The Egyptian Journal of Radiology and Nuclear Medicine (2013) **44**, 547–561

Egyptian Society of Radiology and Nuclear Medicine

The Egyptian Journal of Radiology and Nuclear Medicine

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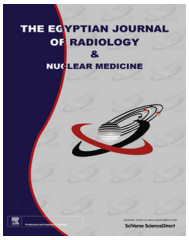

REVIEW

Sickle cell anemia: Imaging from head to toe

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Received 4 June 2013; accepted 10 June 2013
Available online 4 July 2013

KEYWORDS

SCA;
Imaging modalities;
Frequent embolism;
Super added infections;
Extramedullary hematopoiesis;
Stem cell

Abstract SCA is hemolytic anemia with deformed RBCs leading to frequent hemolytic crisis, extramedullary hematopoiesis and multisystem repeated emboli.
Aim: To emphasize the role of different imaging modalities in early accurate diagnosis.
Patients and methods: We present different types of complications of SCA, encountered in patients of Eastern Province-KSA, between 2009 and 2013.
Results: Complication may involve any system of the body, thus different types of imaging modalities are needed for correct diagnosis.
Conclusion: Being familiar with radiological signs of expected complications of SCA in different systems, helps much to control advance of the disease and protect against early organ damage.

Abbreviations: ACS, acute chest syndrome; AVN, avascular necrosis; CT, computed tomography; CTA, CT angiography; CVA, cerebrovascular accidents; DSA, digital subtraction angiography; ET, endothelin; Hb, hemoglobin; HbS, sickle hemoglobin; HbSC, sickle-hemoglobin C disease; Hb S-tha, Hb S-thalassemia; KSA, Kingdom of Saudi Arabia; MI, myocardial infarct; MRI, magnetic resonance imaging; PHT, pulmonary hypertension; RI, resistive index; RBCs, red blood cells; SCA, sickle cell anemia; SCD, Sickle cell disease; US, ultrasound

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Peer review under responsibility of Egyptian Society of Radiology and Nuclear Medicine.

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Contents

1. Introduction

Sickle cell disease (SCD) is an inherited disorder, characterized by defective hemoglobin (Hb) synthesis with production of an abnormal form, known as sickle hemoglobin (Hb S). Under low oxygen concentrations, red blood cells (RBCs) that contain (Hb S) become irreversibly deformed (sickle shaped) and rigid. This, in turn, impedes their ability to pass through narrow capillaries, with frequent clotting and thrombosis. Eventually, this leads to multiple repetitive vascular occlusion with frequent attacks of intractable painful episodes and progressive organ damage (1,2).

1.1. Incidence

Sickle cell anemia (SCA) affects millions throughout the world. It is particularly common among people whose ancestors come from sub-Saharan Africa; Spanish-speaking regions (South America, Cuba, and Central America); Saudi Arabia; India; and Mediterranean countries such as Turkey, Greece, and Italy. In the Unites States, it affects around 72,000 people, most of whose ancestors come from Africa. The disease occurs in about 1 in every 500 African-American births and 1 in every 1000–1400 Hispanic-American births. About 2 million Americans, or 1 in 12 African Americans, carry the sickle cell trait (3). SCD in Saudi Arabia is considered one of the major public health problems in the Eastern province (4,5).

1.2. Pathophysiology

SCD is caused by mutation in the β-globin chain, whose gene is located on chromosome number 11, causing the hydrophilic glutamic acid to be replaced with the hydrophobic amino acid Valine at position 6 of the beta chain. The association of two α-globin subunits with two mutant β-globin subunits forms hemoglobin S (Hb S). Under environmental low oxygen concentrations or increased body oxygen demands (e.g. high altitude or exercise stress), this mutant hemoglobin will cause aggregation of hemoglobin molecules. These aggregates permanently distort RBCs into a sickle shaped ones with lost elasticity i.e. RBCs fail to return to normal shape when normal oxygen tension is restored. Consequently, these rigid deformed RBCs fail to pass smoothly through the narrow capillaries, leading to vessel occlusion and ischemia (6) Fig. 1 (7).

There are different forms of the disease determined by the inherited genotype. If it is of homozygous pattern i.e. (Hb SS), the blood will have no normal hemoglobin particles and phenotypically termed sickle cell anemia (SCA). Heterozygous genotype, in which the patient inherits a sickle cell gene from one parent and a normal gene from the other parent forming Hb SA, is phenotypically expressed as sickle cell trait. Also, other heterozygous types of Hb S may form due to

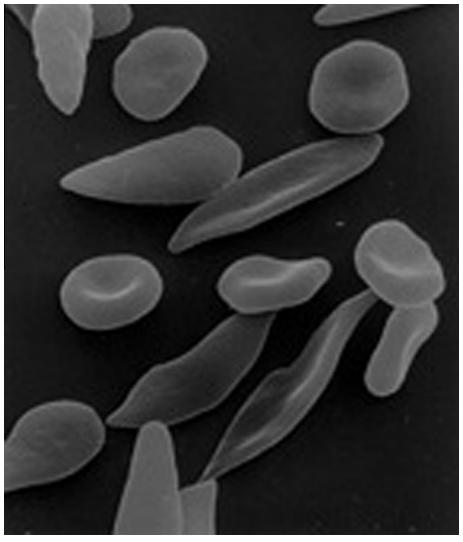

Fig. 1 Scanning electron micrograph showing a mixture of cells, some with round normal morphology, some with sickling showing elongation and bending (7).

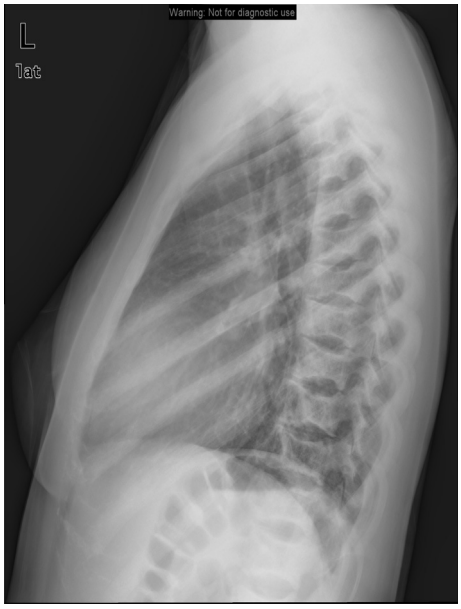

Fig. 2 Lateral X ray of dorsal spine showing central vertebral body depression of multiple dorsal vertebrae with typical H-shaped vertebrae.

combination with another different abnormal gene, such as sickle-hemoglobin C disease (Hb SC) or Hb S-beta thalassemia (Hb S-tha) (8).

Normally, the adult blood is formed mainly of hemoglobin A (96–97%), which consists of two alpha and two beta chains. The remaining small percentage is formed of hemoglobin A2 (two alpha and two delta chains) and hemoglobin F (two alpha and two gamma chains). In Hb SS patients, severe anemia is caused by excessive frequent destruction of the short lived red cells, because of their abnormal shape and elasticity. The bone marrow rate of hematopoiesis is significantly increased, but does not match the rate of destruction. Sickle cells survive only 10–20 days, in comparison with normal RBCs that live 90–120 days. In sickle trait patients with Hb SA, considering that their normal chromosomal allele is able to produce over 50% of the hemoglobin, there is no severe hemolytic crisis as SCA patients. They may have symptoms only if they are severely deprived of oxygen (9).

1.3. Clinical presentation of SCA

Acute painful vaso-occlusive crises are the most common clinical presentations of SCA. Around 50% of patients with SCA experience a painful crisis before the age of five. The skeletal system is the most frequently affected system with repeated complaints of acute severe pain which may involve different parts. Also, these vaso-occlusive crises may involve any organ with different manifestations according to the affected site (10).

2. Imaging of SCA

This article tries to cover most of the radiological manifestations, with different imaging modalities, in different systems affected by the disease, as organ-based approach. Systems are arranged in a descending order according to frequency, as we encountered in practice. Generally, it is agreed that the most commonly affected system is the musculoskeletal system (9).

