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ULTRASONOGRAPHY IN THE MANAGEMENT OF SICKLE CELL ANAEMIA – NEED FOR A SHIFT IN SUB-SAHARAN AFRICA

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ABSTRACT

Sickle cell anaemia is a genetic condition that results in a chronic hemolytic anaemia. This condition is very common in sub-Saharan Africa. It is associated with vaso-occlusive, anaemic and infarctive crises and infections. These crises and infections often present alike and therefore require the use of imaging to differentiate, as management of each differs. Till date x-rays play a very important role in this. With improved care the patients are surviving longer with increasing incidence of acute and chronic complications. X-rays have a number of disadvantages including radiation hazards particularly on repeated exposures, shortage of power and water supply, unavailability of radiographers and radiologists in the areas where the disease is most common. All these make the use of x-rays as the first and most important imaging modality in this group of patients cumbersome. Ultrasound especially mobile ultrasonography has clear advantages over x-rays including convenience, availability, and safety and could replace x-rays while preserving accuracy and sensitivity in the diagnosis of complications of sickle cell anaemia. Imaging in this condition should shift towards ultrasonography.

KEYWORDS: Sickle cell anaemia, Investigations, Therapy, Ultrasonography.

INTRODUCTION

The term sickle cell disease embraces a group of genetic conditions in which pathology results from the inheritance of the sickle cell gene either homozygously, or as a double heterozygote with another interacting gene.[1] The commonest genotype at birth is homozygous sickle cell (SS) disease. It has the worst mortality, therefore more important than the rest.[1] This review will therefore be limited to this. The 100th anniversary of discovery of the disease was marked in 2010.[1,2] Sickle cell disease is common among people whose ancestors came from sub-Saharan Africa and in the Middle East but studied much closely in the USA where a medical resident in 1910, first likened the shape of the abnormal red cells to "sickle", which he demonstrated under the microscope. [3]

METHODOLOGY

Search was conducted in Google Scholar and Pubmed with various combinations of the following keywords – "Sickle cell anaemia", "Crises and complications", "Radiological changes", "Ultrasonography" in various combinations. Articles on the subject of radiographic/ultrasonographic investigations of the condition were identified. Selected articles were arranged into sub-sections for appropriate sequence and clarity.

Main Text

Disease background and pathology

In hemoglobin SS disease, valine replaces glutamic acid at position 6 in amino acid sequence of beta chain. This amino-acid substitution leads to decreased solubility of the hemoglobin molecule in low oxygen tension hence the cells become sickled.[4] This causes a chronic hemolytic anemia occurring from premature destruction of the deformed erythrocytes. Other manifestations include ischaemic changes resulting from vascular occlusion by masses of sickled cells.[4] These children present with frequent episodes of crisis, described as hemolytic and vaso-occlusive crises.[5] This further is complicated by tissue ischaemia and infarctions. These infarctions can occur with the occlusion of small blood vessels in the bones causing growth disturbances and pathologic fractures,[6] in the brain causing strokes,[7] kidneys and spleen causing atrophy and secondary infections.[8]

In their steady state the hemoglobin level is 6-8g/dl with resultant increase in cardiac output and work load producing cardiomegaly.[9] There is also increased susceptibility to infection especially with encapsulated organisms. Increased susceptibility to *Salmonella* osteomyelitis is due mainly to bone necrosis.[10]

These clinical manifestations are generally detected six months after birth when the fetal hemoglobin begins to fall.[5] Hepatic crises or hepatopathy is characterized by right upper quadrant syndrome including right upper quadrant pain, fever, jaundice, liver enlargement and elevation of the liver enzymes.[11,12] In acute chest syndrome, they present with chest pain, fever, cough, tachypnea, leukocytosis, pulmonary infiltrates in the upper lobes of both lungs.[11] Pulmonary hypertension is another recognized serious complication that results in death if not detected early and managed properly.[11] Anaemic crises include hyper-haemolysis, aplastic crisis and acute sequestration crisis.[1,11]

Use of x-rays

X-rays play a very important role in sickle cell disease. Most of the x-ray changes are secondary to the intra-and-extra medullary hematopoiesis, osteonecrosis and osteomyelitis.[6] One of the earliest radiological changes is the so called ‘‘hair- on- end’’ appearance on a skull radiograph caused by the increased thickness of the diploic space as a result of the hyper-marrow activity.[6] It is pathognomic of hemolytic anemias.[6] Vertebral osteopaenia is responsible for vertebral body compression giving a typical x-ray appearance of multiple H-shaped vertebrae seen commonly in the dorsal spine.[6] Osteonecrosis occurs commonly in the hip and presents with femoral head collapse and sclerosis.[11] The hand-foot syndrome is seen as soft tissue swelling with tubular phalanges and irregular sclerosis, as well as loss of cortico-medullary differentiation.[6] These can be diagnosed with x-rays but they are important draw backs.

