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Case report: Extra pulmonary Tuberculosis in Sickle Cell Disease

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Summary
In apparently healthy individuals, tuberculosis (TB) affects mainly the lungs however, worsening immune status tend to predispose to an increased tendency for extra-pulmonary tuberculosis (EPTB). We report the case of a 22 year old known sickle cell anaemia (HBS) female student with three-month history of bilateral hip pain, weight loss and swelling of the left hip with multiple discharging sinuses, paraplegia and recurrent fever. There was no preceding history of trauma. Full Blood Count (FBC) revealed leukocytosis with neutrophilia, monocytosis, thrombocytosis and Packed Cell Volume (PCV) of 23%. Erythrocyte sedimentation rate (ESR) was 120mm/Hr (Western Green) and retroviral screening was negative. Bacteriologic culture of the discharging sinuses grew *Escherichia coli* and *Staphylococcus aureus*, both sensitive to sparfloxacin. Smear microscopy for acid-fast-bacilli (AFB) was negative. Chest X-Ray was reported normal but X-Ray of the pelvis showed loss of L4/L5 disc space and appearances suggestive of avascular necrosis of the femoral heads. Clinical and haematological profile of the patient started to improve by the second month on therapeutic trial of anti-TB regimen. She had nine-month course of therapy and later discharged to physiotherapy clinic. Management of EPTB requires a high index of clinical suspicion and well-equipped laboratory to support the diagnosis. Therefore, this case report highlights the need to upgrade TB-diagnostic facilities in this environment.

Keywords: *Immune status, extra-pulmonary tuberculosis, sickle cell disease, TB diagnostic facilities.*

Résumé
Aux individus apparemment sain, la tuberculose affecte plus les poumons et ceux ayant un statut immunitaire détérioré prédispose une tendance croissante de la tuberculose pulmonaire extérieure. Nous présentons le cas de 22 ans d'une étudiante drépanocytaire anémique (HbS) ayant une histoire de «3 mois de douleur bilatéral au rein, une perte de poids corporelle et inflammation des reins avec multiple décharge des sinus et des fièvres réguliers. Il n'y avait pas d'histoire précèdent de traumatisme. Le taux de cellules sanguines révélait la leucocytose avec la neutrophile et monocyte thrombocyte et l'hématocrite de 23%. Le taux de sédimentation des érythrocytes était de 120mm/Hr et le test rétrovirale negative.La culture bactériologique des décharges des sinus developaient des Escherichia colis et staphylocoques aureus sensitive a la sperfloxacin. Les lames épaisses des bacilles acides de graisse étaient négatives. Le X-ray de la poitrine était normal mais celui des pelvis demonstrait la perte du disque entre L4/L5 et suggérant la nécrose avasculaire. Le profile clinique et hématologique du patient s'améliorait au 2iéme mois du traitement a regimen antituberculeux. Elle avait en 9 mois de traitement, suivit de physiothérapie clinique. Les soins du EPTB demande un indexe de suspicion clinique élevée et un laboratoire bien équipé pour supporter le diagnostic. Ainsi ce cas illumine le besoin d'améliorer les équipements de diagnostic de la tuberculose dans notre environnement.

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Introduction

The definitive diagnosis of extra-pulmonary tuberculosis (EPTB) is often difficult in sub-Saharan Africa due to poor diagnostic facilities. The need to address the inadequate health care infrastructure in sub-Saharan Africa has been highlighted by some researchers [1,2].

Bacterial infections account for significant morbidity and mortality in patients with sickle cell disease (SCD). Incriminated bacteria are encapsulated pathogens such as *Streptococcus pneumoniae, Haemophilus influenza type b, Neisseria memingitidis* and *Klebsiella pneumoniae*. The pathological basis for susceptibility to infections is complex. Defective splenic function is one of the most important factors. Other abnormalities include defective opsonization, defective alternate complement pathway, inadequate antibody production, ineffective leucocyte function and cell mediated immunity.