2.1. Musculoskeletal complications

The skeletal involvement in SCD is mediated through different pathophysiological mechanisms. These are excessive intramedullary and extramedullary hematopoiesis, ischemic osteonecrosis and increased susceptibility of osteomyelitis. Excessive intramedullary hematopoiesis is stimulated by severe anemia caused by frequent hemolysis, which causes expansion of the intramedullary hematopoietic space (red marrow). These high demands of hematopoiesis stop conversion of red marrow into fatty marrow and re-convert the already formed fatty marrow into red marrow. Widening of osseous medullary spaces leads to osteopenia and thinning of cortical bone, making the bone vulnerable to pathologic fractures. Widening of the skull diploic space, together with some trabecular destruction and thickening of other trabeculae produce the X ray picture of hair-on-end skull, which is pathognomonic for hemolytic anemia. The vertebral osteopenic texture can result in central vertebral body compression giving a typical picture of multiple H-shaped vertebrae that are commonly seen in dorsal spine (11,12) Fig. 2.

Regardless, extramedullary hematopoiesis is not a constant feature of SCA; as it is more commonly seen in thalassemia or

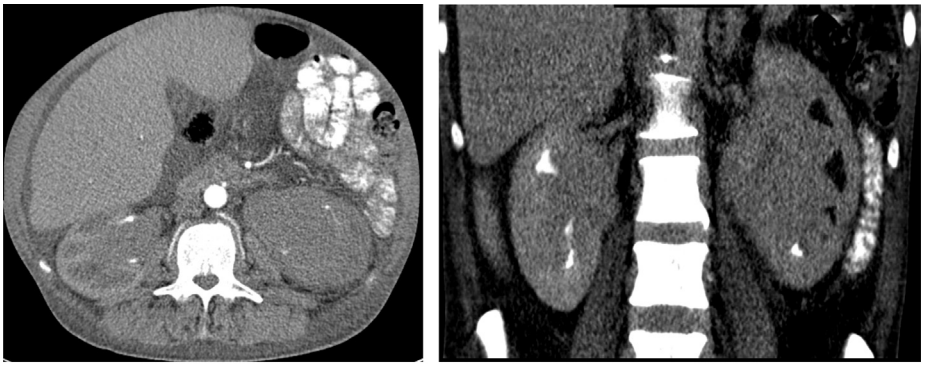

Fig. 3 Triphasic contrast enhanced CT scan (A) Axial nephrographic phase. (B) Coronal reformats in delayed excretory phase showing bilateral hypoattenuated expanding non enhancing soft tissue mass lesions in the area of the renal pelvises.

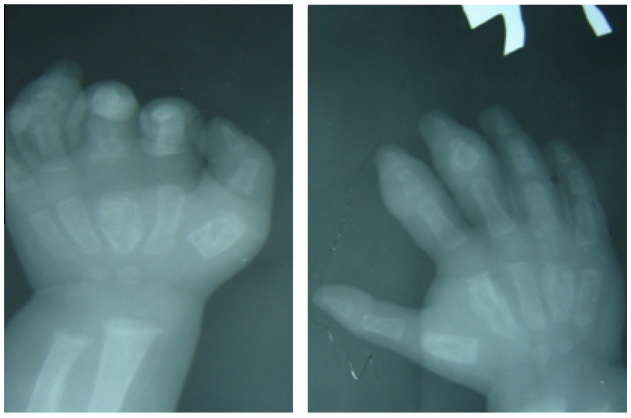

Fig. 4 Plain X ray of right (A) and left (B) hands of an infant showing typical findings of bilateral sickle cell dactylitis, seen as soft tissue swellings, metatarsal and phalangeal expansion and multiple osteopenic patches.

Hb S-tha diseases, it is still reported in considerable percentage of SCA patients (13). It may involve liver, spleen or paravertebral spaces, less likely kidneys, adrenal glands, and skin. Sectional imaging by computed tomography scan (CT) or magnetic resonance (MRI) can perfectly diagnose these masses. They usually show CT isodensity and intermediate signal intensity on both T1-weighted and T2-weighted MR images, with no or minimal post contrast enhancement. Sometimes, biopsy is mandatory to confirm the imaging diagnosis (13–17) Fig. 3.

Osteonecrosis (avascular necrosis or aseptic necrosis) due to ischemic bone insults is one of the most frequently encountered complications of SCA. Ischemia and consequent infarcts mainly involve the medullary cavities of the shafts and epiphyses of long bones, body of spinal vertebrae and pelvic bones. Also, it may involve small tubular bones of hands or feet, which is known as sickle cell dactylitis or hand-foot syndrome. This syndrome usually presents before peripheral skeleton fatty marrow transformation i.e. before the age of six. X ray of affected hands or feet can show soft tissue swelling with periosteal reaction 7–10 days after the onset of severe pain. Later on, it shows medullary expansion, cortical thinning and osseous lucent patches. It mainly involves the metacarpal/metatarsal bones and proximal phalanges. Usually, it is self-limited with spontaneous resolution in few weeks; however bone destruction and resultant deformity may be seen (9,18) Fig. 4.

X rays of AVN in long bone shafts show relative delayed findings of mixed lucent and sclerotic patches, sometimes associated with periostitis and periosteal reaction if the cortex is involved. MRI, which is the most sensitive tool, shows early positive findings that are usually simultaneous with the patient's complaint. First, it shows bone marrow edema as medullary T2w hyperintense and T1w hypointense signal. Shortly afterward, it will show serpentine geographic medullary patch of different sizes according to severity of insult, with T1 low signal and T2w hyperintense signal of granulation tissue surrounded by outer hypointense ring. This can be explained by the formation of central serpentine granulation tissue surrounded by sclerotic ring. Also, this granulation tissue may show enhancement in post contrast scans (9,12,19) Fig. 5.

AVN of long bones epiphysis is considered one of the common features of SCA. The femoral head is the most common site, followed by the humeral head. It can occur in a single or several bones at the same or different times. X ray is usually normal in the early stage of the disease or may show regional osteopenia. Afterward, it usually shows mixed lucent and sclerotic patches, crescent shaped subchondral lucency, collapse, fragmentation and eventually, secondary osteoarthritis (9,12,19). MRI is the most sensitive means of diagnosing

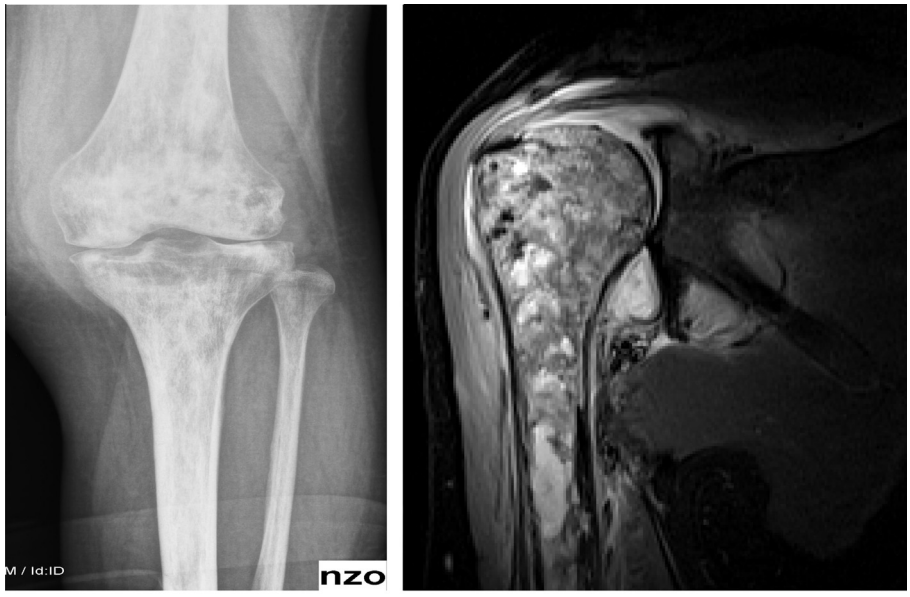

Fig. 5 (A) X ray AP of knee joint showing distal femoral and proximal tibial metadiaphyseal sclerotic patches. (B) Coronal STIR MRI of right shoulder showing extensive humeral head, metaphysis and upper shaft heterogeneous signal intensity, both due to osteonecrosis.

