A RARE CASE OF VISCERAL LEISHMANIASIS IN NON-ENDEMIC STATE OF MAHARASHTRA, INDIA

Warpe BM¹, Adharsh A², More SV⁴, Rane SV³

1-Department of Pathology, IGGMC, Nagpur.  
2,3-Department of ENT, IGGMC, Nagpur.  
4-Department of Biochemistry, SRTR medical college, Ambajogai.

ABSTRACT:
Visceral leishmaniasis (VL), also known as Kala-azar (black fever) and Dumdum fever is the most severe form of leishmaniasis. This disease is caused by parasites of Leishmania genus, especially by Leishmania donovani parasite in India through the bite of female sand flies. Systemic signs and symptoms are known to occur in VL with peripheral cytopenia and organomegaly and of particular concern is its HIV association. VL is endemic in north-east India especially in state of Bihar but rarely seen in the western state of Maharashtra, as very few cases have been reported. We present a rare Indian VL case of a young HIV positive lady in the state of Maharashtra, the rarity being the pure mucosal lesion at presentation and the non endemicity of the area where she resides.

KEYWORDS: Visceral leishmaniasis (VL), Leishmania donovani, HIV, Kala-azar.

1. INTRODUCTION:
Leishmaniasis is a parasitic disorder transmitted by the bite of infected female sandflies which inoculate the promastigotes into the skin of the human host.¹ In humans, the disease presents with four different forms with varied clinical features: visceral leishmaniasis or kala-azar (severe form); cutaneous leishmaniasis; mucocutaneous leishmaniasis and diffuse cutaneous leishmaniasis.² In India, kala-azar is believed to be confined to the endemic north-eastern part of the country.³⁴ The latter is not known to occur in western part of Maharashtra except in some immuno-compromised or migrants from north-east. Also, isolated cases have been reported in the capital city of Mumbai.⁵ The nearest state suspected but unproven endemic area is Goa.⁶

2. CASE DETAILS:
A 29-year-old pregnant female with G2P2L1A0 from Gondia district, Maharashtra state came with complaints of left buccal mucosal ulcer since 3 months and left neck swelling since 2 months (Figure 1). She also complained of gradual loss of weight from 6 months and chronic productive cough since 4 weeks. The seven months ANC lady had married four years back with a healthy 3-year-old child. The lady had no history of any blood transfusion / high risk behavior with no significant family or personal history. She had pallor but there was no evidence of icterus, cyanosis, clubbing or oedema.

The oral examination of the lady revealed mild trismus with 7x4 cm submucosal proliferative lesion in the left side of gingivobuccal sulcus involving the retromolar-trigone area (Figure 1-inset). Also the adjacent buccal mucosa showed scattered ulcerated areas with mild induration and tenderness. The lady showed a left sided neck mass of 10x10 cm involving level I, II,III,IV and V lymph nodes- indiscrete, firm in consistency, mobile, non-fluctuant, non-tender and the skin over the swelling was normal and free from the mass. The frail patient had mild hepatosplenomegaly. Accordingly the following clinical provisional diagnoses were made:
1. Oral malignancy with secondaries in neck.  
2. Extra pulmonary tuberculosis.  
3. Lymphoma.  
4. Immunocompromised state with opportunistic infection.
Lab investigations were advised which revealed pancytopenia. The supplementary investigations showed a twice repeated HIV–ELISA test as ‘reactive’ with CD4 count of 71 cells/cu mm of blood. Also her HBSAg was negative with negative Mantoux test. The sputum tests revealed Gram-negative cocccobacilli on Gram staining and negative AFB stain.

The USG investigation from the neck mass showed features of ill-defined heterogenous, hypoechoic, non-encapsulated mass with area of necrosis, flecks of calcification with moderate vascularity with compression of left External carotid artery. The FNAC from cervical lymph node mass revealed smears in a hemorrhagic background showing cystic macrophages, histiocytes, epitheloid cells, intracytoplasmic bodies, possibly Leishmanianodonavi or toxoplasma. No evidence of any malignancy noted in the FNAC smears. (Figure 2).

Also on histopathology, the punch biopsy report from oral mass showed thickened non-keratinised squamous epithelium with acantholysis, with underlying tissue showing sheets of macrophages and histiocytes containing Leishman-Donovan (LD) bodies (intracytoplasmic granules) as amastigote form of the protozoan (Figure 3). The hypoplastic bone marrow aspirate smears showed plenty of amastigotes forms of Leishmania donovani (also known as LD bodies) both intracellularly within the macrophages as well as extracellularly (Figure 4). The splenic aspiration was not done as she was pregnant. Also, the serological dipstick test for leishmaniasis like rK39 was positive.

Thus the final diagnosis made was: Pregnant immune-compromised HIV-AIDS patient with visceral leishmaniasis. She was counseled for regular ART centre visits with HAART therapy. Proper informed consent were taken and Pentostam® (Sodium stibogluconate) was started and given for 30 days by intravenous therapy in the dose of 20mg/kg/day (max-850 mg) with 100 mg/ml vial diluted in 10 ml of 5% dextrose given over 30 minutes. The patient showed a good response to this treatment, her appetite improved slowly, there were no petechial rash, fever or vomiting with therapy. The cervical swelling and her oral lesions subsided after 30 days. Though there is high level of resistance to Sodium stibogluconate in endemic areas of India, our patient developed response to this therapy and her CD4 counts also improved fairly well after 20 days of therapy.

