Case report

Visceral leishmaniasis in a patient with disseminated malignancy

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Journal of the Ceylon College of Physicians, 2018, **49**, 72-74

Key words: Visceral leishmaniasis, malignancy, pyrexia of unknown origin

Introduction

Leishmaniasis, caused by species of *Leishmania*, can present in three main clinical forms; cutaneous, mucocutaneous and visceral leishmaniasis (VL). In Sri Lanka VL is recognized as an emerging infectious disease. VL is reported among immune-compromised hosts and the clinical manifestations and outcomes of the disease in these patients are largely unknown¹. We report a case of atypical visceral leishmaniasis and metastatic cancer of unknown primary presented with pyrexia of unknown origin (PUO).

Case report

A 72-year-old male, a manual worker from Kurunegala, presented with a two-month history of continuous fever associated with chills and malaise. He had loss of appetite and had lost 10 kg over two months. He had no arthralgia, cough, rashes and urinary or bowel symptoms. There was no improvement in fever with antibiotics given as an out-patient. There was no previous history of cutaneous leishmaniasis or foreign travel. He had a history of 30-pack-years of smoking and drank alcohol occasionally. On examination, he was febrile and cachectic. The rest of the clinical examination was normal.

Preliminary investigations revealed high erythrocyte sedimentation rate (127 mm 1st hour), mild anaemia with normal white cells and platelet counts. Chest x-ray showed hyper-inflated lung fields. Abdominal ultra

sound, echocardiogram, upper gastrointestinal endoscopy, colonoscopy and bronchoscopy were normal.

As he continued to have fever, a bone marrow biopsy was done to look for evidence of haematological malignancy, disseminated malignancy or tuberculosis. Bone marrow trephine biopsy showed malignant secondary deposits (Figure 1), ill-formed granulomas, lymphocyte and plasma cell infiltrate co-existing with few macrophages containing Leishman-Donovan bodies (Figure 2). The bone marrow culture and molecular assay became positive for leishmaniasis. However, rK 39 Serology tests were negative for VL. Tuberculosis polymerase chain reaction (TB PCR) was negative. Immunohistochemistry showed negative prostate specific antibody (PSA), thyroid transcription factor 1 (TTF1), cytokeratin 20 (CK 20) and strongly positive cytokeratin 7 (CK 7) in secondary deposits (Figure 3). Serum PSA, carbohydrate antigen (CA-19-9) level and carcinoembryonic antigen (CEA) levels were within normal limits.

Figure 1. Secondary deposit in bone marrow trephine biopsy (arrow) (Haematoxylin and eosin staining (H&E) (x400).

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Figure 2. Bone marrow trephine biopsy showing Leishman-Donovan bodies (Amastigote) (arrow) (Haematoxylin and eosin staining, H&E) (x400).

Figure 3. Bone marrow trephine biopsy showing CK₇ positivity in secondary deposits (immunohistochemistry (IHC) (x100).

He was treated with intravenous sodium stibogluconate (20mg/Kg/day -700 mg per day) for 28 days, and the fever resolved in 7 days. However, there was no improvement in his weight loss, constitutional symptoms and loss of appetite. Subsequent clinical examination three weeks after the admission revealed 1.5 cm hard immobile lymph node in the left supraclavicular region. Fine needle aspiration cytology (FNAC) of the lymph node showed undifferentiated

highly pleomorphic cells. Contrast CT of chest, abdomen and pelvis revealed an ill-defined soft tissue attenuating lesion on the left perinephric space encasing kidney and renal vessels. There was also a 2.6 cm focal lesion at segment 4B of liver. There were several sclerotic bone lesions in spine and right anterior inferior iliac crest. Few small lymph nodes were found in left supraclavicular and paratracheal regions. FNAC of the liver lesion was inconclusive.

Repeat bone marrow biopsy performed 6 weeks after the first biopsy revealed metastasis only. Extensive investigations failed to reveal primary site of malignancy.

Though his fever responded he continued to deteriorate with frailty, anorexia and weight loss. He was referred for palliative care due to the disseminated nature of the malignancy.

Discussion

Visceral leishmaniasis is a chronic infectious disease primarily caused by *Leishmania donovani* and transmitted by phlebotomine sandflies. VL is a serious parasitic disease, causing high morbidity and mortality in the developing world. Pathogenesis of VL is complex, and the clinical presentation ranges from asymptomatic infection to severe and fatal disease².

Although VL is commonly seen in healthy adults, it is infrequently reported in immunocompromised hosts. There are reported cases in patients with AIDs, haematological malignancies and renal transplant recipients¹. In such patients the clinical manifestations are atypical, and outcome of the disease is largely unknown. In most patients the diagnosis was made during an evaluation for PUO¹. Our patient who presented with PUO did not have typical clinical features of VL and the diagnosis was confirmed by bone marrow trephine biopsy and molecular assay.

In a case series of 120 suspected cases in Sri Lanka only 7 were confirmed as VL. It was not considered as the primary diagnosis in any of them as the clinical presentations were non-specific with fever being the commonest. Hairy cell leukaemia, typhoid, lymphoma and diabetes were identified as co-illnesses in 4 of them³. Although co-existence of two diseases is possible, a review by Kopterides et al concluded that leishmaniasis can directly or indirectly affect the clinical presentation, diagnosis and course of various malignant disorders⁴. Simultaneous diagnosis of leishmaniasis and a neoplastic disorder in the same tissue samples like in our patient has been described⁴.

Multiple approaches to diagnosis which include microscopy of smears, histopathology, in vitro culture, serology and molecular analysis by DNA is recommended to maximize the positive results^{5,6}. Bone marrow is the preferred site for obtaining a specimen for diagnosis; enlarged lymph nodes, spleen and liver are other potential sites⁵. Anti-leishmaniasis treatment relies on pentavalent antimonials such as sodium stibogluconate and anti fungal drugs. Our patient is likely to have acquired infection locally as he had no history of foreign travel. Sodium stibogluconate (first line) and amphotericin B (second line) are the drugs recommended in the local protocol and resistance to these compounds is not yet reported in Sri Lanka⁷.

Conclusion

VL should be considered as a differential diagnosis in patients presenting with pyrexia of unknown origin. With increasing prevalence of Leishmaniasis in Sri Lanka, infection in immunocompromised individuals is likely to rise, warranting increased awareness by the treating physicians.

References

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