Radiographic features are nonspecific and initially are often normal.[12] The earliest changes may not be evident for 8-10 days.[12] Radiation hazards exist, especially since x-rays must be frequently used to diagnose and follow up in each crisis. Timeliness is a factor that discourages the use of x-rays. This is because in many centres in environments with high sickle cell disease load conventional x-rays are still used. It requires expertise, is time consuming and mostly requires electricity and running water.[13] Mobile and digital x-rays are yet to be popular in many of these centers.[13] These patients who require regular x-rays during painful and other crises are then put through the stress of being transported to the x-ray department and sometimes outside the healthcare centre to where light and the proper x-ray machines are available.[13] Sometimes the unavailability of a trained radiographer and a radiologist can further hamper this process.[14] Battery operated mobile x-ray machines and digitally obtained x-ray films, transferred to the big cities for reports, are yet to be accessible in many parts of the developing world where the majority of people with sickle cell disease are.[13,14]

The imperative of ultrasonography in the management of sickle cell disease

Ultrasonography which is more readily available, relatively cheap, safe with no radiation hazards and does not require much expertise to interpret,[15] is therefore imperative. Many of the morbid changes during crises and chronic pathologies, can be more easily, safely and cost effectively assessed by ultrasonography.[16] Mobile operated units can easily be used in remote environment thus removing the need to transport these very ill children through long distances and addressing the problem of limited electricity power supply in these environments.[17] There is also an added advantage of telesonography as the images acquired in the remote centres can be shared with the radiologist in the cities.[18]

The following conditions associated with sickle cell anaemia can be conveniently and accurately diagnosed using ultrasonography:

Spleen: The spleen is the most affected organ in sickle cell disease, because it receives the insults of the associated clinical conditions of this pathology earlier than the other vulnerable body organs.[8] Changes in the spleen can be detected early on ultrasound. Such changes include splenomegaly, infarctions, splenic fibrosis and auto splenectomy.[8]

Gall bladder: The most important abnormality detectable on ultrasonography are gall stones. The accuracy of sonography in detecting gall stones is as high as 98%.[19] The onset of gall stones can occur early, 2 to 4 years of age. Other conditions include cholecystitis and fibrosis.[19]

Kidney complications: Sickle cell disease commonly affects the kidneys. The complications include kidney stones, fibrosis, atrophy and papillary necrosis.[20] These can be diagnosed reasonably early with ultrasound.

Cardiac complications: With increased longevity cardiovascular complications are increasingly evident with progressive development of pulmonary hypertension and left ventricular diastolic dysfunction. Other complications include dilatation of the cardiac chambers. Cardiac ultrasonography or echocardiography can detect these conditions and in the earlier stages before discompensation sets in.[21]

Chest: Acute chest syndrome is a severe complication of sickle cell disease that contributes significantly to mortality in adults. It is defined by the imaging pattern of an acute pulmonary disease involving atleast one complete lung segment. Other complications that can be detected by US are: pleural effusions and pneumonias.[22]

Bones and joints: Osteomyelitis and septic arthritis are major infective complications of sickle cell disease.[11] The previous misconception that ultrasound does not penetrate bones such as the skull, long bones and the spine is no longer tenable. Diagnosis such as osteomyelitis, infarctions, arthritis can now be confidently made on ultrasound.[23] Using a high resolution ultrasound, soft tissue characterization, fluid collections, periosteal reaction and localization of the

part of bone that has the greatest pain is diagnostic of osteomyelitis.[24] Septic arthritis is less common than osteomyelitis.[11] Ultrasound identifies the possible site of infection and guides needle biopsy.[25]

Neurological disorders: These are quite common in patients with sickle cell disease, the findings include territorial infarctions, silent ischaemia and intracranial hemorrhage.[11] The commonest are large artery infarctions.[26] In children with homozygous sickle cell disease, trans cranial doppler ultrasound now forms part of the US national standard in screening for asymptomatic vasculopathy.[26] Silent infarcts in combination with elevated trans cranial Doppler velocities must prompt the initiation of preventive treatment in order to reduce the risk of subsequent stroke.[26]

Genitalia abnormalities: They include segmental testicular infarctions, epidydimi-orchitis, scrotal hydroceles and complications of priapism.[27] The imaging modality of choice is colour Doppler ultrasonography.[27] In testicular infarctions ultrasound most frequently depicts a wedge – shaped area in the testicle with no demonstrable flow. Normal flow is however detected in the non-affected areas.[27]

The need for these scans cannot be over emphasized since many sicklers are living into adulthood even in developing countries.[28] This means that more of these complications are seen and must be picked up early to improve prognosis.

Therapeutic procedures

Ultrasonography also plays a therapeutic role especially in drainage of abscesses and in guiding biopsy needles for aspirations and cytologies.[25]

CONCLUSION AND RECOMMENDATION

Sickle cell anaemia is a very common cause of morbidity and mortality in many sub Saharan countries. It affects nearly all systems of the body causing potentially debilitating complications. These are usually recurrent and so require frequent hospital visits. Currently, such crises require the use of imaging techniques. With the event of ultrasonography, safer, more convenient and more accurate diagnoses can be achieved.

This review has shown the advantages of ultrasonography over radiography in the diagnosis and management of the complications of sickle cell disease. It is therefore recommended that there be a paradigm shift to the use of ultrasonography in the management of this condition and similar conditions.

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