3. DISCUSSION:

Although visceral leishmaniasis (VL) is endemic in 62 countries, the disease is clustered around areas of drought, famine, and high population density. 90% of the estimated 500,000 new cases, which occur annually, are confined to the rural areas of India, Nepal, Bangladesh, Sudan and Brazil; as many as one-half of these cases occur in India. The VL cases which are rarely reported in non-endemic western India are patients with a history of residency or travel to the endemic north part of India. The non-endemic state of Maharashtra has few reported cases of VL. Kaneria MV et al (2005) suggested in a case which was a Bihari migrant to Mumbai, Maharashtra that autoimmune disorders are seen with chronic infectious diseases such as tuberculosis, cryptococcosis, etc. They were of the view that since VL and autoimmune disorders were co-existing, they were most probably causally related. Gawade S et al (2012) showed a case of HIV+VL association in a Nepali national working in Kolhapur, Maharashtra. The difference in our case and the former is that our case was Indian national from a non-endemic area for VL without any autoimmune disorder.
Patient photo - Left-sided neck swelling in a 29-year-old pregnant female. Inset showing the oral examination with 7x4 cm submucosal proliferative lesion in the left side of gingivo-buccal sulcus involving the retromolar-trigone area.

Photomicrograph-FNAC from cervical lymph node mass revealed smears in a hemorrhagic background showing cystic macrophages, histiocytes, epithelioid cells, intracytoplasmic bodies, possibly Leishmania donovani amastigotes (WGO, x 400).

Photomicrograph-Tissue section from punch biopsy of oral lesion showing thickened non-keratinised squamous epithelium with acantholysis (Inset H&E, x 0.00), with underlying tissue showing sheets of macrophages and histiocytes containing Leishman-Donovan (LD) bodies (intracytoplasmic granules) (H&E, x 400).

Photomicrograph-Bone marrow aspirate smears showing plenty of amastigotes forms of Leishmania donovani (LD bodies) both intracellularly within the macrophages as well as extracellularly. (Leishman stain, x 1000).
VL is uniformly fatal unless treated. The incubation period of kala-azar ranges in between 10 days to 2 years.\textsuperscript{10} VL has non-specific sub-clinical infection while mild clinical manifestations lasting for more than three weeks include fever, cough, diarrhoea, malaise, mild hepatomegaly and eventually splenomegaly presenting as fluctuating course that evolves over a prolonged period of time. Anaemia is the major and most frequent haematological sign, generally of normocytic and normochromic type\textsuperscript{11}.

The gold standard for diagnosis is visualization of the amastigotes in splenic aspirate or bone marrow aspirate. This is a technically challenging procedure that is frequently unavailable in areas of the world where VL is endemic. Serological testing is much more frequently used in areas where leishmaniasis is endemic. The \textit{rK}_{39} dipstick test is easy to perform, and village health workers can be easily trained to use it.\textsuperscript{12}

The treatment of choice now for VL in India is liposomal Amphotericin-B.\textsuperscript{13} until the early 1990s, pentavalent antimony was the only first-line drug with a well-documented record of success in the treatment of VL. The traditional treatment is with pentavalent-antimonials such as sodium-stibogluconate and meglumine-antimoniate. Resistance is now common in India and rates of resistance have been shown to be as high as 60% in parts of Bihar, India.\textsuperscript{14} We used this drug ‘sodium-stibogluconate’ mainly because the patient was pregnant and she couldn’t afford Amphotericin-B but the patient responded well to this old first-line therapy. Miltefosine, the first oral treatment for VL with a 28-day long course and the oral antibiotic-paromomycin were sanctioned by the Indian government for use since 2002 and August 2006 respectively but are very costly.\textsuperscript{15}

4. CONCLUSION:

As kala-azar is non-endemic in Maharashtra state of India, this patient remained undiagnosed for a considerable period of time. A delayed diagnosis due to atypical manifestations and its frequent association with HIV-AIDS, especially in non-endemic India may lead to a fatal outcome in these patients. Clinical criteria of organomegaly, pallor with simple laboratory findings like pancytopenia, a positive \textit{rK}_{39} dipstick test and bone-marrow or splenic aspirates can help make an early diagnosis even in atypical cases like HIV-AIDS+VL, thereby reducing the mortality of visceral leishmaniasis. Also, sodium-stibogluconate whose resistance is now common in endemic India can be still effective in non-endemic Indian cases of HIV+VL.

5. REFERENCES:

[1]. Extent of problem of Kala-azar in India; National Vector Borne Disease Control Programme (NVBDCP); MOHFW; http://nvbdcp.gov.in/
[15]. New Cure for Deadly Visceral Leishmaniasis (Kala Azar) Approved By Government Of India. (Press release One World Health, September 8, 2006).