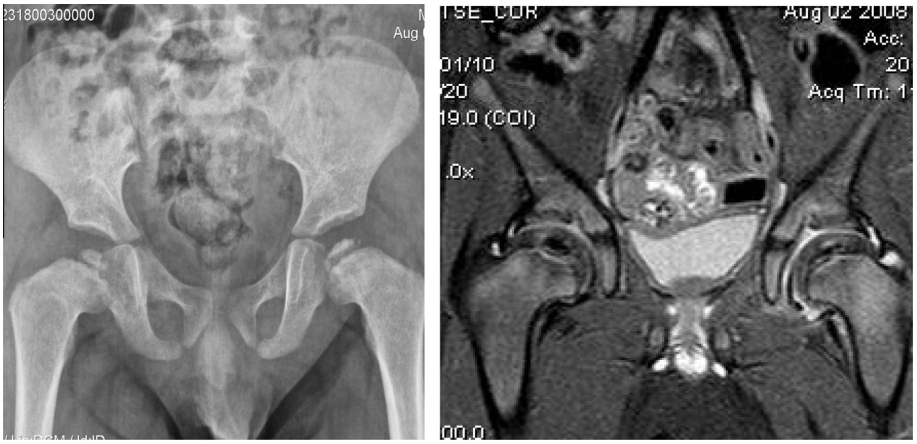

Fig. 6 Bilateral femoral head AVN. (A) Plain X ray AP pelvis showing bilateral femoral head collapse and sclerosis. (B) Coronal MRI STIR showing femoral head double line sign, collapse and secondary osteoarthritis of hip joints.

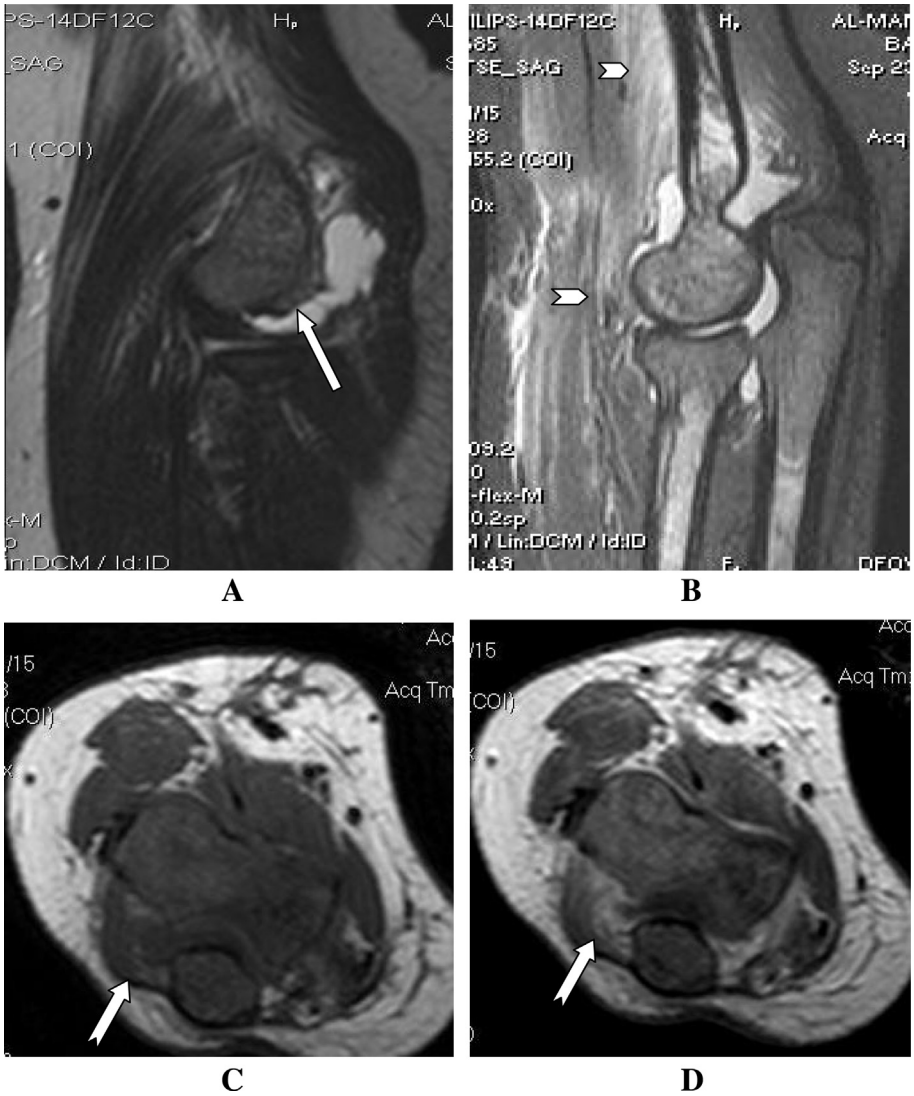

Fig. 7 MRI of young female patient with septic elbow arthritis: Sagittal T2w (A) Sagittal STIR (B), Axial T1w (C) and Axial T1w with contrast, showing joint effusion, marginal cortical destruction (Arrow in A), and synovial thickening showing post contrast enhancement (Notched arrows in C and D), extensive periarticular soft tissue edema (chevrons in B).

epiphyseal AVN, because it is indispensable for early diagnosis and accurate staging. MRI facilitates a better response to treatment because it helps early correct therapeutic application, avoiding complications of delayed diagnosis. MRI may also help and guide interventional procedures such as core decompression as well as judge and check therapeutic response (9,12,19) Fig. 6.

Osteomyilitis and septic arthritis are also common complications in patients with SCA. This may be due to immune compromised status of these patients and the presence of osteonecrotic lesions. Osteomyelitis and septic arthritis were reported in some researches to be 18% and 7% of SCA patients, respectively (9,20,21). Sometimes, differentiating acute osteomyelitis from osteonecrosis in SCA patients is difficult. Plain X ray and CT scan have a limited role in such differentiation, as the major positive signs could be shared by the two pathologies, like periosteal reaction and bone destruction. Also, paraosseous soft tissue and subperiosteal collection, which could be seen by Ultrasound (US) is not clear differentiating point. Even US guided aspiration and culturing the drained collection are not completely reliable, as blood culture was reported to be positive only in 50% of patients. According to variability of tracer uptake in different phases of AVN, also scintigraphy has limited specificity (9,21).

MRI is the most sensitive, specific and promising imaging tool of choice for such differentiation and early diagnosis. Regardless, there are some common shared signs like bone marrow and soft tissue edema, the pattern of enhancement in post contrast images is one of the major differentiating points. Those with osteomyelitis showed a thick, irregular ring enhancement around a non-enhancing center, while medullary infarction showed a long segmental serpiginous medullary enhancement. Also, the presence of sequestra, involucra and paraosseous abscess highly supports the diagnosis of osteomyelitis. So, it is now widely accepted, that MR imaging is the most sensitive and specific imaging tool for early diagnosis of AVN and osteomyelitis, more sensitive and specific than other tools, even scintigraphy. Osteomyelitis may develop on the top of predisposing infarct which makes it quite difficult to detect through imaging (9,21,22) Figs. 7 and 8.

