

Sickle cell anemia - a review of the imaging findings

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Authors: E. Rosado, P. Paixao, W. Schmitt, D. Penha, F. M. P. D. Carvalho, A. Tavares; Amadora/PT
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Learning objectives

To review and describe the manifestations of sickle cell anemia, focusing on the typical imaging findings in the most frequent affected organs.

Background

Sickle cell anemia is an autosomal recessive genetic condition characterized by a defective form of hemoglobin (hemoglobin S), which promotes the aggregation and distortion of red blood cells. Anemia results from the rapid removal of the abnormal red blood cells by the reticuloendothelial system. Another consequence of the presence of abnormal circulating cells is the obstruction of microcirculation, producing ischemia and infarction. Infarcts are common in several organs and they are responsible for most clinical and radiological manifestations.

Findings and procedure details

Sickle cell anemia can affect several organs and systems. Acute vaso-occlusive crisis are the most common and earliest clinical manifestation, usually appearing in the paediatric age. Although bones, brain, lungs and spleen are usually affected, vaso-occlusive crisis may occur in almost any organ. In the following section we will describe most relevant manifestations of sickle cell anemia in the major anatomic areas.

1. Thoracic manifestations

The lungs are frequently involved, with infarcts, emboli and increased propensity to pneumonia. Pneumonia is much more common in patients with sickle cell anemia than in general paediatric population. Most common agents are *Streptococcus pneumoniae*, *Hemophilus influenzae*, *Staphylococcus aureus*, *Chlamydia pneumoniae* and *Salmonella* species. Chest radiographs show a consolidation that help to confirm the clinical diagnosis (Fig.1). Pneumonia may lead to acute chest syndrome, which pathogenesis is probably related to infectious agents or fat emboli from an infarcting bone. Its syndrome is characterized by a combination of fever, chest pain, cough, dyspnea and tachypnea, associated to consolidations in the chest radiograph, usually in the bases (Fig. 2). Acute chest syndrome may progress to respiratory distress syndrome and death. Pleural effusion is very common either associated to pneumonia or acute chest syndrome (Fig. 3 and 4). Repeated episodes of pulmonary insults may lead to chronic pulmonary disease,

which consists of pulmonary fibrosis. Radiological findings include a reticular pattern and at CT septal thickening, traction bronchiectasis and architectural distortion are visible.

2. Musculoskeletal manifestations

Red cell destruction in sickle cell anemia results in increased production of red blood cells in the bone marrow. Thus, appendicular red marrow persists throughout life. In infants, red marrow extends to all bones, including little bones of hands and feet. In older children it persists in the ankles, wrists and shafts of long bones.

Infarction is the main manifestation of sickle cell anemia, and it may occur anywhere in the skeleton. It results directly from the sickling of the red blood cells in the bone marrow, and typically occurs in the medullary cavities and epiphyses. In infants infarction often occurs in the diaphysis of small tubular bones of hands and feet as a result of the presence of red marrow in these regions. It provokes a dactylitis called "hand-foot syndrome".

Epiphyseal necrosis is common and is frequently seen in the femoral and humeral heads. It is often bilateral. Radiographic signs include lucency and sclerosis within the epiphysis. Later, crescent-shaped subchondral lucencies develop and eventually, depression of the articular surface, collapse, and fragmentation occur (Fig. 5). MR images demonstrate changes earlier. T2-weighted inversion recovery images show regions of high signal intensity indicative of bone marrow edema. T2-weighted images may show the "double line" sign, a serpiginous double line that consists of a hyperintense inner border and hypointense periphery. In weight-bearing joints such as the hip, secondary degenerative changes usually follow collapse (Fig. 5).

Infarction of the long bones is also common both in children and adults. Acute infarcts cause lytic changes. Later, patchy intramedullary lytic and sclerotic areas become evident (Fig. 6). If cortical bone is also infarcted, subperiosteal new bone may form, producing periosteal reaction (Fig. 7 and 8) and thickening of the cortex, causing a laminated, "bone-within-bone" appearance (Fig. 9).

In the spine, infarction of the central growth plate of the vertebral bodies cause endplate depressions. As a consequence, multiple vertebrae become H-shaped (Fig. 10).

Osteomyelitis and septic arthritis are frequent and serious complications of sickle cell disease. It is most common in the diaphysis of femur, tibia and humerus. Vertebrae may also be involved. The most commonly encountered organism is *Salmonella*, followed by *Staphylococcus aureus*. The clinical features are similar to those of painful bone crisis, and differentiation of infection from infarction may be challenging. Radiographic findings features are also nonspecific and initially are often normal. Signs of periosteal inflammation, osteopenia and sclerosis may take 8 to 10 days to become evident and are seen both in infarction and infection. Ultrasonography may be useful on characterization of soft-tissue changes and fluid collections. Although a small volume of pure-fluid may

be expectable adjacent to infarcted bone, a larger, non-pure fluid collection favors the diagnosis of osteomyelitis (Fig. 11). Nuclear medicine may also play an important role in differentiation of these two entities, by means of radiolabeled leukocyte imaging and ^{99m}Tc sulfur colloid scintigraphy. MR imaging is important because it is capable to show pathologic changes before they are visible in radiographs. T2-weighted fat-saturated sequences show fluid collections as area of high signal intensity, with or without sequestra. Contrast-enhanced T1-weighted sequences demonstrate peripheral bone marrow enhancement around as non-enhancing center. Septic arthritis is less common than osteomyelitis and often arises in conjunction with bone infarction.

Painful crisis may also involve skeletal muscle and soft tissue. Vascular occlusion may lead to inflammation, edema and necrosis. Ultrasound and MR imaging are the best methods for characterization of muscle and soft tissue changes.

3. Abdominal manifestations

Pigmented gallstones are the most common gastrointestinal manifestation of sickle cell anemia and are observed in around 50% of patients (Fig. 12). Gallstones are rare before 3 months of age and thereafter the incidence increases with age. Intrahepatic biliary duct stones and cholestasis may occur.

The spleen is also frequently involved. It has a slow, tortuous microcirculation that favours sickling of red blood cells and, as consequence, splenic infarctions are very common. Over time, multiple infarctions progress to autosplenectomy. At imaging, a small, calcified spleen is seen (Fig. 13). Another splenic complication is sequestration syndrome (Fig. 14). It consists of a rapid pooling of blood within the spleen, which becomes larger than expected for a child or adult with sickle cell anemia. Resulting intravascular volume depletion may progress rapidly to cardiovascular collapse and death.

The kidney is also susceptible for sickling of red blood cells and infarction, especially in the medulla, where vasa recta flow through a hypertonic interstitium. Capillary obliteration result in medullary and papillary necrosis. At imaging, up to 50% of patients have enlarged kidneys. At ultrasonography kidneys may have normal echogenicity, may be diffusely hyperechogenic or may have increased medullary echogenicity with normal cortical echogenicity (Fig. 15). Later in life, if renal failure develops, kidneys become small and hyperechogenic.

4. Central nervous system manifestations

In the brain, infarcts occur at young ages, causing atrophy and cognitive impairment. Infarcts in patients with sickle cell anemia are usually ischemic and tend to occur in the white matter, at the peripheral supply zones of the anterior cerebral and middle cerebral

arteries (Fig. 16). Silent infarction is twice as common as clinical infarction. MR imaging is the best technique for detection of both silent and clinical infarctions. Acute infarcts show low signal intensity on T1-weighted images and high signal intensity on T2-weighted images. Chronic infarcts are characterized by cystic cavitation, which results in further decrease in signal intensity on T1-weighted images and increase in signal intensity on T2-weighted images. The margins become better defined and focal atrophy, manifested by dilatation of adjacent sulci and ventricles, develops (Fig. 16).

