



CHRONIC OSTEOMYELITIS DUE TO SALMONELLA TYPHI IN A HEMOPHILIA PATIENT-A CASE REPORT

Surgery

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ABSTRACT

Salmonella causes various intestinal and extra intestinal manifestations. Chronic osteomyelitis is commonly seen in patients with patients of haemophilia. Most common cause of chronic osteomyelitis is Staphylococcus aureus. Very rarely Salmonella typhi causes chronic osteomyelitis. So here we report a case of Chronic osteomyelitis with recurrent discharging sinus caused by Salmonella typhi in patient who was a known case of haemophilia highlighting the pathogenesis which would have resulted in such a clinical presentation. If not treated in time would lead to permanent disability.

KEYWORDS

INTRODUCTION

Osteomyelitis due to *Salmonella typhi* is uncommon and accounts for 0.45% of cases and 0.8% of all Salmonella infections (1-5). Most common organism causing chronic osteomyelitis include *Staphylococcus aureus* (60%) followed by *Enterobacteriaceae*, *Pseudomonas* and *Streptococcus sp* (6).

Amongst haematological abnormalities, Salmonella infection has been reported in sickle cell disease and haemoglobinopathies, very rarely in haemophilia (2-4). So here we report a case of Chronic Osteomyelitis due to *Salmonella typhi* in a haemophilia patient.

Case Report

A 26 year old male, student from Latur district of Maharashtra, known case of Hemophilia A, presented to hematology OPD in January 2018 with chief complaints of low grade intermittent fever since a month associated with left knee swelling of insidious onset which gradually aggravated till the patient had difficulty in walking and restriction of movement. Orthopedic evaluation revealed tenderness and restricted movements of left knee with a bleeding sinus with purulent discharge and about 3x2 cm on the lateral aspect of the knee.

Investigations revealed his WBC counts to be 13,700cells/cu mm (83%polymorphs) with CRP levels of 29.12 mg/dl. X-ray and MRI of left knee were suggestive of hemophilic arthropathy with osteomyelitis of distal femur. Pus discharging from the sinus was sent for microbiological evaluation. Gram's stain showed few polymorphonuclear leucocytes with Gram negative bacilli. The Acid fast stain and modified Acid fast stain of smear made from pus was negative. Bacteriological culture of this discharge yielded non lactose fermenting colonies confirmed as *Salmonella Typhi* by phenotypic tests followed by agglutination with antisera (7-9). The same identification was also obtained by Vitek2 compact. Swabs sent for fungal culture didn't yield any isolate till 6 weeks post inoculation.

The isolate was a pan-susceptible strain except to quinolones being susceptible to ampicillin, amoxicillin-clavulanic acid, cotrimoxazole, chloramphenicol, azithromycin, piperacillin-tazobactam, cefoperazone- sulbactam, ceftriaxone, cefipime & resistant to ciprofloxacin and levofloxacin (9). Blood culture and stool culture did not yield any isolate. Patient was started on Injection Ceftriaxone intravenously along with conservative wound care for 3 weeks, discharged on oral co-amoxiclav with a scheduled follow-up. Patient failed to follow-up and presented with a more aggravated picture in July 2018.

Discharge from the sinus was sent for bacteriological culture. *Salmonella Typhi* with same antimicrobial susceptibility pattern as demonstrated previously was recovered. Significant clinical improvement was observed after core decompression of the bony lesion with bone graft and internal fixation along with Inj.

Ceftriaxone for a month. On subsequent follow up the swelling had

decreased in size and patient was able to walk with assistance of proper physiotherapy.