2.2. Neurological complications

Cerebrovascular accidents (CVA) are the most common cerebral insults reported in SCA patients, accounting for about 12% of deaths in these patients. Vasculopathy of the major cerebral vessels is the main responsible pathology. CT angiography (CTA) or magnetic resonant angiography (MRA) or

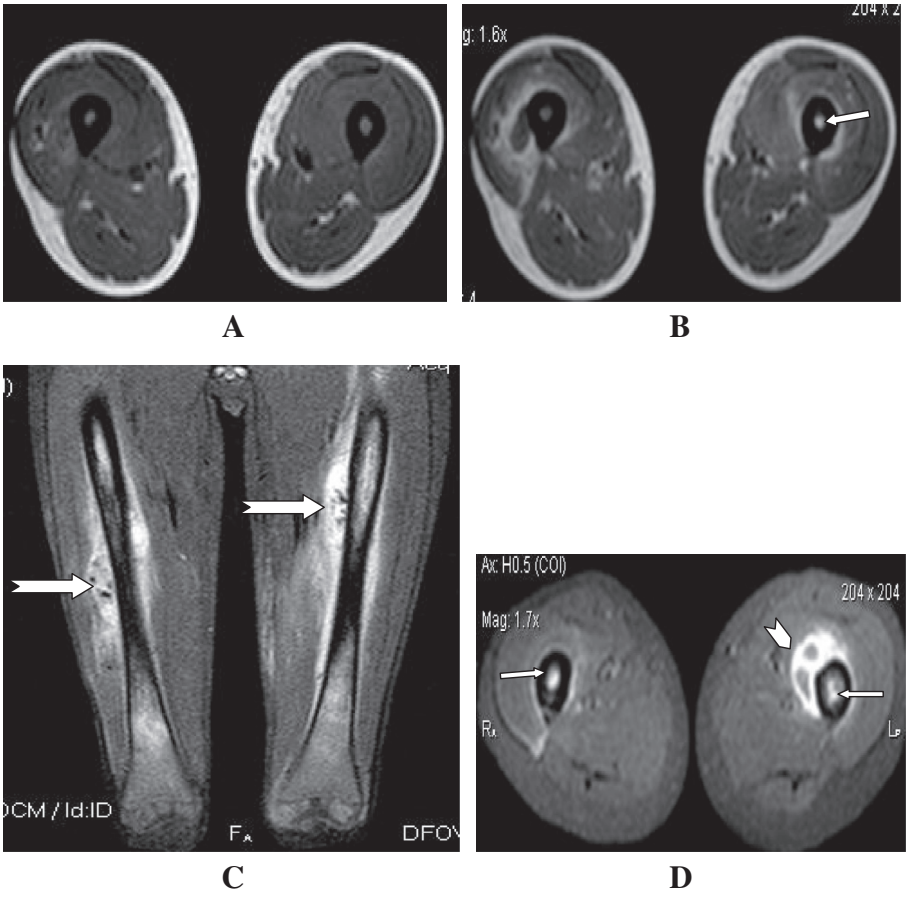

Fig. 8 MRI of bilateral femoral multifocal osteomyelitis. (A) Axial T1w. (B) Post-contrast axial T1w. (C) Coronal STIR. (D) Post-contrast axial T1w. Fat sat sequences, showing patchy enhancing medullary foci (arrows) and paraosseous extensive soft tissue edema (notched arrows) and ring enhancing collections (chevron).

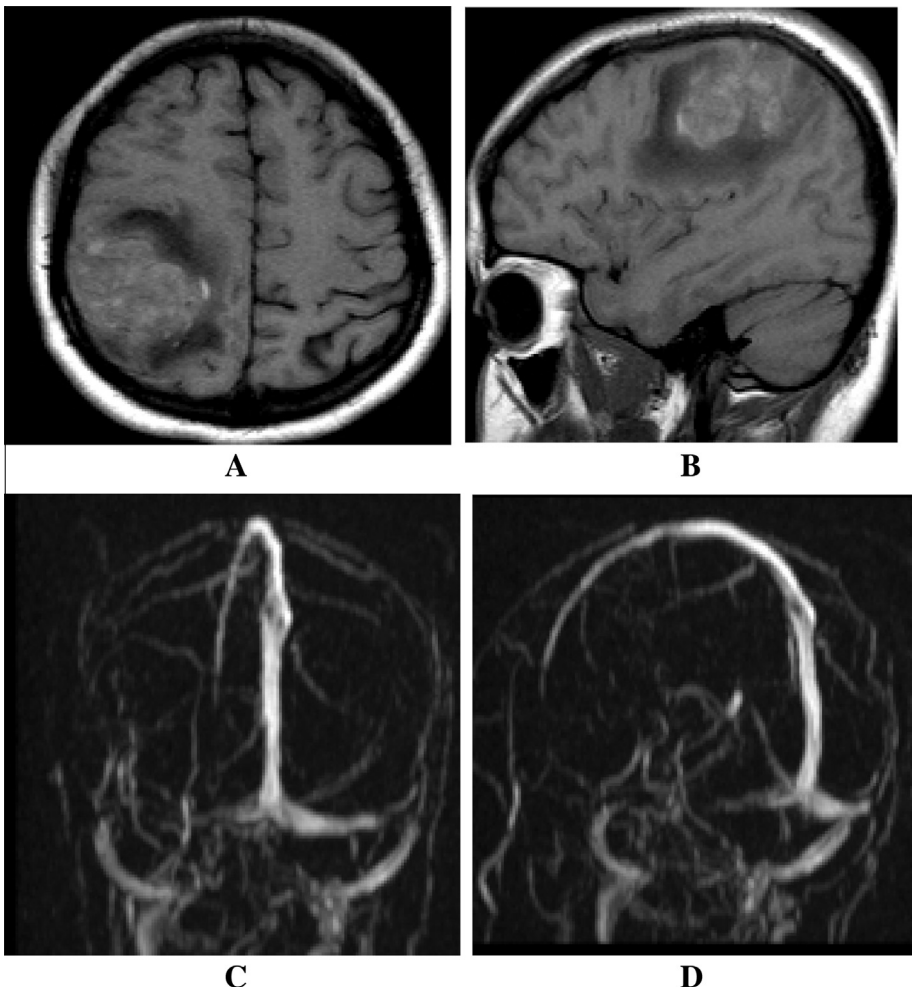

Fig. 9 MRI T1w axial (A) and Sagittal (B) show right high parietal hemorrhagic infarction. MRV coronal (C) and Sagittal (D) reformat clearly show right transverse sinus thrombosis, supporting diagnosis of hemorrhagic venous infarct.

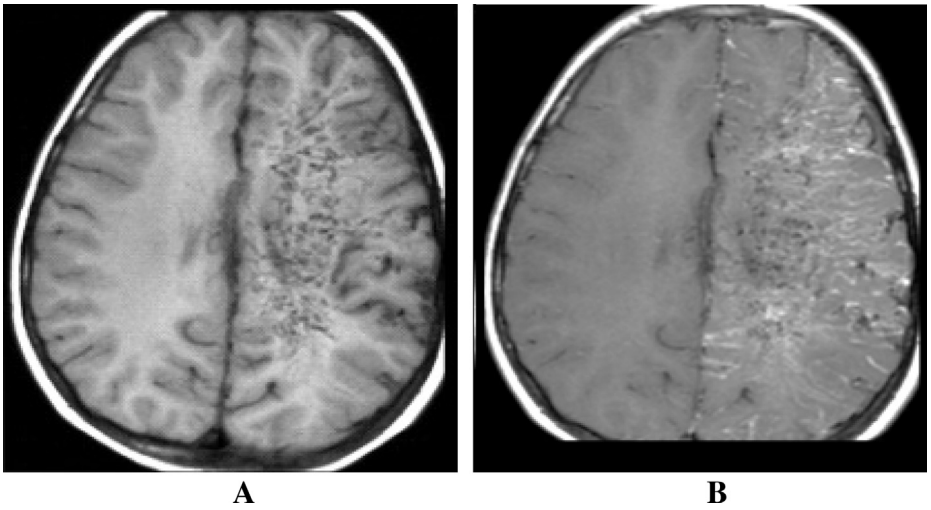

Fig. 10 MRI axial T1w sequence with (A) and without (B) contrast showing extensive left parietal intraaxial vascular collaterals secondary to left internal carotid ischemia (moyamoya).

conventional digital subtraction angiography (DSA) can show this cerebral vasculopathy as arterial tortuosity, stenosis or occlusion Fig. 9. Also, arterial intimal damage may be precipitated by a high velocity blood flow and the sickle RBC

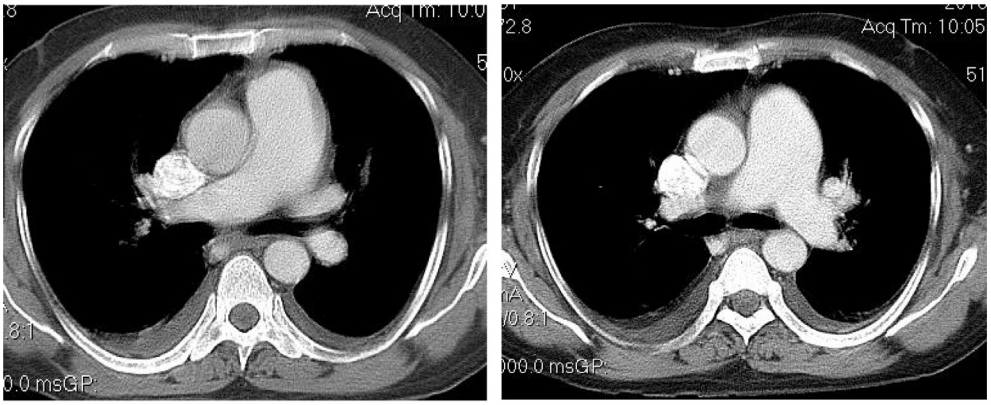

Fig. 11 (A and B) Axial IV contrast CT scan chest showing enlarged main pulmonary trunk and the major right and left divisions, consistent with pulmonary hypertension.