Reduced cerebral blood flow after vascular occlusion may result in the development of fine collateral vessels. This process is named moyamoya for its angiographic appearance. It usually develops in talamoperforate and lenticulostriate arteries in response to occlusion of the distal internal carotid artery.

Propensity for aneurism formation is also characteristic. Aneurisms are usually multiple and approximately 30% originate in the posterior circulation. Manifestations include intraparenchymal and subarachnoid haemorrhage.

Images for this section:

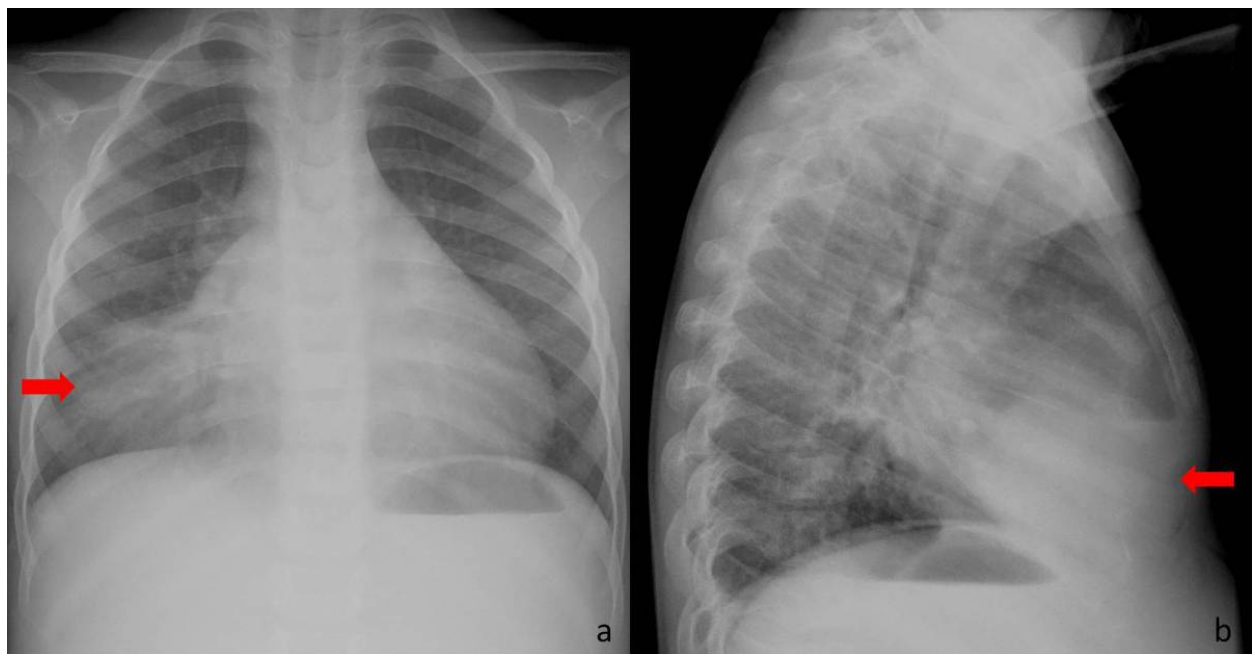


Fig. 1: Fig. 1: Frontal (a) and lateral (b) chest radiograph of a 4-year-old boy showing condensation of the middle lobe (arrow). Symptoms were suggestive of pneumonia.

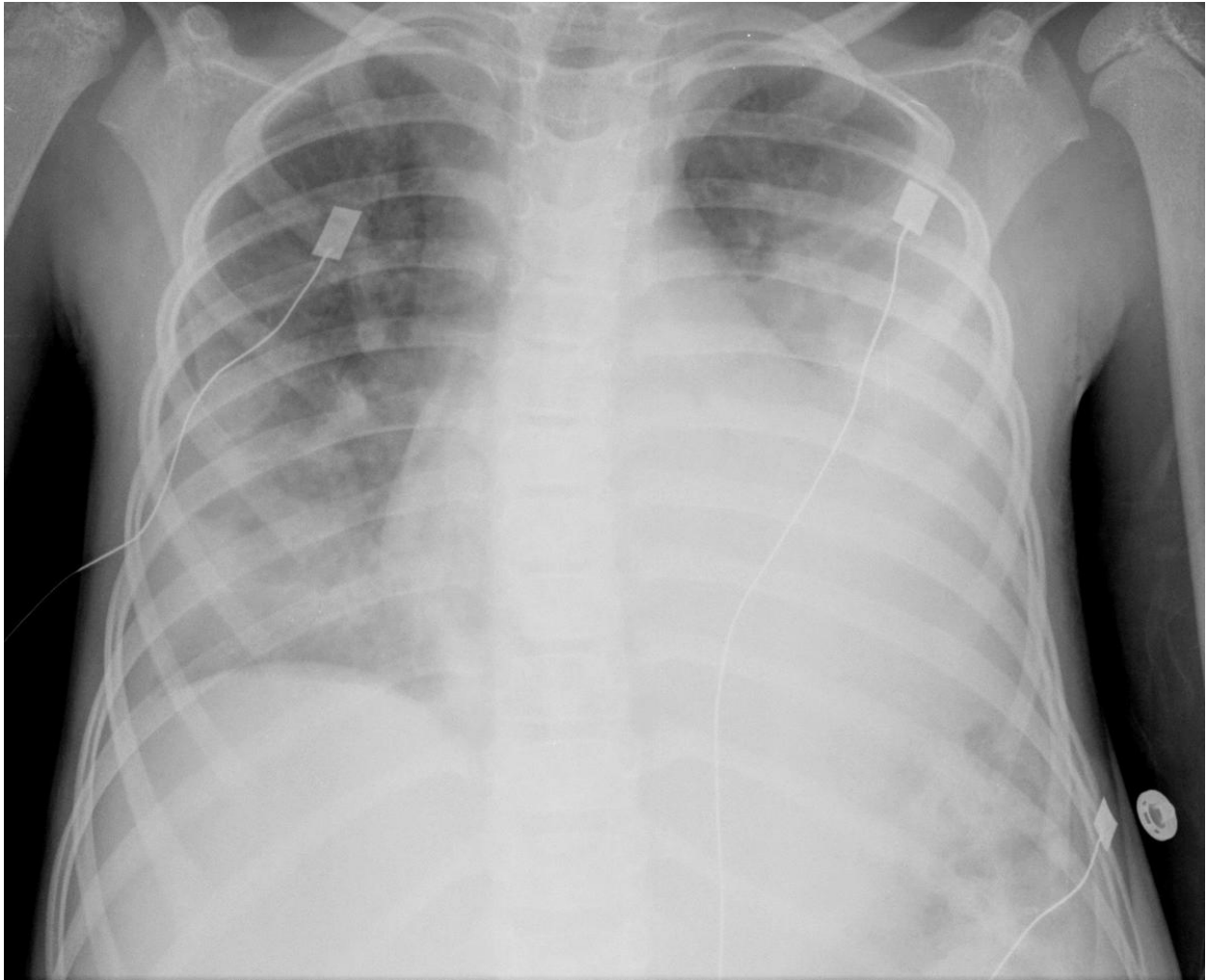


Fig. 2: Fig. 2: Frontal chest radiograph of a 6-year-old girl showing multiple and bilateral areas of parenchymal condensation. Clinical syndrome included fever, chest pain, dyspnea and hypoxemia, suggesting acute chest syndrome.

