

*CASE REPORT*

**Pancytopenia due to lepromatous involvement of the bone marrow: Successful treatment with multidrug therapy**

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*Summary* Leprosy is a chronic infectious disease with a wide spectrum of signs and symptoms depending on the ability of the host's immune system to resist the infection. The disease is frequently associated with sensory loss in skin lesions and damage in peripheral nerve trunks leading to nerve function impairment. In lepromatous leprosy, the immune system offers no protection against the multiplying bacilli and this results in heavy infiltration of the internal organs. We report a case of florid lepromatous leprosy with bone marrow suppression due to the disease, presenting with anemia, leukocytopenia and thrombocytopenia. The hematological abnormalities were fully reversed by multidrug therapy for leprosy. We suggest that infiltration of the bone marrow by *Mycobacterium leprae* can cause pancytopenia, which can be cured by treatment of the leprosy alone.

**Introduction**

Lepromatous leprosy (LL) is the most severe form of leprosy, in which unchecked multiplication by enormous numbers of bacilli results in systemic manifestations. The heavy load of *M. leprae* found in the reticuloendothelial system is due to bacilli from the blood and lymph circulation deposited in the liver, spleen, bone marrow and lymph nodes.<sup>1</sup> Anemia,<sup>2</sup> leukopenia,<sup>3</sup> and both anemia and leukopenia occurring simultaneously,<sup>4</sup> secondary to bone marrow involvement in LL, have been demonstrated. Immune thrombocytopenic purpura with bleeding manifestations in a case of borderline lepromatous leprosy on multidrug therapy (MDT) for 6 months, has been reported. The good response of the thrombocytopenia to prednisolone confirmed the immune etiology, though the possibility of it occurring as a

result of leprosy has also been suggested.<sup>5</sup> Causes of thrombocytopenia in leprosy include drug-induced thrombocytopenia due to rifampicin.<sup>6</sup> Thrombocytopenia can also be a manifestation of anti-phospholipid syndrome, which can be due to infections including leprosy.<sup>7</sup> To the best of our knowledge, LL primarily causing bone marrow suppression leading to thrombocytopenia has not been reported. We report a case of LL with pancytopenia which could be attributed solely to the disease, and which resolved fully with anti-leprosy treatment.

### Case Report

A 24 year old male presented with a 1 year history of generalised, asymptomatic skin lesions, along with numbness and weakness of the hands and feet. There was no history of an acute exacerbation of the symptoms or appearance of new lesions or sudden weakness of the limbs. He had not taken any treatment for his symptoms.

Physical examination revealed multiple, soft, non-tender enlargement of the cervical, axillary and inguinal lymph nodes. There were numerous hyperpigmented papules, small plaques and nodules varying between 3 mm to 3 cm in size, on the face (Figure 1), limbs (Figure 2) and trunk, along with infiltrated nodules on the pinnae of the ears (Figure 3) and hyperpigmented papules on the soles (Figure 4).

Many of the lesions had a rough, verrucous surface. There was loss of hair over the eyebrows, eyelids, trunk and limbs. On ocular examination, scleral nodules were noted at the nasal limbus of the right eye. Ophthalmological examination was otherwise normal.



**Figure 1.** Hyperpigmented papules, plaques and nodules on the face.



**Figure 2.** Papules and small plaques on the limbs.

Palpation of the peripheral nerves revealed tenderness and thickening of the right ulnar and both common peroneal nerves, with non-tender thickening of both greater auricular nerves and right sural nerve. Examination of the sensory system revealed loss of fine touch, temperature and pain sensations over the distal parts of both upper limbs up to the mid-forearms, and over both lower limbs distal to the lower two-thirds of the legs. There was ulnar clawing of both hands, with mild clawing of the thumb and weakness of the small muscles of the hands. There was no evidence of Type 1 or Type 2 reaction.

Slit-skin smears from lesional skin and normal skin were positive for acid-fast bacilli, with a bacillary index of 5+ and 4+ respectively, and a morphological index of 30. Complete blood cell count (CBC) showed a hemoglobin level of 7.9 g/dl, a white cell count of  $2100/\text{mm}^3$  with 85% neutrophils, 9% lymphocytes and 5% monocytes, and a platelet count of  $78,000/\text{mm}^3$ . Liver function tests were normal except for serum proteins, in which albumin was 2.2 and globulin was 3.5 gm/dl, indicating a reversal of the A:G ratio. Renal function tests, serum electrolytes, blood sugar and chest radiograph were normal. Tuberculin skin testing, sputum for acid-fast bacilli and cytology, retrovirus, hepatitis B antigen, anti-hepatitis C virus and anti-nuclear antigen tests, VDRL, anti-platelet antibodies and blood culture showed negative results. Peripheral smear examination showed hypochromic, microcytic anemia with mild thrombocytopenia and leukopenia. An abdominal ultrasonogram revealed hepatomegaly, with a liver size of 14 cm (normal 10 cm) and spleen 13 cm (normal 10–12 cm). Fine needle aspiration cytology (FNAC) from the enlarged cervical and inguinal lymph nodes showed a scanty aspirate with a few lymphocytes and macrophages. Skin biopsy and axillary lymph node biopsy showed features of lepromatous leprosy and



**Figure 3.** Infiltrated nodules on the pinnae of the ears.

pyogranulomatous lesion, respectively. Bone marrow examination was not performed as the patient declined to give permission for the procedure.