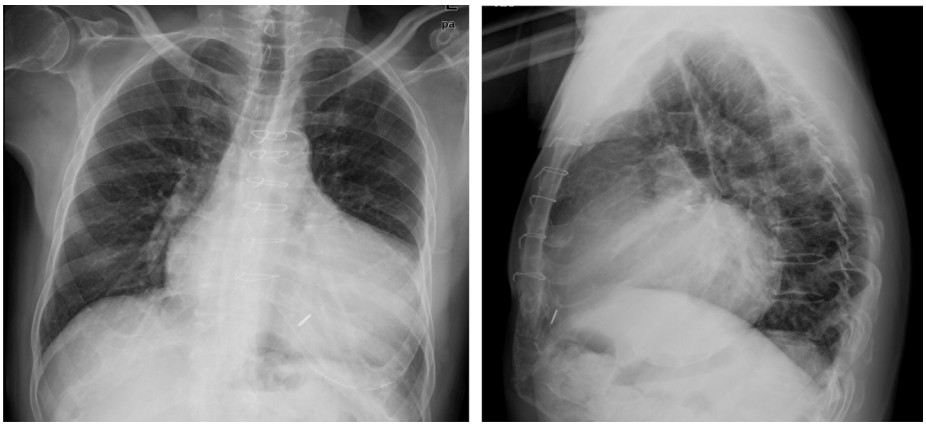

Fig. 12 (A) PA and (B) left lateral chest X ray showing segmental dilatation of the left ventricle due to post MI aneurysm (echo proven).

aggregates that permit the adherence of RBCs to the vascular endothelium leading to intimal hyperplasia, thrombosis or aneurysmal formation. Severe forms of intracranial arterial stenosis may cause chronic ischemia, which promotes development of many types of collateral, termed moyamoya which is a Japanese word meaning puff of smoke. It is a non-specific sign that could be seen in other types of chronic ischemia (23,24) Fig. 10.

2.3. Cardiovascular complications

Previously, owing to a short life span of SCA patients, there were no considerable recognized cardiovascular complications. However nowadays because of the relatively increased longevity of those patients, cardiovascular complications are more pronounced. The most frequent cardiovascular complications are pulmonary hypertension (PHT), myocardial infarct and heart failure (25).

Precapillary type of PHT, which may develop in older SCA patients, may be explained by the vasoconstrictive effect of the high-viscosity sickled RBCs in the pulmonary arterial circulation. Also, surgical splenectomy or functional asplenia, pulmonary thromboembolism, interstitial lung fibrosis, other vasoactive mediators such as placental growth factor and endothelin (ET)-1 may contribute to the development of PHT. Best diagnostic clue is dilatation of the central pulmonary arteries with rapid tapering and right ventricular hypertrophy, which is easily seen in plain chest X-ray. Also, it can be clearly identified in CT or CTA scans, in which accurate measures of the diameter of the main pulmonary artery can be done (Normally = 28.6 mm). It is measured at the site of the arterial bifurcation, perpendicular to long axis. Normally, the normal main pulmonary artery is smaller in diameter than the adjacent ascending aorta. MRI is less sensitive and technically difficult in these patients, because they are commonly dyspneic with difficult breath hold (25) Fig. 11.

Also, chronic anemia in SCA patients causes cardiac chamber dilation and a compensatory increase in left ventricular mass, which can be accurately estimated by Echocardiography. This is often accompanied by left ventricular diastolic dysfunction. Direct myocardial damage can occur in SCA patients without predisposing coronary artery diseases. This may be explained by the fact that disproportion between myocardial oxygen supply and demand results in myocardial ischemia and infarction. So, young SCA patients or even children may have ECG ischemic changes with reported cases of myocardial infarcts in children, with possible chronic complications e.g. ventricular aneurysms. This may be one of the possible

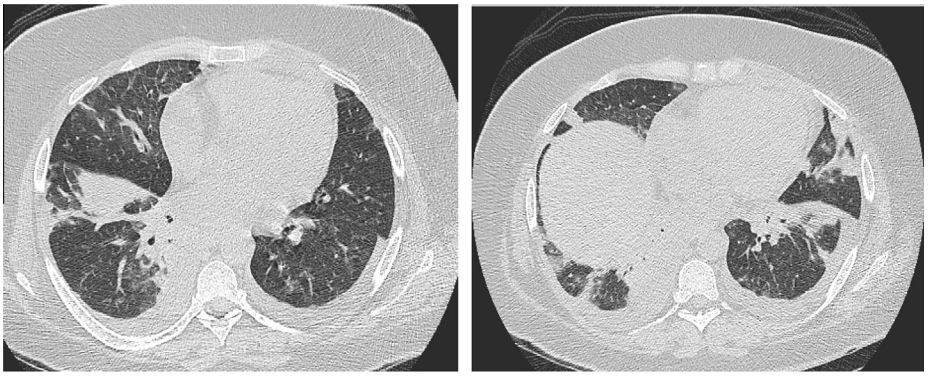

Fig. 13 HRCT scan (A and B) showing bilateral multiple infiltrates of ACS as well as bilateral pleural effusion.

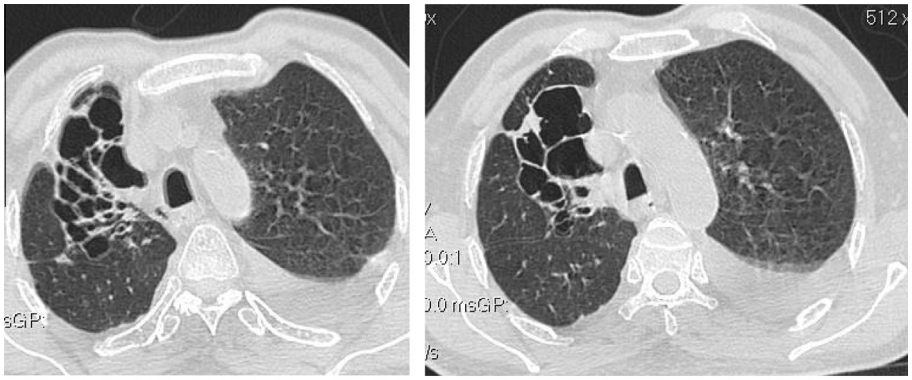

Fig. 14 (A and B) HRCT scan showing right upper lobar anterior segment cystic bronchiectatic changes.

etiologies of sudden death, which is an increasingly recognized problem among SCA patients, thus cardiac investigations are mandatory to recognize and treat high-risk patients (26,27) Fig. 12.

Multidetector CT scan (MDCT) and newly introduced fast MRI sequences had confidently replaced the previous widely used isotope scanning, in the diagnosis of MI. MDCT can provide additional helpful information about cardiac cavities' dimensions and wall thickness, as well as MI complications e.g. aneurysms or intracardiac thrombi. Also, MRI can show acute MI and accurately delineate the size of the infarct segment within 30 min of its outset. Infarct is seen as hyperintense myocardial edema on black-blood T2-weighted images (e.g. Half-Fourier, single-shot fast spin echo with double inversion recovery). MI diagnosis by MRI can be made well before classic troponin positive test. Flow up MRI studies can show the previously mentioned complications as well as a permanent myocardial scar, which is inevitable sequel of infarct, as an enhancing patch in delayed post contrast images (28,29).