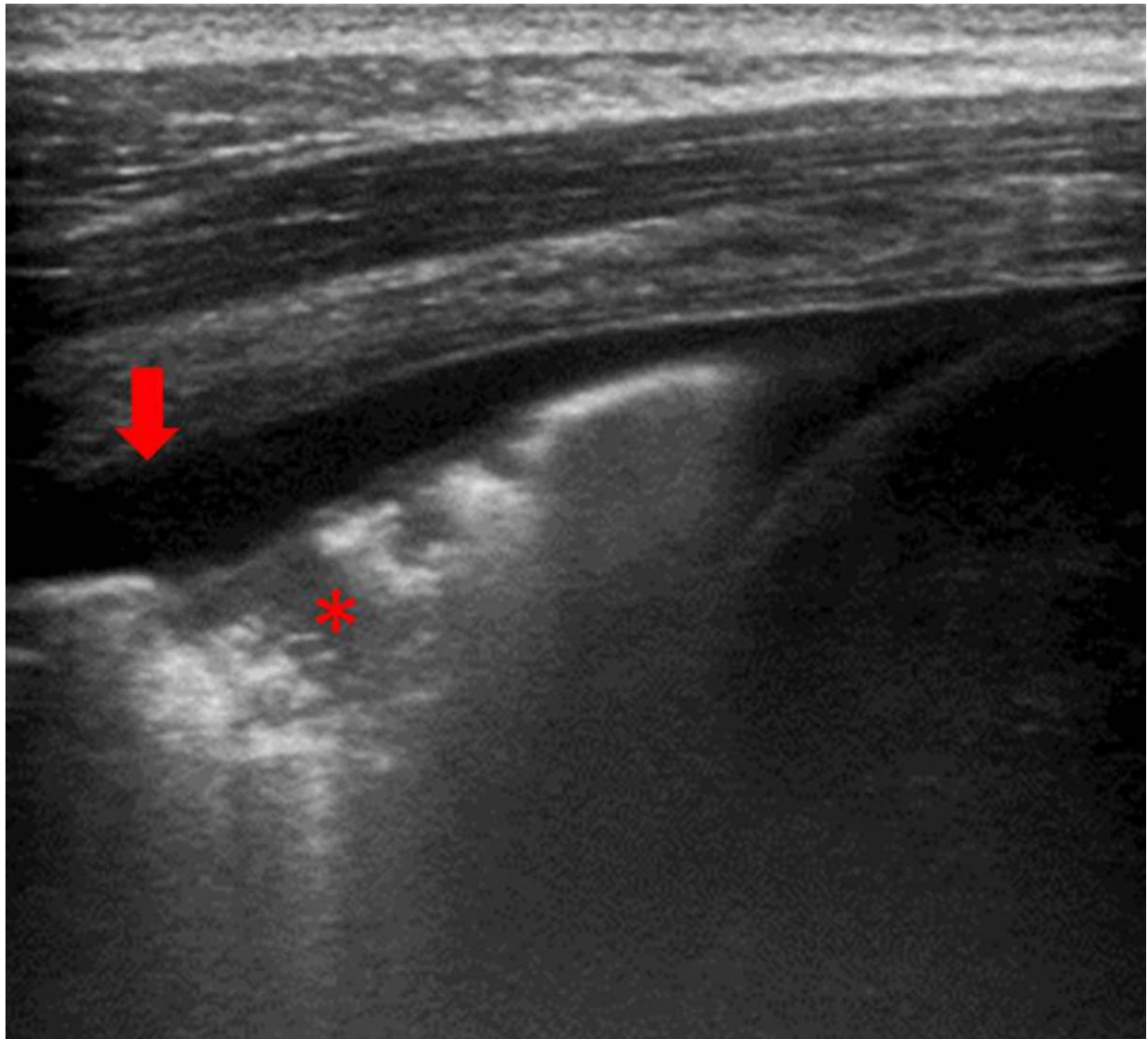


Fig. 3: Fig. 3: Thoracic ultrasound performed with a high-frequency probe in a 13-year-old girl with sickle cell anemia and symptoms of pneumonia. Pure fluid (arrow) is seen in the pleural space near the costo-phrenic angle. Lung subjacent to the pleural effusion is partially condensed (*)

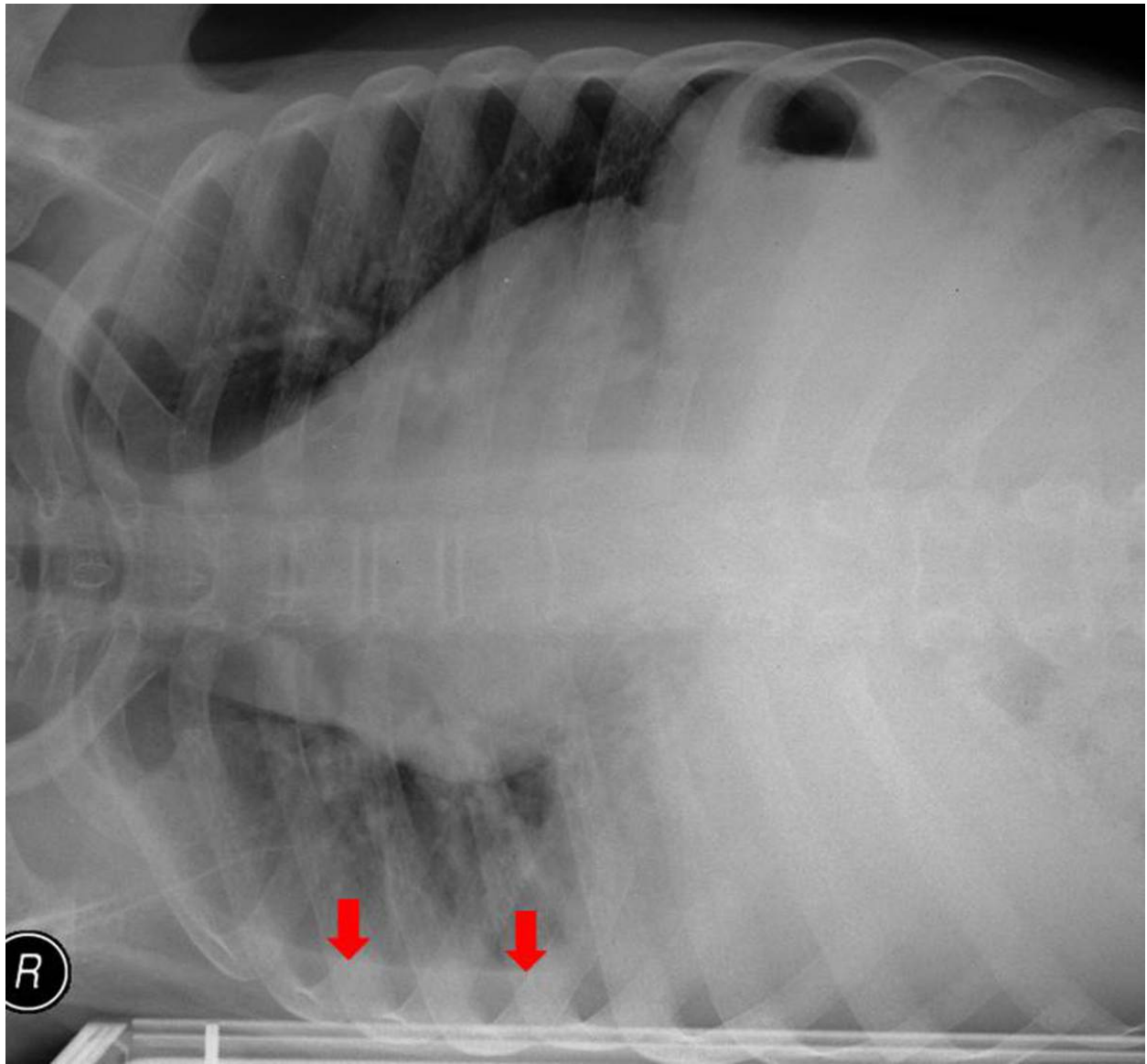


Fig. 4: Fig. 4: Right lateral decubitus chest radiography showing pleural effusion in the same young girl with sickle cell anemia shown in Fig. 3.

