

Ward Round: A 43-year-old diabetic man with multiple joint pains

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We admitted a forty-three year old man who had initially presented at the diabetes clinic at Queen Elizabeth Central Hospital, Blantyre with a two week history of multiple painful and swollen joints. The joint pains started gradually over two weeks involving bilateral metacarpal, proximal interphalangeal, left wrist, ankle and knee joints. On further inquiry, he reported to have had right knee swelling for 5 months. This had earlier been attributed to trauma in another health facility and he had been prescribed a non-steroidal anti-inflammatory drug. However, the patient denied any history of trauma. The joint pains were worse in the morning and were associated with marked stiffness, lasting over two hours. This was associated with swelling of the affected joints. His presentation to the clinic had been prompted by his inability to walk in the previous five days.

He had a five-day history of watery diarrhea which started after the symptoms of arthralgia and self resolved three days prior to admission. There was no history of mouth ulcers, eye symptoms, skin rash or genito-urinary symptoms. He denied weight loss, coughing, night sweats or fever. There was no family history of joint disease.

He had been diagnosed with type II diabetes and hypertension in March 2010. His diabetes and hypertension were well controlled. He had received insulin, metformin and lisinopril. He tested HIV negative in July 2010. He reported no previous episodes of arthralgia or joint swelling.

He had a 15 pack-year history of smoking and moderate alcohol consumption (< twenty units a week) for twenty years but had stopped smoking and drinking when he was diagnosed with diabetes. He is married with two children. His wife is a nurse, and is well. He worked as an electrician but had stopped since his symptoms started.

On examination, he was in pain and was unable to rise from his wheelchair. His Blood Pressure was 119/82, pulse rate 84 per minute, respiratory rate 24 per minute and a temperature of 36.8 degrees celcius. His cardiovascular, respiratory, neurological and abdominal examinations were normal. There was no lymphadenopathy. In the upper extremities, the right metacarpo- phalangeal, proximal interphalangeal joints of the 4th and 5th digits and the left wrist were swollen, warm and tender (figure 1).



Figure 1: Swollen right metacarpal-phalangeal, proximal interphalangeal joints of the 4th and 5th digits and left wrist.

In his lower extremities, he had bilateral knee swelling. The right knee was more swollen than the left. He had a positive patellar tap sign indicating knee effusion. There were no nodules around the joints (see figure 2 below).



Figure 2: Swollen right knee

There was no muscle atrophy. He had no signs of peripheral neuropathy. Fundoscopy examination was normal.

His initial investigation results showed that he had a hemoglobin of 11.9 g/dl (11.0-18.8), a white cell count of $6.6 \times 10^9/L$ (4.0-11.0), Platelets of $130 \times 10^9/L$ (150-400). Urine dipstick showed no white cells, protein was trace. He tested HIV Reactive on admission with a CD4 cell count of 126 per micro liter.

Discussion

When arthritis is symmetrical and involves small joints the differentials include rheumatoid arthritis (RA), reactive arthritis, psoriatic arthritis and undifferentiated arthritis. Undifferentiated arthritis refers to arthritides that do not fit into well-known clinical disease categories¹. Rheumatoid arthritis (RA) primarily affects the small joints of the hands particularly the proximal interphalangeal, carpal joints and metacarpophalangeal joints, wrists and cervical spine. The larger joints may also be involved². Painful, swollen and stiff joints are characteristic of RA, with the stiffness being worse in the morning after a period of inactivity. These symptoms and signs had been found in our patient. In view of the positive patellar tap sign on his right knee, it must be noted that septic joint effusions are not uncommon as a complication of RA.³

Reactive arthritis may be secondary to diarrheal illness caused by some strains of Salmonella, Shigella or Yersinia enterocolitica⁴. However, the diarrheal illness in our patient started after the symptoms of arthritis had already developed. The temporal relation makes it unlikely that the diarrheal illness was the cause.

The possible contribution of HIV also needs consideration in this patient. HIV has been described to play a role in reactive arthritis immunopathogenesis by it acting directly as an arthritogenic agent or indirectly causing immune dysfunction and promoting infection by other opportunistic

arthritogenic pathogens.⁵

Gout is another possible cause in view of the history of alcohol. However, this is unlikely in our patient as this tends to present with asymmetrical arthritis.

Further investigations should include erythrocyte sedimentation rate (ESR) and level of C-reactive protein to look for evidence of inflammation. Serum autoantibodies, which have variable specificity and sensitivity for various joint diseases, should be considered. X-rays are important in joint diseases and can be diagnostic in certain conditions. Radiographs of both hands revealed joint space narrowing with periarticular osteopaenia and had evidence of erosion mainly affecting the right second MCP joint and interphalangeal joints (figure 3).