2.4. Pulmonary complications

Acute chest syndrome (ACS) is one of the most common causes of hospitalization and even death of SCA patients. ACS is defined as a new pulmonary infiltrate on chest radiograph, associated with fever, cough, wheezes, dyspnea and tachypnea. There is no clear single pathogenesis of this syndrome; however multiple different factors (separate or combined) may be incriminated e.g. pulmonary fat embolism, hypoxemia and atelectasis due to shallow breath secondary to painful rib infarction, as well as pulmonary vascular obstruction. X ray shows single or multiple areas of pulmonary infiltrate mainly involving the middle and lower lobe airspace (30) Fig. 13.

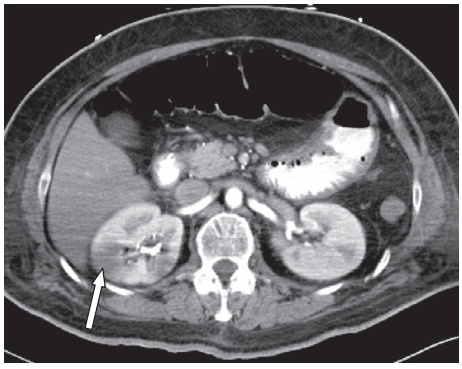

Fig. 15 Nephrographic phase contrast enhanced CT scan shows right renal wedge shaped cortical infarct (arrow).

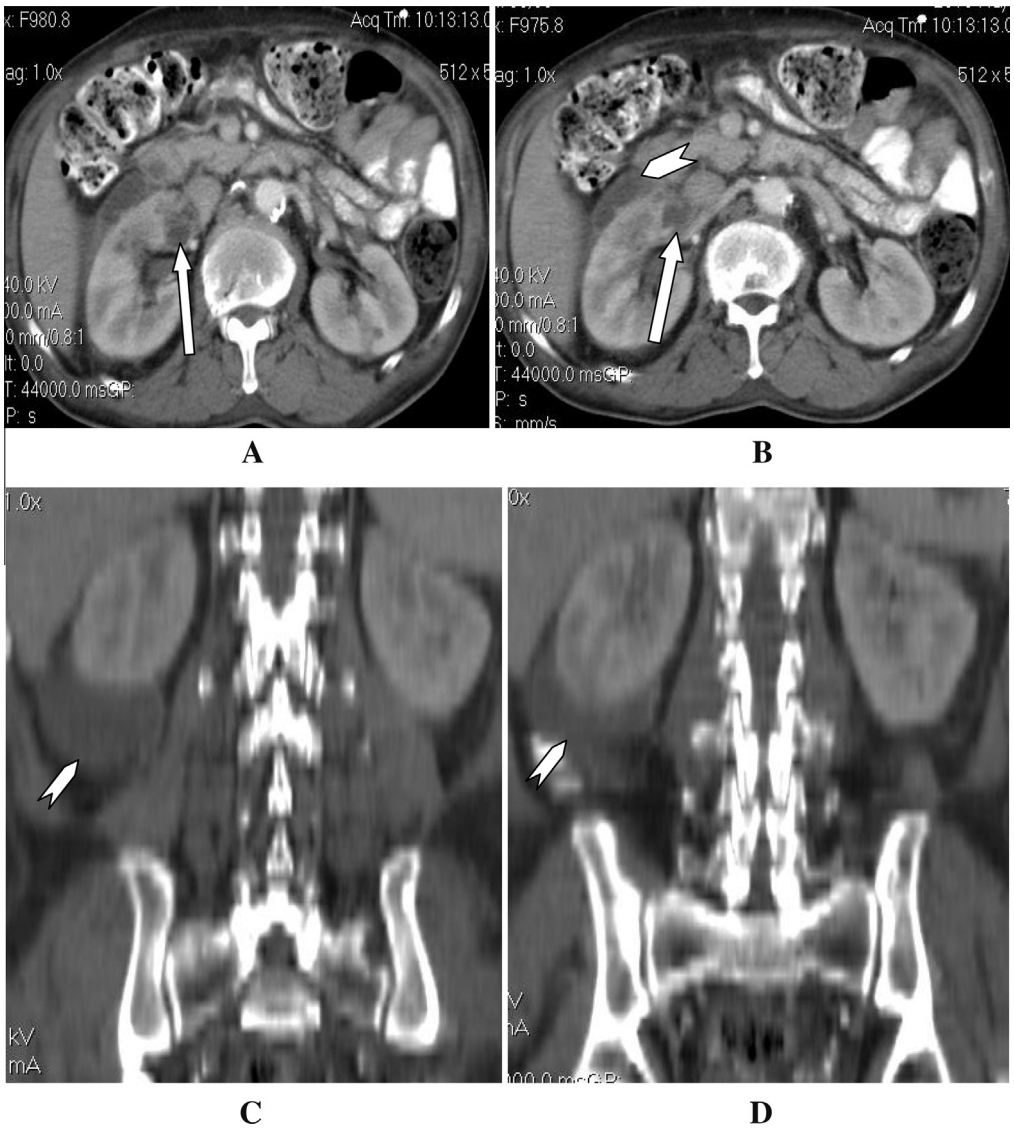

Fig. 16 Post contrast CT scan Axial (A and B) and coronal reformat (C and D) showing right renal upper polar carbuncle (Arrow) with massive perinephric collection (chevron).

Pleural effusion may be seen, however it does not help much to differentiate infectious from non-infectious causes of ACS. Non-infectious infiltrates will clear more rapidly than infectious ones, so, follow up chest X rays are recommended to monitor the resolution of the disease. Sputum and blood cultures should be done in non-resolved types to identify responsible bacterial agents, if present. Also, fiberoptic bronchoscopy and broncho-alveolar lavage (BAL) can provide much help in the diagnosis of fatty embolism (30,31).

Patients with SCA may develop obstructive or restrictive lung diseases, when there is a progressive decline in the pulmonary functions after a preceding history of several attacks of acute chest syndrome. This may be explained by established fibrotic lung changes from repeated episodes of pulmonary infective and vaso-occlusive events. High resolution CT scan (HRCT) shows these interstitial changes, that are of reticular or reticulonodular pattern and may be associated with traction bronchiectasis (32) Fig. 14.

2.5. Renal complications

Sickle cell nephropathy is another debilitating complication of SCA, which develops as a result of sickling of RBCs in renal circulation. This leads to ischemia causing cortical infarctions and papillary necrosis, as well as renal tubular injury Fig. 15. It may be associated with proteinuria, nephrotic syndrome, azotemia, hyperuricemia, uremia and finally renal failure. US is a good diagnostic imaging modality for nephropathic changes, as it shows cortical echogenicity accentuation, loss of corticomedullary differentiation, increased resistive index (RI) on Doppler examination and shrunken size. The deterioration in renal function tests with decreased creatinine clearance are the most important landmarks and may precede or be disproportionate to imaging findings. Also, there is a possible superadded bacterial infection of the scarred renal tissues and functional tubule abnormalities in conjunction with the

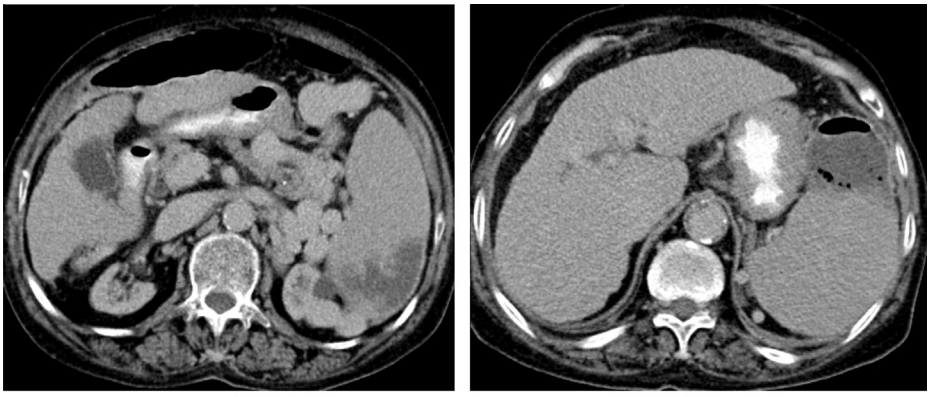

Fig. 17 Non contrast CT scan in two different SCA patients showing splenic infarct (A), seen as capsular based irregular triangular shaped hypodense patch (Arrow) and splenic abscess (B), seen as splenic cystic swelling showing air fluid levels (arrow).