DISCUSSION

Chronic bacterial osteomyelitis is a persistent infection of bone and bone marrow which incapacitates the patient. Healthy bone is relatively resistant to infection. Bacteria adhere to bone matrix and orthopaedic implants via receptors to fibronectin and to other structural proteins (10). They subsequently elude host defences and antibiotics by hiding intracellularly, by developing a slimy coat, or by acquiring a very slow metabolic rate. The presence of an orthopaedic implant also causes a local polymorphonuclear cell defect which leads to decreased ability to kill phagocytosed bacteria. Other risk factors are Diabetes, peripheral vascular disease, obesity, smoking (10). These bacteria occlude the vascular channels leading to patchy ischemic necrosis which in turn provide an ideal culture medium for the growth of the bacteria. Osteolysis is determined locally by the interaction of bacterial surface components with immune system cells and subsequent cytokine production. Gram negative endotoxin its lipopolysaccharide fraction, N acetyl muramyl dipeptide and cytokines destroy the bacteria and further promote Osteolysis (10). Most common causes of chronic osteomyelitis are due to *Staphylococcus aureus* (60%) followed by *Enterobacteriaceae* (23%), *Pseudomonas sp.* (9%) and *Streptococcus sp.* (9%) (10).

Salmonella species causes enteric fever, acute gastroenteritis, bacteremia/sepsis and asymptomatic infection. Osteomyelitis due to *Salmonella* is a rare clinical presentation accounting for about 0.45% of osteomyelitis and 0.8% of *Salmonella* infections (1-5). Species associated with rare presentation are usually *Salmonella typhimurium*, *Salmonella typhi* and *Salmonella enteritidis* rarely *Salmonella virchow* (11). Rare causes like *Salmonella panama*, *Salmonella virchow*, *Salmonella arizonae* have also been reported in literature (12). In the present case report *Salmonella typhi* was the infection causing organism. This condition is associated with haemoglobinopathies, malignancy, chronic liver disease, diabetes, in extremes of ages and in patients with previous history of Trauma or surgery. It is very rare in healthy persons as seen in present study that the patient was a known case of hemophilia (2-4). It is not always associated with gastrointestinal manifestations and also the usual signs of osteomyelitis like fever, bone pain, soft tissue swelling, pathological fractures and leukocytosis. *Salmonella* osteomyelitis occurs due to hematogenous dissemination associated with underlying disease, rarely due to trauma or direct inoculation or translocation of organisms across intestinal mucosa. Most commonly diaphysis of long bones like femur followed by humerus is affected (3, 13).

Hemophilia is an X-linked recessive bleeding disorder, characterized by absence of one of the clotting factors, VIII in Hemophilia A and factor IX in Hemophilia B. Lack of these factors makes the person prone to abnormal bleeding manifestations (6). The abnormal bleeding in hemophilia patients causes release of iron from hemoglobin, thus inducing chronic inflammatory process by cytokines and proangiogenic factors which result in bone damage. Bone turnover induced by inflammatory mediators is controlled by a molecular triad osteoprotegerin (OPG), Receptor activator of nuclear factor κ B (RANK) and RANK ligand (RANKL). RANKL is a transmembrane ligand which is expressed on the surface of osteoblast/stroma cells of bone and is responsible for inflammatory cytokines mediated osteoclastic activity resulting in bone resorption which is controlled by OPG (14). This results in osteomyelitis in hemophilia patients.

Salmonella osteomyelitis is clinically and radiographically indistinguishable from osteomyelitis caused by other organisms, with most patients presenting with pain and variable swelling of the affected limb. Successful management of Chronic salmonella osteomyelitis is achieved with multiple bone debridements with suitable antibiotics followed by delayed bone reconstruction surgeries (2, 12, 15) which was also followed in present study. Antibiotics like ampicillin, chloramphenicol, azithromycin, third generation cephalosporins like ceftriaxone and fluoroquinolones are effective in these cases. Fluoroquinolones have potent activity against Salmonella and also has good bone penetration. Hyperbaric oxygen therapy may hasten the healing process (12). In addition to this in hemophilia patients any surgical procedure should be supplemented with clotting factor concentrates (CFC) to prevent recurrences (6, 14, 15).

CONCLUSION

Early diagnosis, surgical intervention & appropriate antibiotics for the right duration play a pivotal role in successful management. The close co-operation between the hematologists, orthopedic surgeons, microbiologists, rehabilitation physicians and physiotherapists is important for the successful management of such cases.

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