other hand, arterial occlusion or stenosis was seen in 16 patients on initial MRA. Moyamoya vessels were seen in 20% (6 of 30). Anterior circulation was more involved than posterior circulation. Their results suggest that cortical infarction is often unilateral and in the frontoparietal location and seems to be related to a macrovascular process while white matter infarction is often bilateral and likely related to a microvascular process. Follow up MRA showed marked improvement of major arterial stenosis in one patient suggesting that prolonged transfusion therapy slows progression of stenosis and decreases the risk of stroke. Unusual findings included diffuse linear enhancement in the white matter.

In 2003, Steen et al.\textsuperscript{17} with 8 years experience in evaluation of pediatric patients with SCD, reported a high prevalence of ischemic brain injury in pediatric SCD patients. They reported 44% (82 out of 185) prevalence of infarction, ischemia, or atrophy in pediatric patients with a mean age of 10 years. They found that imaging abnormalities depend on patient age, patient clinical history and diagnosis as well as imaging methods. While an earlier, but the largest study to date, reported a 22% (70 of 312) prevalence of infarction, ischemia, or atrophy in pediatric patients with a mean age of 8.3 years.\textsuperscript{18} In comparing our results to that study, we have a significantly higher prevalence of infarctions and atrophy because our patients are selected based on clinical findings and are of a higher age group and also due to the use of newer imaging methods. The sensitivity of MR for stroke detection was 100% in the Cooperative Group Study of Sickle Cell Disease,\textsuperscript{18} and lesions typically involved both cortical and deep white matter whereas silent infarctions usually involved deep white matter in a border zone distribution. In that study, the most common site of MR abnormalities was the frontal and parietal lobes.

The deep white matter is perfused by arterioles and is more liable to inadequate perfusion and subsequent infarction. Small vessel disease in SCD is due to formation of intravascular masses of dense or less flexible sickled erythrocytes in the peripheral arterioles and post capillary venules.\textsuperscript{13} The prevalence of small vessel disease based on combined MRI and CT findings in our 36 patients was 38.9% (14 out of 36). The average age of patients with small vessel disease was 18.4 years (range 1.6-30.5 years). Involvement tends to be bilateral as this was the case in 9 patients and unilateral in 5 patients only. In our study, involvement of deep white matter was more than basal ganglia and caudate nucleus was the most commonly involved site in basal ganglia. Moritani et al.\textsuperscript{13} reported similar results.

Iodinated contrast medium carries the risk of intravascular sickling. So prior to conventional angiography, it is recommended that the patients should be well hydrated and receive a blood transfusion to decrease HB S level to 30%.\textsuperscript{14} However, new non-ionic contrast agents with low osmolarity have the potential to decrease further the risk of contrast media.\textsuperscript{14}

Al-Hawsawi and Ismail\textsuperscript{19} reported a 10% (9/90) prevalence rate of stroke among children with SCD in Madina Maternity and Children hospital, Saudi Arabia. Brain CT showed cerebral infarction in 8 patients while only one patient had normal CT brain scan. They found that a low hematocrit level was a risk for stroke as previously reported in other studies, but a high leukocyte count is not a risk factor. Al-Hawsawi\textsuperscript{20} reported the development of intracranial hemorrhage in a 5-year old Saudi girl with splenic sequestration. Hemorrhage was attributed to repeated blood transfusion with associated increased blood viscosity. The author recommended not to over transfuse patients with splenic sequestration. Wang et al.\textsuperscript{21} performed brain MRI and MRA for 39 very young children with SCD aged 7-48 months. The overall prevalence of CNS abnormalities in the asymptomatic group was 4 of 36 (11%). One child had a silent infarction on MRI and a stenotic lesion on MRA, and 3 other children had stenotic lesions on MRA. The remaining 3 patients with seizures had infarction on MRI. This study suggests a need for early diagnosis early in life to start a therapeutic intervention to prevent CNS complications in SCD.