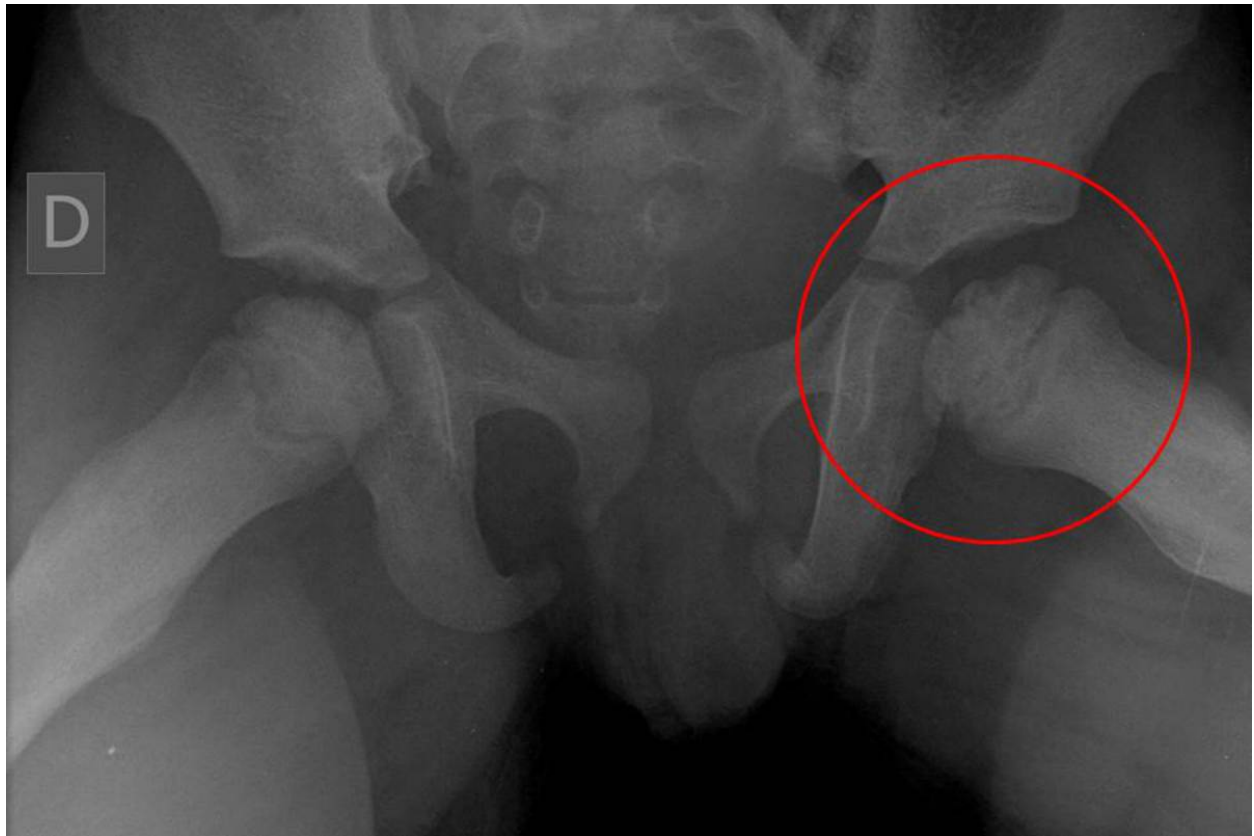


Fig. 5: Fig. 5: Plain radiograph of a 4-year-old boy with sickle cell anemia, showing left hip avascular necrosis (circle). Left femoral head has an irregular border and multiple lytic and sclerotic areas with a patchy distribution.



Fig. 6: Fig. 6: Plain radiograph showing lytic and sclerotic areas with a patchy distribution in the tibial shaft of a 7-year-old girl with history of infarction.

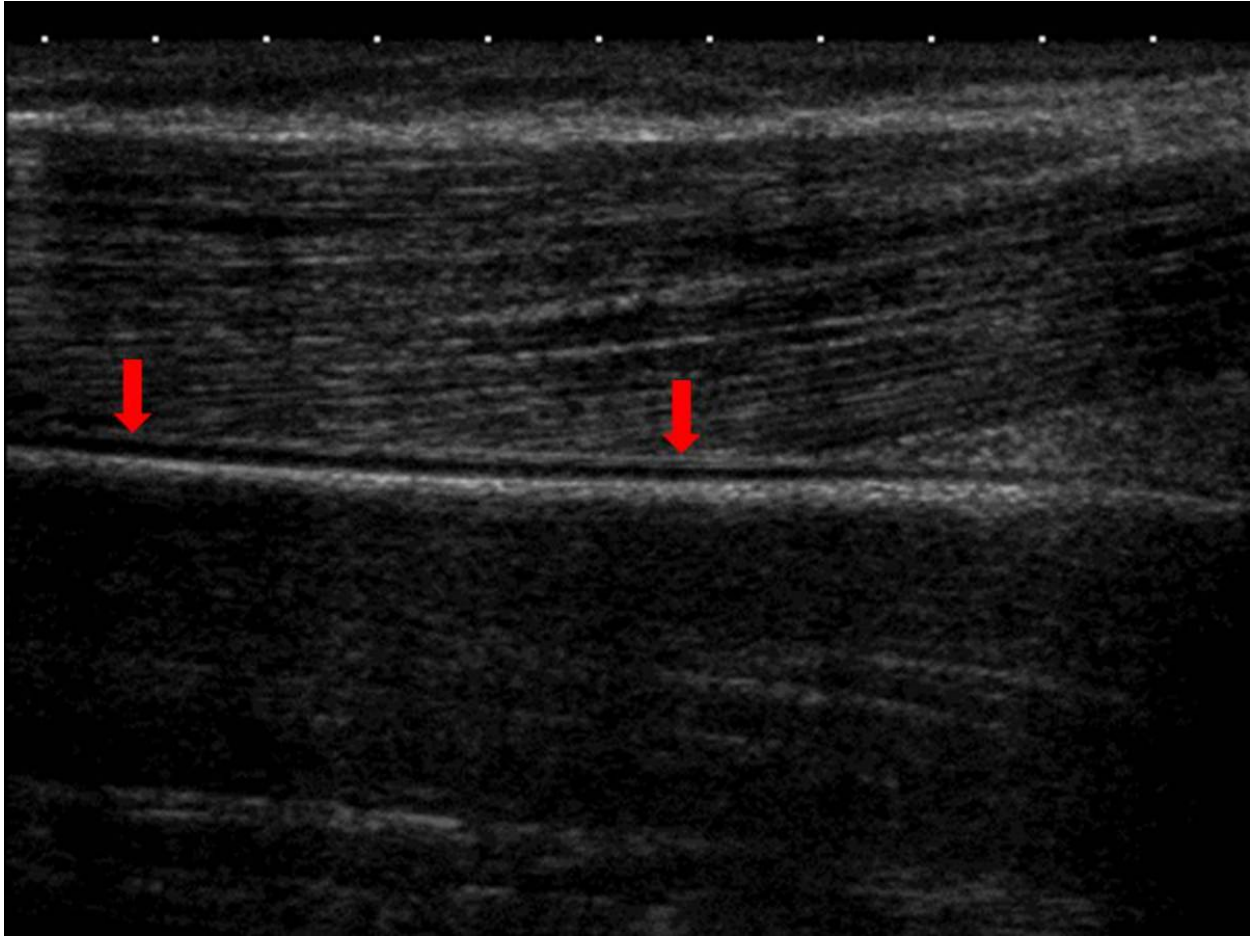


Fig. 7: Fig. 7: Musculoskeletal ultrasound performed with a high-frequency probe showing the tibial shaft of a 12-year-old boy with sickle cell anemia. The periosteum is separated from the tibial cortex (between the arrows).