Figure 3: X-rays of the right and left hands.

The radiographs of the right knee and left ankle were normal. The radiographical findings from his hands of periarticular osteopenia, joint erosion and loss of joint space combined with the history of morning stiffness of his joints makes RA likely to be contributing to this patient's presentation.

The right knee was aspirated. The aspirate was straw coloured and turbid. Although joint effusions are not uncommon in RA, the colour of the effusion is translucent and thin.⁶ The fact that the effusion was straw coloured made the effusion unlikely to have been secondary to his RA.

The white blood cell count was 4500/mm³ with a differential of 5% lymphocytes, 95% neutrophils. In RA, the white cell count varies between 5 and 50,000/L; Polymorphonuclear cells predominate. A synovial fluid white blood cell count >2000/L with >75% polymorphonuclear leukocytes is highly characteristic of inflammatory arthritis, although not diagnostic of RA⁷.

Microscopy done on the fluid from the knee revealed acid fast bacilli following Ziehl Neilsen (ZN) staining. Gram stain was negative. There was no growth from the synovial fluid on bacterial culture and he did not have antibiotics prior to the knee tap.

The predominance of polymorphs could suggest that the preexisting rheumatoid arthritis was superimposed by a reactive arthritis. It is unlikely that the Mycobacterium isolated from the joint on ZN stain was causing articular tuberculosis (TB) for two reasons: (i) The increase of polymorphs is usual with articular TB, (ii) There was no evidence of joint destruction including local deformity on the X-rays of his knee. Articular TB is more often associated with joint destruction⁸.

The plausible explanation of his arthritis would therefore be

in a form of a reactive arthritis. This would be supported by the increased number of polymorphs in the joint as well as the symmetrical joint exacerbations in the rest of his joints. In the setting that no bacteria were grown from the synovial fluid, it is possible that he had TB arthritis in one joint and reactive arthritis in the rest of the joints. With these considerations, and a chest X-ray whose features were consistent with Pulmonary TB, the patient was started on TB treatment and his symptoms had completely resolved in the following two weeks. At the end of two weeks, he was ambulating without joint problems. He continued to take his TB drugs and was since booked to start Anti-retroviral treatment for HIV on the basis of a low CD4 count.

Cases of reactive arthritis complicating mycobacterial infection have been reported.^{9, 10, 11} However, all these have had no mycobacterium isolated from synovial fluid. We recognize that mycobacterium culture could have been important, as there is a possibility that the mycobacterium could have been a contaminant and this could be reactive arthritis due to pulmonary TB.

TB reactive arthritis was first described by Antonin Poncet in 1897 and named after him as Poncet's disease.⁹

Poncet's disease is a reactive polyarthritis associated with non-articular tuberculosis. It is a rare form of polyarthritis thought to be a reactive arthritis secondary to active Tuberculosis infection. The arthritis is aseptic in nature and, although the pathogenesis is uncertain, it is thought to occur due to a hypersensitive immune cell mediated response to the tuberculo-protein, resulting in an inflammatory reaction in the joint spaces. Due to the rarity of Poncet's disease despite the frequency of TB, a genetic predisposition has been suggested in the pathogenesis, with links to the HLA DR3 and HLA DR4 haplotypes. HLA DR4 has been implicated in rheumatoid arthritis and studies have shown DR4 positive patients to be hyper-responsive to mycobacterium antigens. However this link between Poncet's disease and HLA haplotypes requires further studies.

Clinically the disease is different to the well recognized TB monoarthritis; a septic mycobacterium infection of a joint leading to its destruction. From the cases previously described, Poncet's arthritis is non-destructive and resolves completely following TB treatment.

The arthritis mainly affects the larger joints, with the knee being the most commonly affected, followed by the ankle and wrist joints. Small joints may become involved as well as was the case with our patient. The axial skeleton tends not to be involved. The onset of arthritis is usually acute or subacute but chronic cases, although rare, have been reported. It is described as a symmetrical polyarthritis but many studies have suggested it to be a pauciarticular arthritis, mainly of the larger joints. Other common symptoms include lymphadenopathy (mainly cervical and axillary), grumbling fevers (which may be present many weeks prior to developing the arthritis) and skin changes; classically erythema nodosum.⁸

The diagnosis is usually one of exclusion and should be considered in all patients with a symmetrical arthritis in TB prevalent regions. Extra-pulmonary TB, particularly lymph node TB, is traditionally thought to be the main culprit.¹⁰ Very few cases of Poncet's arthritis with HIV have been reported. TB is often difficult to diagnose in HIV positive patients and due to the rarity and relatively unfamiliar nature of Poncet's disease it may be easily missed.¹⁰

The case serves to remind us to consider Poncet's disease

as a differential diagnosis in patients who present with symmetrical joint complaints.

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