Although, bacterial sepsis has been reported to be the commonest cause of morbidity in SCD patient in Nigeria [3], occurrence of EPTB has not been documented in this environment. We report a case of SCD patient who was managed therapeutically with anti-TB regimen following a three-month presentation of painful swelling of the left hip.

Case Report

Initial presentation and history

A 22-year-old female student, a known HBS patient of University College Hospital (UCH), Ibadan, Nigeria diagnosed at age one year but defaulted however, her

past medical history was uneventful. Immunization record shows that she had BCG, oral polio and DPT at seven months. She was admitted on 10th September 2003 through a referral from General Out-Patient Department (GOPD) of the hospital with three-month history of bilateral hip pain, swelling of the left hip with multiple discharging sinuses, recurrent fever and yellowness of the eyes. She has lost significant weight and was unable to walk. She was the only affected sibling of the three children in a monogamous family of a low socioeconomic status. There was no history of trauma.

Physical examination

On examination, She was a chronically ill-looking girl, cachetic (weighing 25kg at presentation), small for age, afebrile, moderately pale, mildly jaundiced and mildly dehydrated. Multiple discharging sinuses were found on the left gluteal regions. Right gluteal region was apparently normal. She had bilateral tender inguinal lymphadenopathy. Other significant findings include diffuse atrophy of both lower limbs with reduced muscle bulk. Examination of the spine did not reveal any obvious gibbus. Power was grade two in both lower limbs with normal muscle tone and brisk reflexes. Abdominal examination showed no remarkable findings.

Laboratory and imaging studies

The initial full blood count showed marked leukocytosis with neutrophilia (White Blood Cell count of 17,900mm^3). There was lymphocytosis (absolute lymphocyte count of 5,594/mm^3) and monocytosis (absolute monocytes count of 1,194/mm^3). There was also severe thrombocytosis (platelet count of 1,057,000/mm^3). Blood smear showed few occasional nucleated red blood cells. Her packed cell volume (PCV) was 23% and erythrocyte sedimentation rate (ESR) was 120mm/Hr (WG method). Retroviral screening was non-reactive.

Culture of the discharge from the sinusis grew *Escherisia coli* and *Staphylococcus aureus*, both sensitive to sparfloxacin. Both tuberculin (Mantoux) skin test and Ziehl- Neelsen staining of the discharge for acid-fast-bacilli were negative. Culture for *Mycobacterium tuberculosis* and histological stain of the discharging abscess were ordered but not done due to lack of facilities. Also, fine needle aspiration biopsy (FNAB) of the enlarged inguinal nodes revealed inflammatory cells.

Radiological examination of the spine and pelvis (X-Ray) revealed lumbar spine lordosis, loss of L4/L5 disc space, osteopenia with trabeculae pattern and appearances suggestive of avascular necrosis of the femoral heads. The chest X-Ray was reported normal.

Clinical course

The patient was placed on sparfloxacin 200mg twice daily for one week. Despite this therapy, clinical condition of the patient continued to deteriorate as evidenced by weight loss of 0.25 kg over a period of one week, elevated ESR from 120mm to greater than 150 mm (Western Green), a gradual fall in PCV from 23% to 17% and persistence of discharging sinuses of the gluteal and the left hip pain.

A clinical diagnosis of tuberculosis of the spine was then considered based on the above radiological findings and this was reinforced by orthopaedic surgeons' review. The patient was placed on therapeutic trial of anti tuberculosis regimen for nine months (Tab isoniazid 300 mg daily, tab. rifampicin 600mg daily, tab pyrazinamide 1.5g daily and tab.ethambutol 1.2g daily for initial period of two months. This was later followed by tab. isoniazid 300mg and tab ethambutol 1.2g for seven months).

The drop in ESR from greater than 150mm/Hr to 100mm/Hr by 22nd day on anti-tuberculosis drugs and reversal of white cell count, absolute lymphocyte and monocytes count, and platelet count to normal further support the diagnosis. Erythrocyte sedimentation rate eventually became normal (10mm in 1st Hr) and her steady state PCV stabilize at 23%. Her weight appreciated to 31kg by 40th day of therapy.