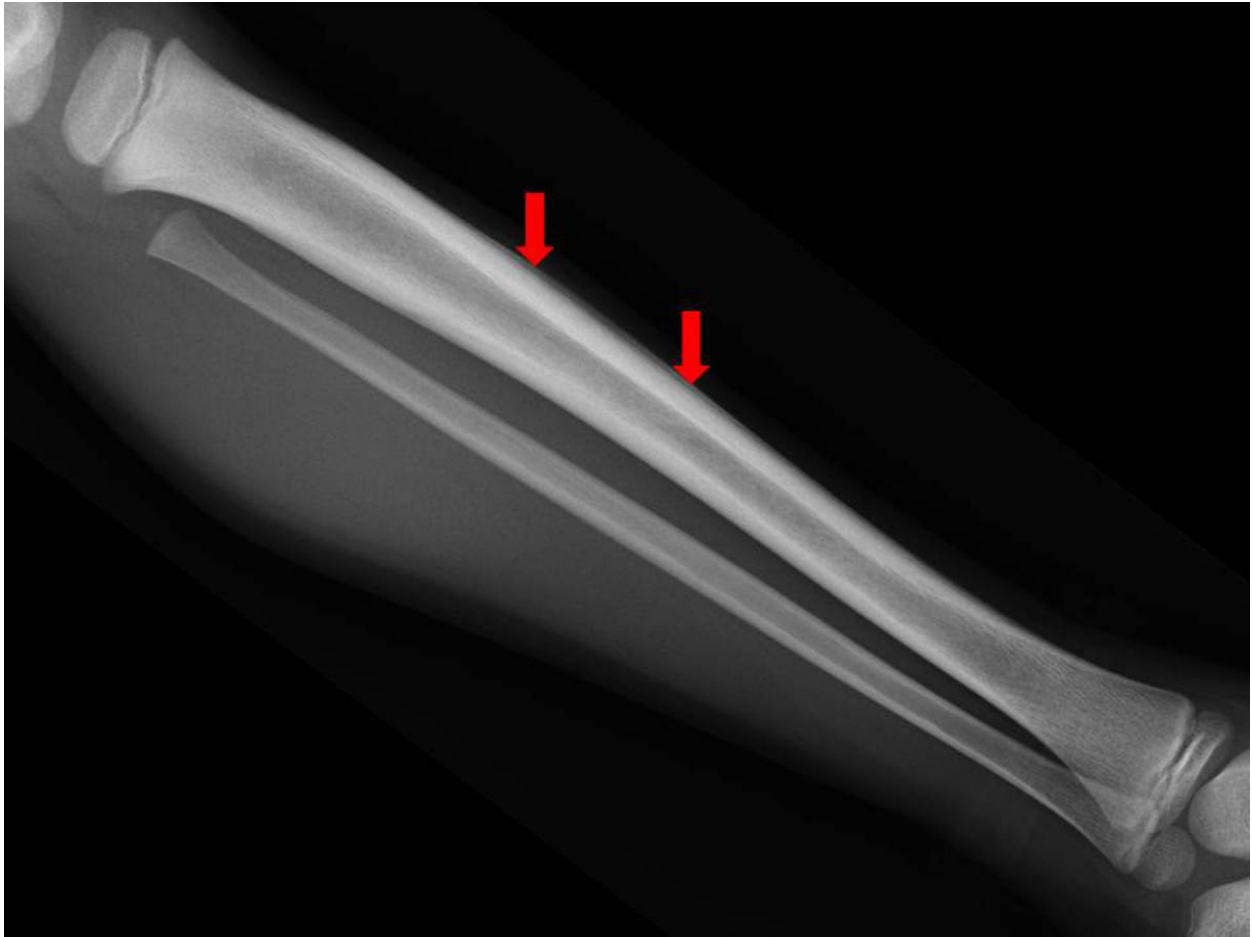


Fig. 8: Fig. 8: Plain radiograph of a 12-year-old boy with sickle cell anemia, showing separation of the periosteum from the tibial cortex (between the arrows).

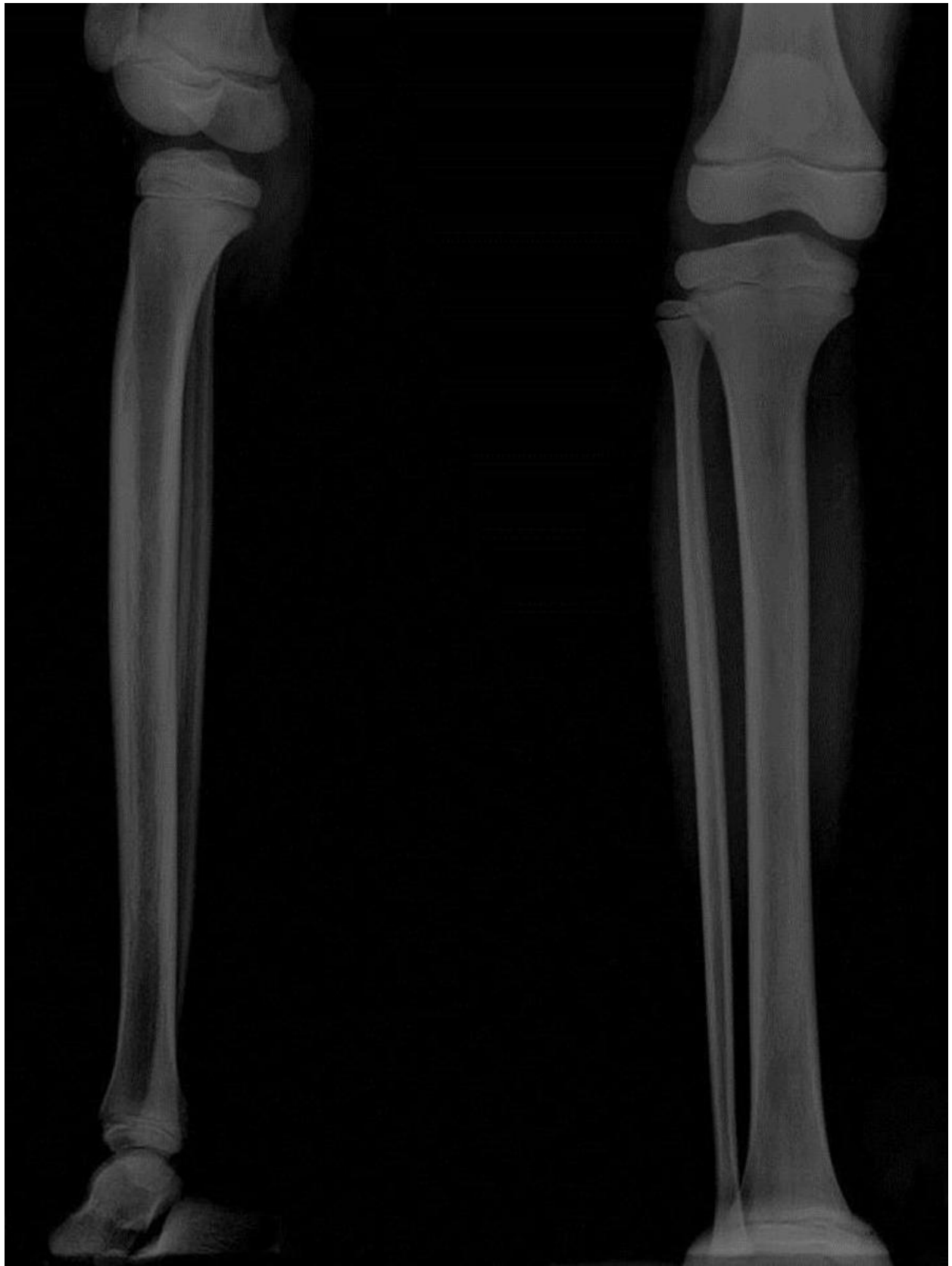


Fig. 9: Fig. 9: Plain radiograph of an 8-year-old girl with sickle cell anemia, showing thickening of the cortex of the tibia, with a laminated appearance (bone-within-bone).