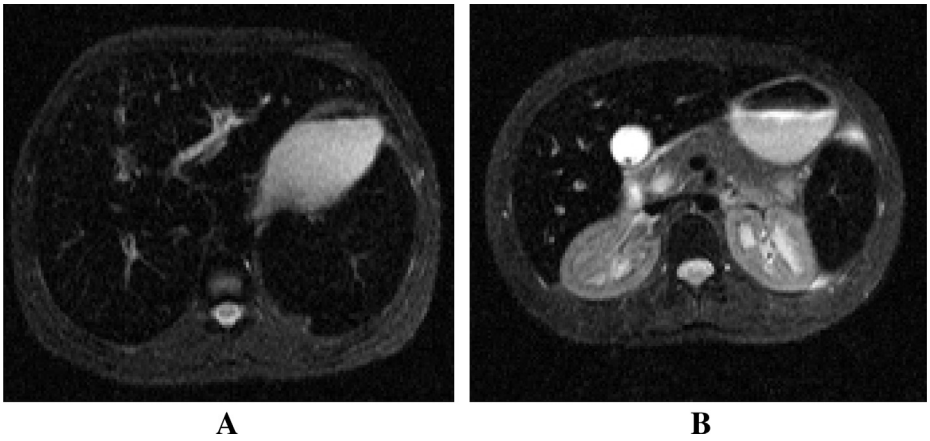

Fig. 18 (A and B) Axial fat-saturated fast spin-echo (SE) T2-weighted MR image shows the significant hypointense signal of the liver and spleen, sparing the kidneys and pancreas, supporting diagnosis of secondary hemochromatosis.

compromised immunity, leading to suppuration and sometimes abscess formation (33,34) Fig. 16.

2.6. Abdominal complications

2.6.1. Spleen

Sickle cell clots cause ischemic vascular occlusion, which frequently affects different parts of the abdominal structures. The most commonly involved organ is the spleen, which is affected in almost all patients with SCA. Repeated splenic infarctions that start within the first 18–36 months of life, in association with the dates of disappearance of protective Hb F, result in hyposplenism or even asplenism. Splenic atrophy is a major etiology of compromised immune status of these patients and increased susceptibility to infections (35,36) Fig. 17A.

Splenic infarction usually presents with left upper quadrant pain and sometimes nausea, vomiting, friction rub over the splenic area, and leukocytosis. Imaging appearance of splenic infarction depends on the timing of imaging and the size of the infarct. In well-established cases both ultrasound and CT are almost equally sensitive, however in early acute stage, contrast enhanced CT scan is the most sensitive tool of imaging. The typical infarct is seen as a hypodense non- or poorly enhancing wedge, with apex pointing toward the hilum. Later on, these infarcts may resolve completely or leave a permanent scar seen as contracted segment, or liquefy with possible abscess formation. Also, multiple small infarcts or global infarct of the whole spleen are reported in the imaging findings (37–39) Fig. 17B.

2.6.2. Liver

Liver infarction in SCD was reported in 34% of autopsies. Regardless the dual hepatic blood supply, the sickle blood high viscosity predisposes to infarction. Acute sickle hepatic crisis affects about 10% of patients admitted for painful crisis. It usually simulates acute cholecystitis with right upper quadrant pain, fever and leucocytosis, however unlike cholecystitis; the liver is enlarged and tender. Intrahepatic cholestasis is rare; however it is considered severe and may be a fatal form of hepatic crisis due to acute massive hyperbilirubinemia. MDCT is the most sensitive imaging tool for the diagnosis of these insults (40,41).

Mainly, chronic liver disease in SCA is due to the development of secondary hemochromatosis or hepatitis, which may lead to end stage hepatic cirrhosis, even among young patients.

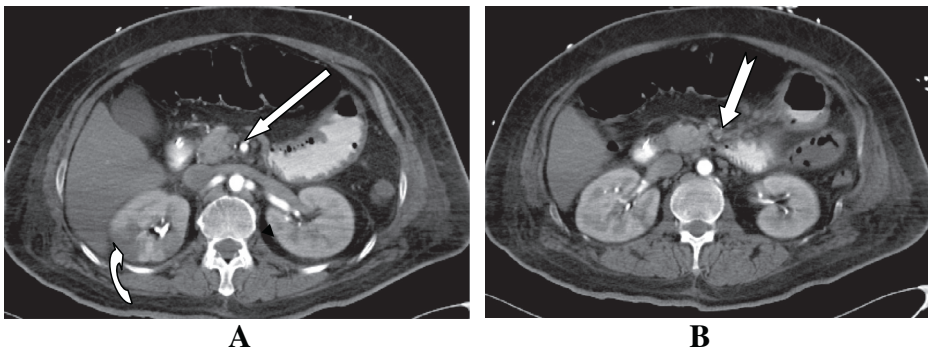

Fig. 19 Arterial phase contrast enhanced CT scan abdomen shows: (A) Normal filling of the celiac artery (arrow) and (B) lack of filling of the thrombosed superior mesenteric artery (notched arrow). Right renal cortical infarct is seen as well (curved arrow in A).

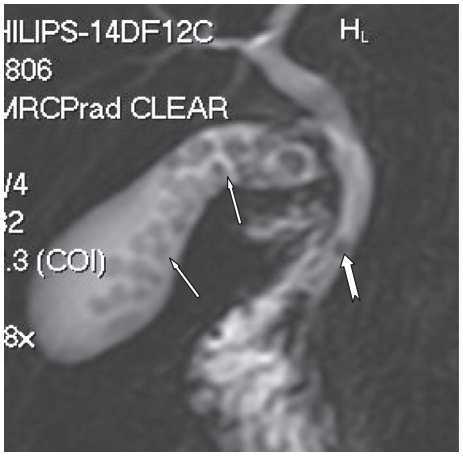

Fig. 20 MRCP showing multiple small gall stones (arrows) and CBD stone (notched arrow) with minimal CBD dilatation.

It is considered one of the major causes of high mortality scores among SCA patients. Hepatic hemochromatosis is due to hepatic iron overload secondary to excessive accumulation of transfused iron leading to increased total body content of iron to 50–60 gm. (normally, less than 6 gm.) This is explained by increased gastrointestinal absorption as a result of intensive erythropoiesis, and continuous hemolysis. Non contrast CT scan shows homogeneously increased liver density (75–135 HU (normal 45–65 HU)). MR findings are generalized decrease of signal intensity of the liver and spleen in T1w and T2w images. Involvement of the spleen differentiates this type of secondary hemochromatosis from primary type, in which the spleen is spared (42) Fig. 18.

2.6.3. Mesenteric vaso-occlusive crisis

Though it is not so common, mesenteric arterial or venous thrombosis could be a life-threatening complication of SCA. After, the advent of MDCT scan, CTA is now considered the diagnostic tool of choice for this insult with high sensitivity scores. This is because; MDCT allows rapid volumetric data acquisition allowing perfect spatial resolution of large anatomic volume. From these data, retrospective post-processing is done with application of one or more reformat software e.g. Multiplanar reformat (MPR), maximum intensity projection (MIP), curved multiplanar reformatted images (CMPR) and 3D volume rendering (VR) visualization. These applications significantly increase the sensitivity of the images to approximate or even it may overcome the results of invasive conventional angiography, which was previously considered the ideal tool of investigation. CTA was reported in some studies to have a specificity of 94% with a sensitivity of 96% in the diagnosis of such mesenteric vaso-occlusive insults (43,44) Fig. 19.

2.6.4. Gall bladder

A high incidence of gall bladder multiple pigmented gall stones is clearly demonstrated among SCA patients due to high bilirubin levels. Ultrasound is sufficient for the diagnosis of these stones, except if complicated by biliary tree or CBD obstruction, then MRCP is recommended for the diagnosis (45) Fig. 20.