With the clinical findings of ear lobe infiltration, generalised skin lesions, sensory loss and motor weakness, along with the demonstration of acid-fast bacilli in the skin smears, the final diagnosis was LL with Grade 2 disability of the hands, Grade 1 disability of the eyes and feet, and nerve function impairment (NFI) of both ulnar, both common peroneal and both posterior tibial nerves.

Since the patient did not have any other disease and was not on any drugs which could possibly cause pancytopenia, we concluded that the bone marrow suppression could be due to leprous infiltration of the bone marrow. He was given MDT with dapsone being substituted by 400 mg of ofloxacin daily because of the anemia, along with 50 mg of clofazimine daily and once-monthly pulse of 300 mg of clofazimine with 600 mg of rifampicin. In addition, the patient received prednisolone for the NFI as well as iron and vitamin supplements. Daily monitoring of the CBC was done. The platelet count had risen to  $152000/\text{mm}^3$  by the sixth day of treatment, and  $228000/\text{mm}^3$  by the tenth day.

The improvement in the white cell count was slower and was  $5300/\text{mm}^3$  by the tenth day, while the hemoglobin level was 8.9 g/dl by the tenth day. The reversal of serum A:G ratio was corrected by the fifth day of treatment, with albumin level 3.7 and globulin 2.9 gm/dl.

The patient showed satisfactory improvement during monthly follow-up examinations, and all haematological parameters returned to normal. At the end of 3 months the lymphadenopathy and hepatosplenomegaly were still present, though a slight reduction in the size was noted.



**Figure 4.** Hyperpigmented papules on the soles.

## **Discussion**

In lepromatous leprosy, the inability of the host's immune system to resist the infection, results in a heavy bacterial load, estimated at  $10^5$  organisms/ml of blood.<sup>8</sup> Our patient was seen in an advanced stage of the disease. The anemia and leukopenia observed in our case is a manifestation of bone marrow involvement by circulating lepra bacilli.<sup>4</sup> The occurrence of thrombocytopenia in LL has not been reported before and can also be attributed to the same mechanism. The presence of lepra bacilli and microgranulomas composed of foamy macrophages, plasma cells and lymphocytes interfering with the normal functioning of the bone marrow could be responsible for the pancytopenia, which resolved within 2 weeks of initiation of anti-leprosy treatment. Our patient was not on any concomitant drug therapy and did not have any other detectable cause for the pancytopenia. The pancytopenia could not have been drug-induced as it was detected before initiation of multidrug therapy. He had no episodes of deep vein thrombosis, arterial occlusion or other features of antiphospholipid syndrome. He was given corticosteroids for the NFI. Immune thrombocytopenic purpura responds rapidly to prednisolone treatment.<sup>5</sup> However, he was not in reaction and there were no antiplatelet antibodies or evidence of an immune etiology for the thrombocytopenia. Hence the improvement of the thrombocytopenia cannot be attributed to corticosteroids in this case. The non-tender hepatomegaly and lymphadenopathy seen in our patient are documented findings in lepromatous cases. Numerous miliary lepromas consisting of macrophages packed with bacilli are found in the liver, lymph nodes and spleen. Macrophages replacing lymphocytes in the thymus-dependent areas of the spleen can

contribute to the nonspecific suppression of cell-mediated immunity in advanced LL.<sup>9</sup> The reversal of albumin:globulin ratio seen in our patient is also a feature of bacillated leprosy, which tends to normalise with regression of the disease.<sup>10</sup> The normal liver function tests and FNAC studies of the lymph nodes indicated that there was no functional impairment of the liver or lymph nodes. The lymphadenopathy, hepatomegaly and splenomegaly in our patient had not subsided after 3 months of MDT, indicating that the resolution of the granulomas and leprosy infiltration is a slow process.

This case underscores the importance of early detection and treatment in the prevention of multi-organ involvement and its sequelae in LL. The possibility of bone marrow suppression due to the disease itself has to be considered in patients with LL presenting with pancytopenia. To our knowledge, this is the first reported case of anemia, leukopenia and thrombocytopenia occurring simultaneously due to leprosy infiltration of the bone marrow, which we recommend can be treated without any specific treatment other than MDT.

## References

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