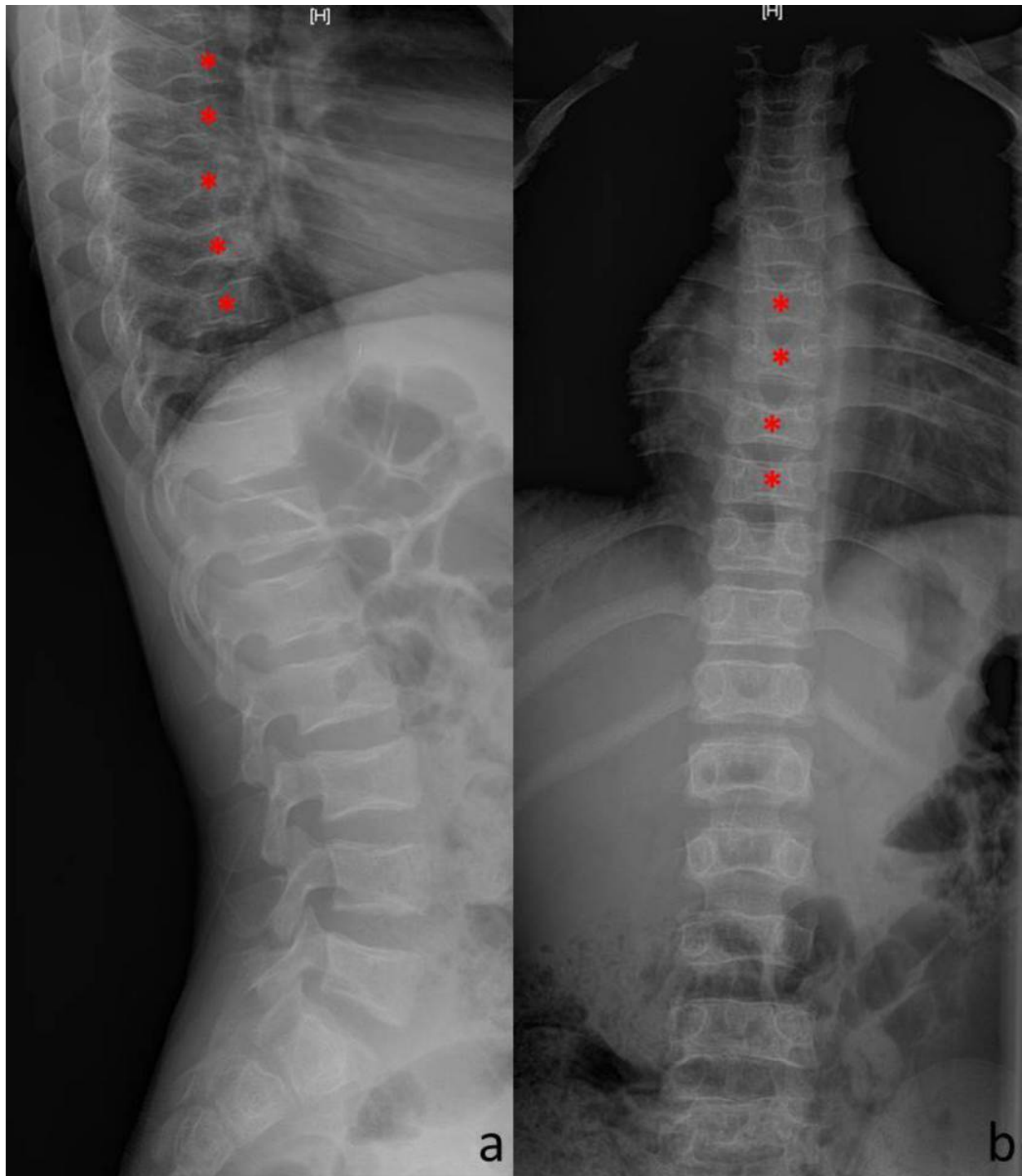


Fig. 10: Fig. 10: Lateral (a) and frontal (b) plain radiographs of the spine showing multiple H-shaped vertebral bodies (*) in a 16-year-old boy with sickle cell anemia.

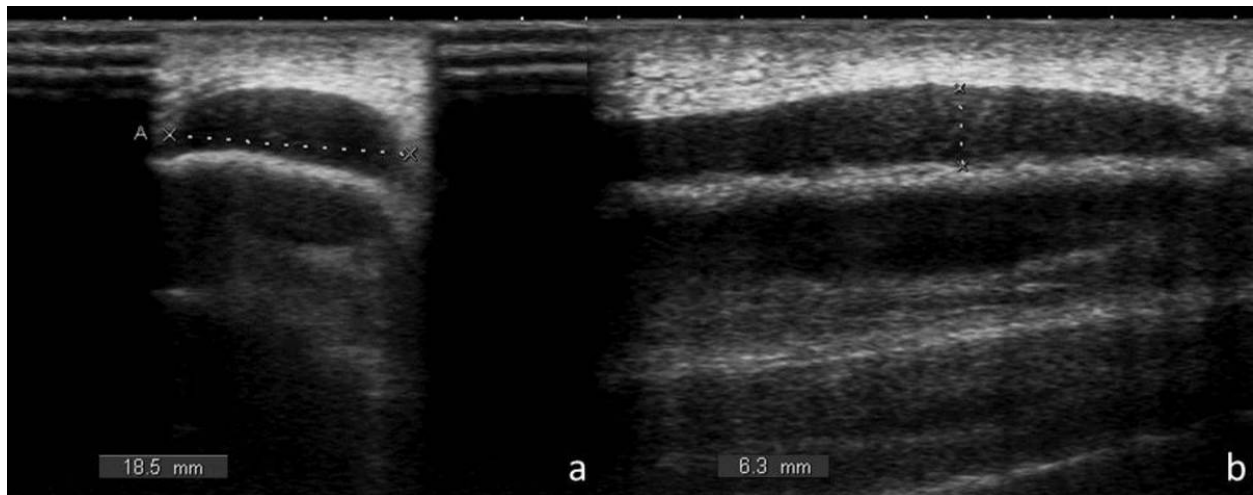


Fig. 11: Fig. 11: Musculoskeletal ultrasound performed with a high-frequency probe showing a fluid-collection adjacent to the tibial shaft in an 8-year-old girl. The dimensions of the collection (6mm thickness) and the non-pure fluid content are suggestive of osteomyelitis.