There are few published articles discussing perfusion MRI in SCD. Kirkham et al.\textsuperscript{22} studied 48 patients with SCD with MRI, including perfusion imaging, and MRA. Abnormalities on perfusion were seen in 25 cases. The perfusion lesion was larger than the area of infarction in 9 cases and was seen in an arterial distribution with no infarction in a further 9. In 6 other patients, perfusion abnormalities were seen despite normal MRI or MRA. So, perfusion abnormalities are associated with neurological symptoms in SCD, even if MRI and MRA are normal. The authors suggested that it is likely that perfusion MRI may guide management in individual patients. Recently, Grueneich et al.\textsuperscript{23} investigated the relation between neuropsychological function and imaging findings in children with SCD. Twenty-two patients underwent MRI including MR perfusion studies. Imaging abnormalities were found in 45% of patients and abnormalities were found to be correlated with disease severity and increased variability in neuropsychological level of performance. These results underscore the high rate of vascular pathology in SCD. Perez-Defin et al.\textsuperscript{24} found that cortical atrophy is the most frequent brain lesion among 78 asymptomatic patients with SCD from Cuba. Their study showed that 35.7% of adults and 10% of children have silent brain lesions. While in Moritani et al’s study,\textsuperscript{13} brain
atrophy was seen in 14 patients out of 30 in initial MRI studies. Moser et al\textsuperscript{18} reported 11% prevalence of atrophy among 312 children with SCD. In a subset of 16 patients with history of cerebrovascular accident, they reported atrophy associated with ischemic changes in 13 of their patients giving a prevalence of 81%. In our study, atrophy was seen in 52.8% (19 out of 36) patients based on either CT or MR, or both. The prevalence of atrophy based on MRI was 61% and CT 46.9%. Our results showed that atrophy is the most common finding in patients with SCD in both MRI and CT. So radiologists interpreting brain and CT images of sickle cell patients should not overlook the presence of global or focal atrophy, and always assess that based on the patient’s age.

Headache, which may be severe, is a frequent symptom in SCD. It could be due to anemia, cerebrovascular disease, stress related, or other causes including pseudotumor cerebri, or it may be the result of an unknown factor that predisposes sickle cell patients to headache.\textsuperscript{25} Prenger et al\textsuperscript{26} suggested that anemia in sicklers results in compensatory hyperemia and hypervolemia and the resultant cerebral vasodilatation causes headache. In addition, abnormalities in MR perfusion studies were correlated with neurological complications of SCD including headache.\textsuperscript{25} In our study, 16 (44.4%) of our patients had severe headache. In 11 patients headache was the only presenting symptom. In this subgroup, brain MRI and CT revealed cortical infarction in one patient, small vessel disease in 3, and cerebral atrophy in 5 (Table 1). We encountered a 10 year-old boy with severe headache, fever, and hyperreflexia. The MRI revealed multiple abnormal signal intensity areas involving the skull with associated epidural hematoma, and abnormal subcutaneous signal intensity areas. Additional bone scan revealed multiple infarctions in the skull bone. The patient was managed successfully conservatively with hydration, antibiotics, and blood transfusion. In SCD, bone infarction usually affects the long bones, vertebral bodies, or ribs although there are infrequent reports describing skull infarctions.\textsuperscript{27} Presenting symptoms usually include bony tenderness, fever, local heat, and induration. Bony skull infarction should be considered as the cause of headache in SCD patients if there is associated scalp edema.\textsuperscript{28} The differential diagnosis includes osteomyelitis and soft tissue infection. Epidural hematoma may coexist with skull bone infarction. Resar et al\textsuperscript{27} reported multiple skull bone infarctions associated with epidural hematoma in a 14-year-old-boy with SCD. The development of spontaneous epidural hematoma is attributed to bone marrow infarction with subsequent periosteal elevation and subperiosteal and epidural hematoma.\textsuperscript{29,30} Our case, and others reported in the literature, emphasizes that the non-surgical conservative approach in treating combined skull infarction and epidural hematoma should be attempted first to avoid complications of surgical intervention.\textsuperscript{30}