2.6.5. Sequestration syndrome

It is rapid pooling of the blood within solid organs, commonly the spleen, less commonly the liver, causing acute organomegaly. If this sequestration happens, it definitely occurs before the development of hyposplenism. This pooling, in turn, results in intravascular volume depletion and depreciation of hematocrit values (a drop of >2 g/dL is considered significant). If severe, children may present with a rapidly enlarging spleen, abdominal fullness, pallor, tachycardia, and tachypnea. Fulminant cardiovascular crisis is the expected fate of suddenly resolved sequestration, due to rapid rise in Hb with resultant hypervolemia, heart failure, and intracerebral hemorrhage. Therefore, the diagnosis of sequestration syndrome must be considered in a child with any of the above symptoms or signs, especially the unexplained acute splenic enlargement. Lifesaving treatment consists of blood transfusion, or the infrequently applied splenectomy (46).

2.6.6. Less common complications

Acute pancreatitis may develop with or without clear predisposing factors e.g. gall stones. If there is no clear predisposing factor, it may be a result of microvascular occlusion and ischemic injury. Non-doubtfully, CECT scan is the most reliable imaging tool of acute pancreatitis with accurate determination of the degree of severity, according to the widely used Balthazar grading system. This imaging grading score guides

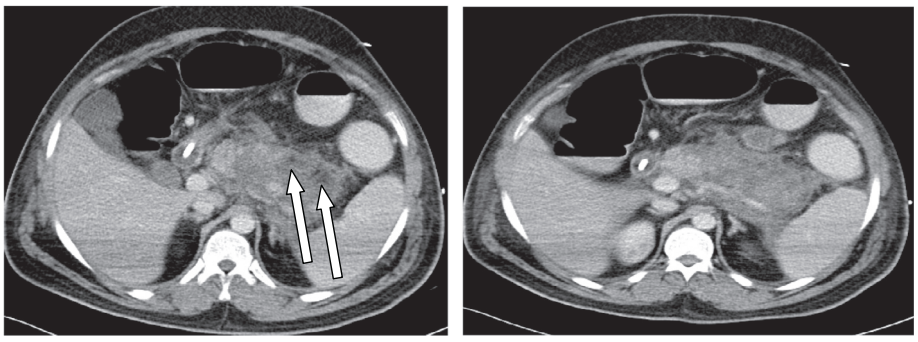

Fig. 21 (A and B) CT scan with IV contrast shows severe diffuse pancreatic swelling with heterogeneous patchy enhancement and multiple non enhancing necrotic foci (arrows).

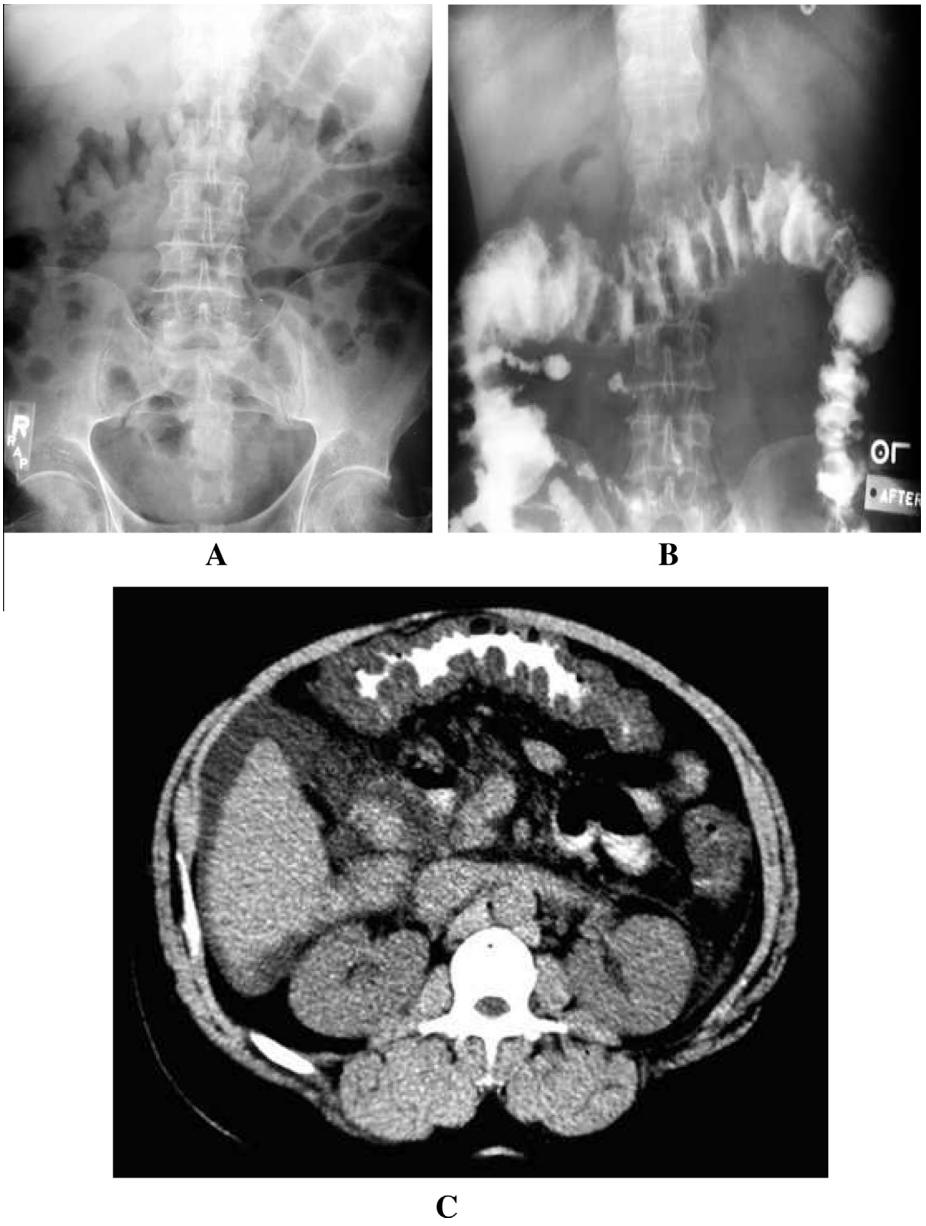

Fig. 22 (A) Frontal abdominal radiograph showing nodular haustral thickening, (B) Barium enema showing serrated appearance of transverse colon and (C) CT scan showing the classic accordion sign of pseudomembranous colitis (52).

the management of acute pancreatitis, whether conservative or interventional, according to the degree of severity and complications that may rapidly develop e.g. abscess, splenic or mesenteric vein thrombosis. Also, CT scan can detect possible chronic complications on delayed examinations, like chronic pancreatitis or pseudocysts (47) Fig. 21.

Peptic ulcer is infrequently encountered in patients with SCA, however it is characteristically not associated with high acid outputs. This may suggest chronic mucosal ischemic insult as possible etiology, so it is resistant to medical treatment (48). Reports of uncommon colonic abnormalities include acute necrotizing colitis in adults, pseudomembranous colitis (PMC) in a child, ischemic colitis, and life threatening toxic megacolon. Pathogenesis of these inflammatory complications seems also to be due to intestinal ischemic microvascular occlusion (49). Barium enema is contraindicated for imaging of these intestinal lesions, if associated with acute abdomen due to a high risk of perforation. CECT with oral water soluble contrast is the imaging tool of choice, and may show a long segmental intestinal wall thickening which is irregular and shaggy, compared to symmetrical homogeneous pattern in Crohn's disease. Also, it may show the famous accordion sign which represents trapped contrast between thickened edematous colonic haustral folds (50) Fig. 22 (51).

3. Treatment of SCA

So far, SCA has no definite curative therapy, however the different therapeutic tools are applied in an attempt to relieve symptoms and treat complications. Blood and marrow stem cell transplants still have lower successful indices, with reported many complications and high rejection scores of non-matching donor's stem cells. However this stem cell transplant is still the only promising curative therapy for those children suffering from SCA. Regardless, it is still not a recommended therapeutic option for adults; researches are going-on for covering older age groups (51).

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