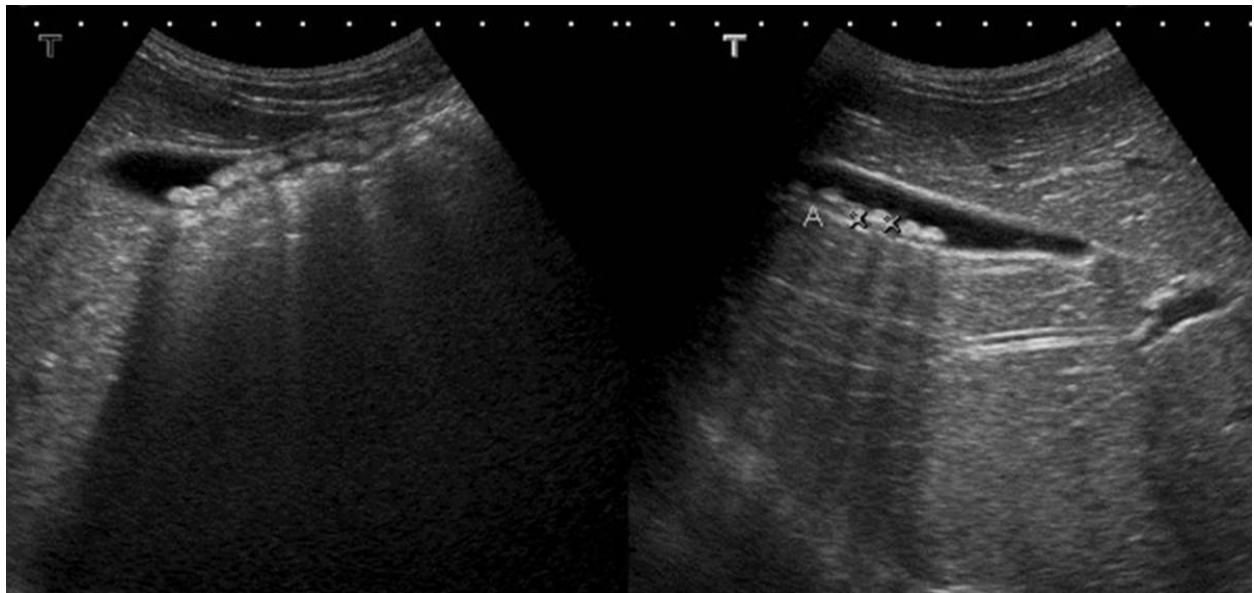


Fig. 12: Fig. 12: Abdominal ultrasound showing multiple, small gallbladder calculi in a 13-year-old boy with sickle cell anemia.

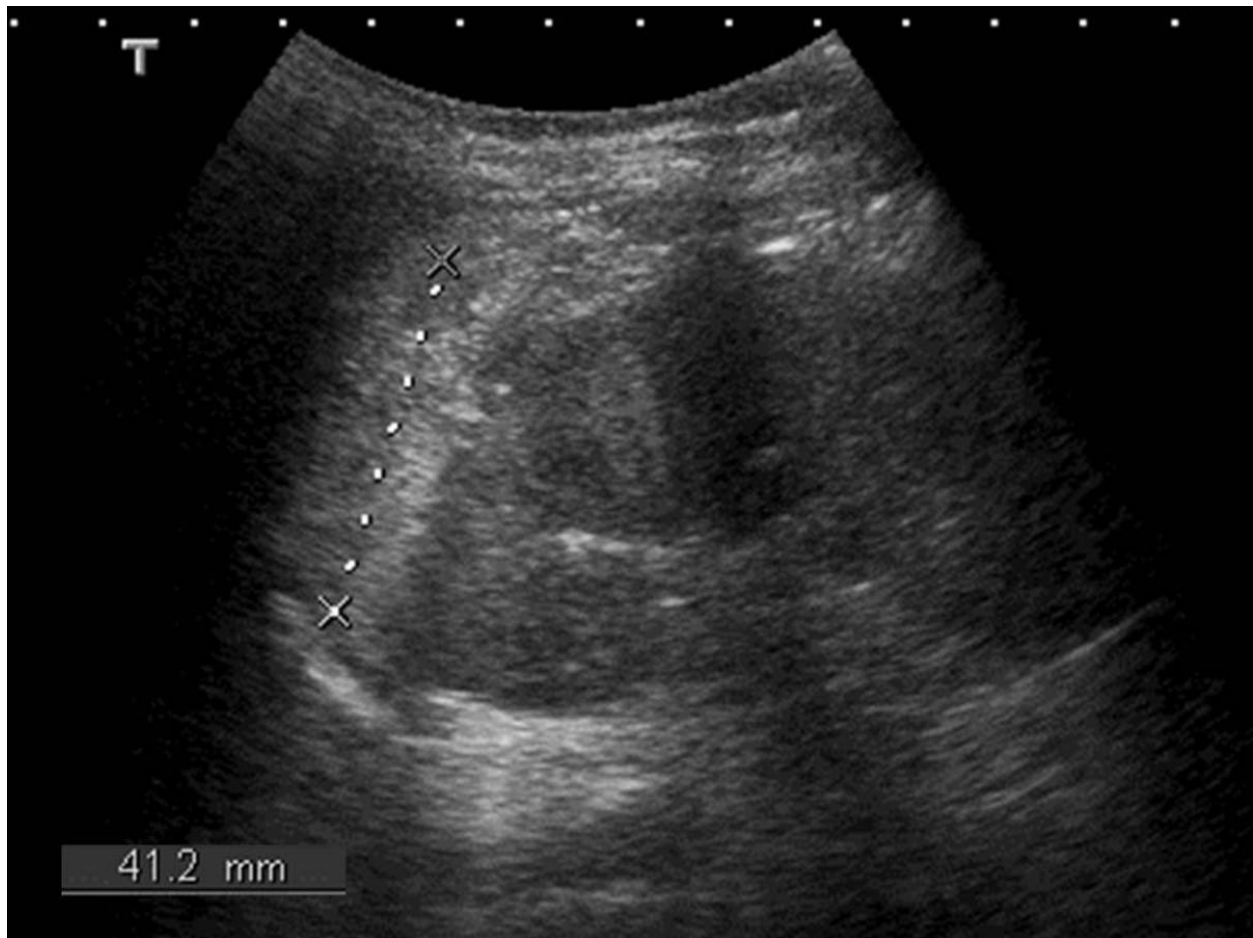


Fig. 13: Fig. 13: Abdominal ultrasound showing a small (4cm major axis), hyperechoic spleen, corresponding to autosplenectomy in a 9-year-old girl with sickle cell anemia.



Fig. 14: Fig. 14: Abdominal ultrasound showing an enlarged spleen (13,5cm major axis) in a 12-year-old girl with sickle cell anemia (since older children have autosplenectomy, an apparently normal sized spleen indicate an enlarged spleen).