Epilepsy is more common in sickle cell patients than in the general population. Liu et al\textsuperscript{31} reported a prevalence of 13.9% among their 152 patients with SCD. While Adamolekun et al\textsuperscript{32} found a 10.4% prevalence of epileptic seizures in their 96 patients. The later found that seizures in SCD patients are difficult to be controlled and patients were unlikely to present voluntarily for treatment. They concluded that physicians should specifically elicit a history of seizures in SCD patients. In our study, 9 patients (25%) had seizures either alone or associated with other symptoms. Focal MRI or CT abnormalities were seen in 4 patients including cortical infarction in one patient, combined cortical infarction and small vessel disease in 2 patients, and hemorrhagic infarction in another one patient. Cerebral atrophy was diagnosed in only one patient. On the other hand, Liu et al\textsuperscript{31} found that the majority of their epileptic sickle cell patients have nonfocal CT and MRI findings but demonstrate focal EEG abnormalities.

The incidence of adenotonsillar hypertrophy in SCD appears increased and likely represents compensatory lymphoid tissue enlargement rather than infection.\textsuperscript{32} In our study, there was remarkable prevalence of adenoid hypertrophy in 72% (26 of 36) of patients based on sagittal images of brain MR, and scout lateral view of CT exams. Robertson et al\textsuperscript{33} and Wali et al\textsuperscript{34} independently reported a cerebrovascular incident in a SCD child with severe sleep apnea syndrome due to adenotonsillar enlargement. Sidman and Fry\textsuperscript{35} reported complete remission of frequent vaso-occlusive crisis, due to obstructive sleep apnea, in a 12-year-old black girl following tonsillectomy and adenoidectomy. They believe that oxygen desaturation during periods of apnea was the cause of the frequent vaso-occlusive crisis. Physicians should be aware of possible exacerbation of SCD by sleep apnea syndrome, so definite diagnosis and proper treatment should be employed.

Alteration of cranial marrow signal intensity on T1-weighted images may be the first clue to the radiologist to suspect underlying systemic or hematologic disease. Homogeneous diploic or clival marrow that is hypointense relative to white matter in adults older than 20 years should suggest underlying disease and require correlation with clinical and laboratory findings. However in a small percentage of patients, this finding may represent normal variation.\textsuperscript{37} In our study, 6 patients showed marked low signal intensity of the calvarial bone marrow compared to gray matter on T1-weighted MR images due to iron overload from repeated blood transfusion. Moritani et al\textsuperscript{39} reported iron deposition in 17 out of their 30 patients with SCD using MRI. In our study, a high prevalence of thickening of diploic space of skull was observed in more than one fourth of the patients (27.8%).
The relative small number of patients and its retrospective nature limits our study. However, there are very few reports, with even smaller number of patients, describing brain imaging findings in SCD patients from Saudi Arabia.

In conclusion, cerebrovascular complications of SCD are common and are a major source of concern to the hematologist and neurologist. Based on our results, cerebral atrophy is the most common imaging finding followed by small vessel disease and then by cortical infarction. An unusual finding was an epidural hematoma associated with skull bone infarctions and scalp edema that was successfully managed conservatively. There was an increased incidence of adenoid hypertrophy in our patients based on CT and MRI findings. We hope that our study would highlight the need for a multi-center cooperative study both at a national and international level to address the use of imaging in prevention (for example using transcranial Doppler ultrasound) and diagnosis of cerebrovascular and even other complications of SCD using the recent techniques and the exchange of accumulated knowledge.

Acknowledgments. We thank Dr. Sattam Lingawi for his thoughtful review of the manuscript and all the radiologists, clinicians, and technicians who contributed in the care of the sickle cell patients.

References