Physiotherapist review indicated that there was gross muscle weakness of both lower limbs with reduced range of movement at the hip joint. The patient was commenced on exercises to improve both muscle tone and the range of movements at the hip joint. By the third month on anti-TB trial, her weight increased from 25 kg at admission to 34kg at discharge. She was commenced on wheelchair training and discharged home three months later to be followed up by Medical Out Patient department and orthopaedic unit at Surgical Out-Patient clinic. Daily dressing of the wound was continued at home. She started walking with the aid of walking stick by May 2004 and She completed her nine-month anti-Koch's therapy by August 2004.

Discussion

Tuberculosis (TB) is among the top ten causes of global mortality [6]. It kills nearly two million a year- 5,000 human beings every day- mainly in the poorest communities in the developing world. It is caused by a bacterium, *Mycobacterium tuberculosis*, a microorganism whose principal reservoir is human. *Mycobacterium tuberculosis* is spread by patients with pulmonary TB especially those with positive sputum smear [5,6]. Of those infected, 10-12% will develop TB disease after a period ranging from weeks to decades [6].

Patients with sickle cell anaemia are severely immunocompromised and suffer considerably from infections. This is due to their defective immune mechanism, which accounts for their high susceptibility to EPTB. In fact, bacterial infection is the most common cause of death among such patients [4]. Aken'Ova *et al* [3] reported that Klebsiella species was the commonest cause of sepsis in SCD patients. Sickle cell patients are not immune to *Mycobacterium tuberculosis*, being an intracellular

pathogen, which flourishes well in patients with defective cell mediated immunity. Sickle cell disease patients, through blood transfusions, are also prone to other blood-borne viral infections like hepatitis B, C and even HIV infections, which might further compromise their immune status.

There is little information in sub-Saharan Africa about how to make the diagnosis of EPTB. In a study done in Tanzanian hospital, only 18% of patients with EPTB had a laboratory confirmation of the diagnosis [8]. This highlights the fact that EPTB has been poorly managed in sub-Saharan Africa and this might serve as one of the impediments to global TB control.

Tuberculosis is a preventable and curable disease. Reports all over the world have shown that the treatment of this disease is not only effective but is among the most cost-effective ways of prolonging healthy living [9,10].

World Health Organization (WHO) recommended strategy for TB control is "DOTS" (Directly Observed Treatment Short Course) and this forms the basis for TB control in the 22 high burden TB countries including Nigeria.

Weak laboratory services has been reported as one of the major constraints undermining the success of DOTS strategy most especially in poor resource countries [11]. Thus, smear microscopy which is the hallmark of TB diagnosis according to WHO regimen was not only unsuitable to diagnose EPTB as shown in this patient but also in latent infections, paediatric cases and in patients with TB/HIV co-infections [11]. Hence new diagnostic tools such as radiometric liquid culture medium (Bactec 460^{TB}) and alternative new solid culture media (TK medium, Salubrics InC) [12] are needed to accurately diagnose these categories of patients for TB control efforts to have meaningful impact in the community.

Recently, commercial serologic assays have been developed as alternative to tuberculin skin test (TST), which had been the only diagnostic tool for latent TB for decades. The principle of these assays (QuantiFERON TB GOLD, (Cellestis, Australia) [13] and T-Spot TB (Oxford) [14] is based on the detection of gamma interferon (IF-ã) liberated in the blood incubated in-vitro with antigens specific to *Mycobacterium tuberculosis*. These tests have a higher specificity and sensitivity than TST, they have less cross-reactivity with the BCG vaccine and environmental mycobacteria [13,14]. They are also of immense value in the diagnosis of EPTB, HIV/TB co-infections and in paedriatric TB [13,14]. Laboratory turnaround time is shortened to 24 hours with the use of these assays [15], thus truncating the delay often associated with TB diagnosis in developing countries.

In conclusion, diagnosis of EPTB requires a high index of suspicion and should involve a multi-displinary approach, especially in immunocompromised patients like SCD. Also, newer affordable diagnostic tools with high sensitivity and specificity would be of immense value for TB control programme to have meaningful impact globally.

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