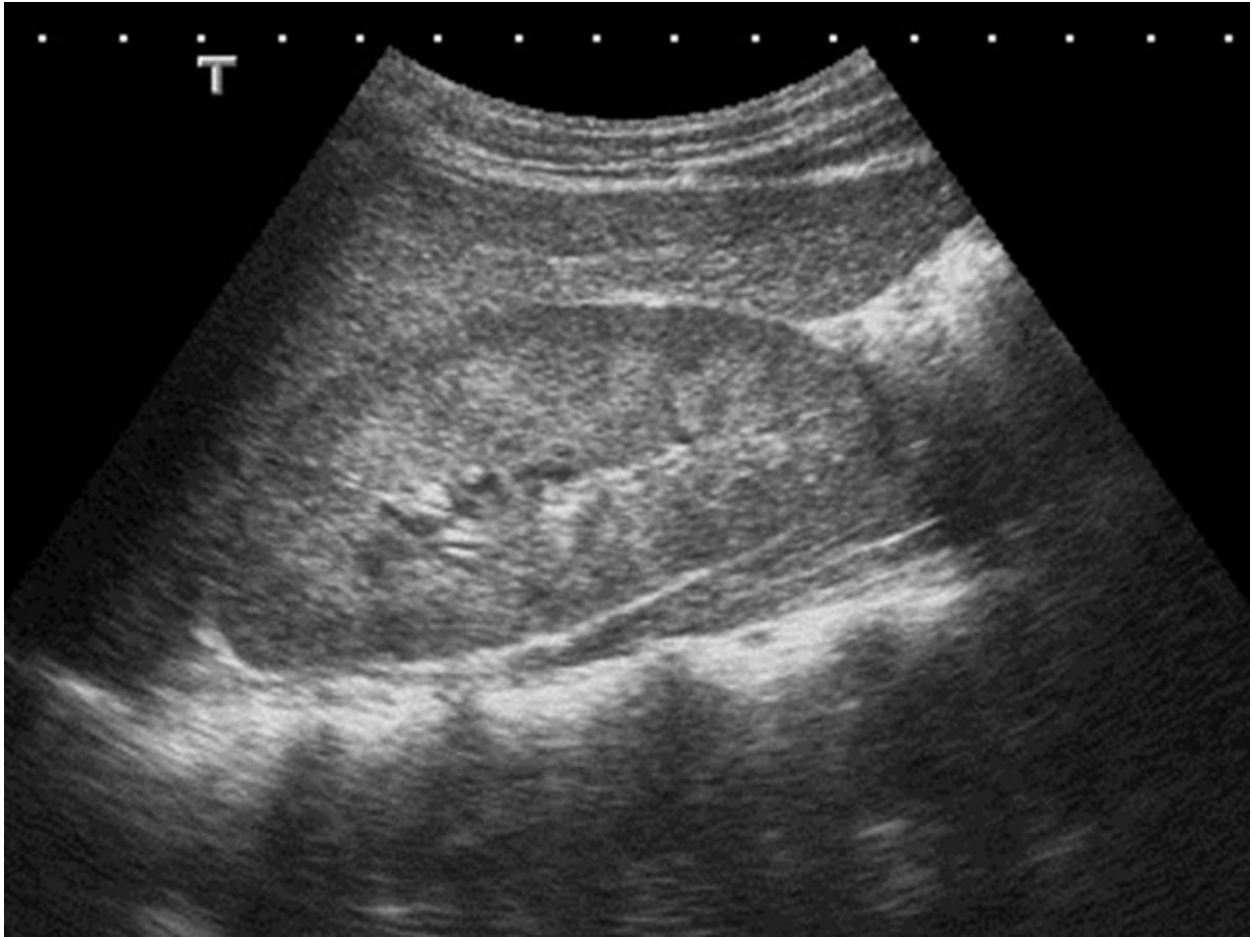


Fig. 15: Fig. 15: Renal ultrasound showing an enlarged right kidney with hyperechogenic medulla in an 11-year-old boy with sickle cell anemia.

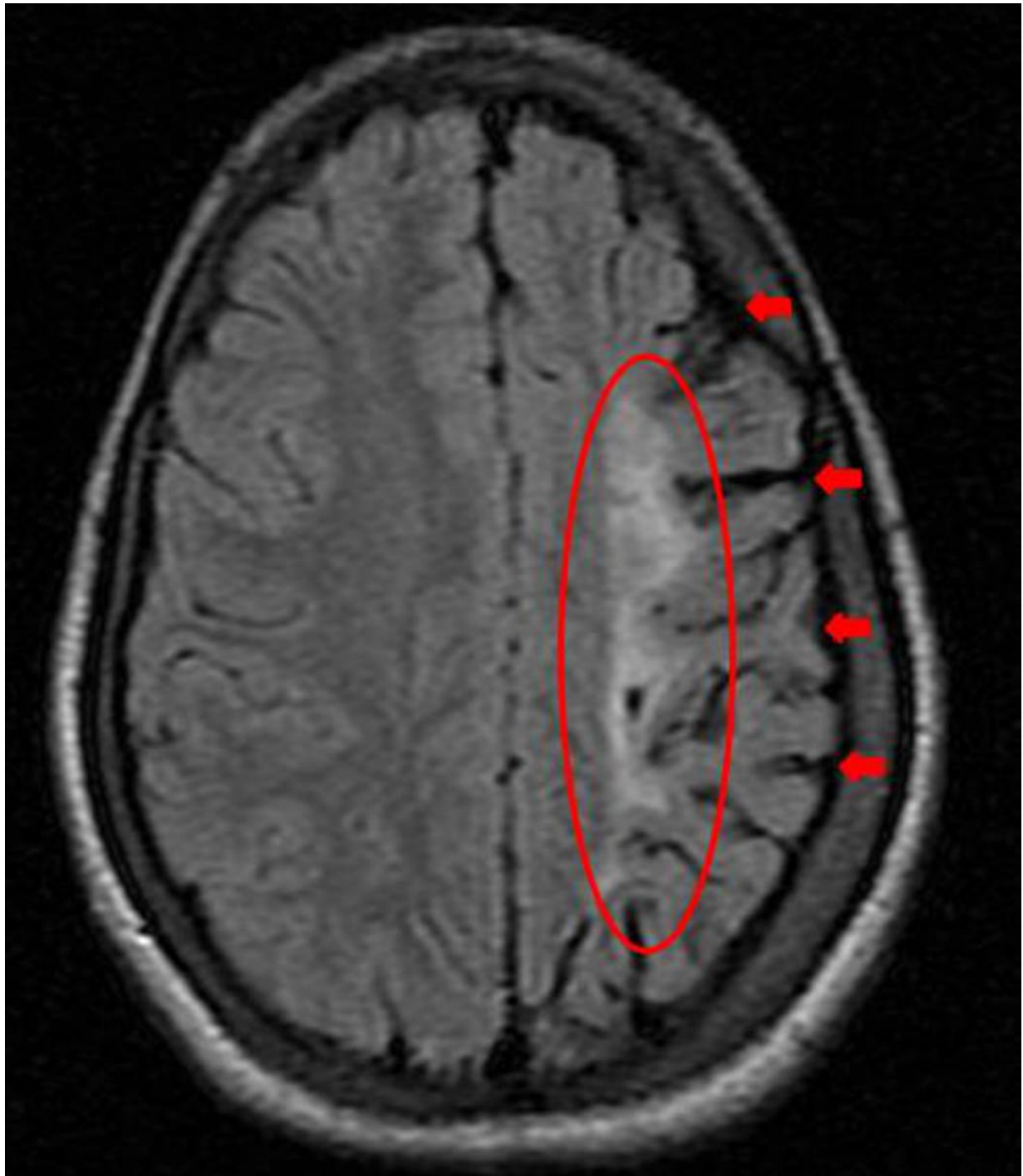


Fig. 16: Fig. 16: Chronic border zone infarction in a 16-year-old girl with sickle cell anemia. Axial FLAIR MR image showing chronic ischemic infarction (inside the circle) in the left frontoparietal white matter. There is moderate dilatation of the regional cortical sulci (arrows).

Conclusion

In patients with sickle cell anemia, most relevant clinical and radiological manifestations are caused by ischemic complications. Lungs, bones, brain, kidneys and spleen are among the most affected organs, with important clinical consequences. Recognising typical imaging manifestations and adequate correlation to the physiopathology and clinical manifestations are essential for diagnosis and for therapeutic implementation.

Personal information

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