Indian J Lepr 2008, 80 : 275-278

Case Report

Systemic Sarcoidosis in a Case of Lepromatous Leprosy: A Case Report

P Sharma, M Bhardwaj**, HK Kar**

Abstract

The clinical features of cutaneous sarcoidosis and leprosy are some times difficult to differentiate and there have been many reports where pulmonary sarcoidosis was treated as pulmonary tuberculosis or a case of sarcoidosis was treated with anti-leprosy multidrug therapy, before a correct diagnosis was made. So far there has been only one published case report of leprosy and sarcoidosis co-infection, where tuberculoid leprosy developed in a case of sarcoidosis, known for over a decade. We are reporting a case of dual affliction, where sarcoidosis was discovered (on routine screening) in a case of lepromatous leprosy, after administration of 2 years of multidrug therapy. The role of mycobacterial antigens (among a vast array of different animate or inanimate particles) in causation of sarcoidosis, is still speculative, as reviewed from literature.

Key words : Systemic sarcoidosis, ENL, MDT, Mycobacterial antigens, Leprosy

Introduction

Sarcoidosis is a multisystem inflammatory disease that mainly affects lymph nodes and pulmonary tissues and is characterized by non-caseating granulomas in the affected organs (Crystal et al 1984). The skin involvement in sarcoidosis is observed in about 20-30% cases. On the other hand, leprosy is a chronic granulomatous mycobacterial infection, primarily affecting the peripheral nerves and the skin, with occasional involvement of eyes and other organs. To our knowledge, there has been only one case report where leprosy developed in a case of sarcoidosis, known for 13 years. We are reporting a case of lepromatous leprosy in which sarcoidosis was diagnosed, as a matter of routine examination for complaints of dry cough, after a period of 2 years of regular administration of MBMDT.

Case Report

A 50 year old female was referred to the Department of Dermatology from the Department of Neurology in March 2005 with clinical findings of facial erythema, symmetrical polyneuropathy with bilateral

* P Sharma, Senior Research Officer, Department of Dermatology, STDs and Leprosy
** M Bhardwaj, Senior Pathologist, Department of Pathology (Histopathology Unit)
*** HK Kar, Professor and Head, Department of Dermatology, STDs and Leprosy
Dr Ram Manohar Lohia Hospital and PGIMER, Baba Kharak Singh Marg, New Delhi-110001, India
Correspondence to : Prof (Dr) HK Kar, Email : hkkar_2000@yahoo.com

ulnar nerve thickening and madarosis. She gave a history of paraesthesia both feet, skin patches over back and infiltration of both ear lobes for past 2 years for which she consulted in private clinics. On examination in the Dermatology Department, she was found to have diffuse erythema and infiltration all over body, especially limbs, face, ears. Bilateral ulnar and lateral popliteal nerves were moderately enlarged and non-tender, patient had glove and stocking hypoesthesia. There was no history of fever with or without rigors or of any eruptions of nodular swellings over the body. A provisional diagnosis of lepromatous leprosy (LL) was made. Her bacteriological index (BI) was found to be 6+ (Ridley's grade) and the histopathological report came as lepromatous leprosy.

She was started on WHO multibacillary (MB) multidrug treatment (MDT) in March 2005 which she continued regularly till March 2007 (partly from our hospital and often from private clinic). In January 2006, she had an episode of erythema nodosum leprosum (ENL) which was controlled by a course of oral steroid (Prednisolone) for 4 weeks. In November 2006, she had another mild episode of ENL which was controlled by NSAID (Ibuprofen). After receiving 24 months of regular MBMDT, she was released from treatment (RFT) in March 2007. Her slit-skin smear examination report for AFB was not available at the time of RFT.

In April 2007, she reported to a physician in the Department of Internal Medicine of our hospital with complaints of dry cough. Her chest X-ray showed bilateral hilar lymphadenopathy (BHL) and the CT scan (Chest) revealed extensive madiastinal and bilateral hilar lymphadenopathy, with bilateral parenchymal small nodular shadows central bronchiectatic changes and septal thickening. Radiologist's opinion was of sarcoidosis with differential diagnosis of tuberculosis. There was no history related to anti-tuberculosis treatment (ATT), diabetes or hypertension. Hemogram was normal except for ESR which was 41 mm in first hour. Liver function tests were normal and urine examination showed few epithelial cells and calcium oxalate crystals. She was admitted to hospital for fibreoptic bronchoscopy and bronchial biopsy which on histopathological evaluation showed a single naked epithelioid granuloma, opinioned likely consistent with sarcoidosis and stain for AFB was negative. Fluid cytopathology from bronchial washings did not show any granuloma or malignant cells. Montoux test was negative and TB ELISA was positive for IgG and negative for IgM. Pulmonary function tests were within normal limits. Serum angiotensin converting enzyme (ACE) level was found to be raised to 228 (normal 8-65 micrograms/L). Serum calcium was 10.7 mg% and 24 hour urine calcium excretion was low, 96 mg/24 hours (Normal value 100-300 mg/24 hours). Serum LDH was 437 U/L (Normal value 340-480 U/L) and serum beta 2 microglobulin was grossly raised (3697 microgm, normal value 510-1470). The thyroid function tests revealed hypothyroidism (TSH 7.14 mIU/L, Normal value 0.35-5.5 mIU/L) for which she was started on Eltroxin. Ultrasound (abdomen) revealed cholelithiasis, though she never had any pain abdomen in the past. Blood CRP, ANA and RA were all non-reactive.

From the clinical signs and symptoms and with the positive findings of investigations, a diagnosis of sarcoidosis (non-cutaneous) was made and she was started on oral steroids around July 2007 (Tab. Deflazacort [Defcort] 60 mg OD). She responded very well to the oral steroid with resolution of her respiratory complaints within 2 weeks of starting steroids and also her serum ACE levels dropped down to 152 micrograms/L from 228 micrograms/L after

one month and to 36 micrograms/L after 10 weeks of starting steroids.

Around the same time when she had started having chest complaints in April 2007, she noticed a new small nodular lesion over the skin below right knee about a month after RFT. The slit skin smear examination from the nodule revealed a BI of 3+. To exclude cutaneous sarcoidosis, skin biopsy was done from the nodule which revealed the histopathological feature of borderline leprosy. In view of concomitant condition of sarcoidosis, for which she was on oral steroids and slit-skin smear positivity for AFB, she was again started on MBMDT in July 2007. In December 2007, her slit-skin smear BI was 2+ and it dropped down to 1.5+ in April 2008. When last seen in June 2008, she was on a tapering dose of oral steroids (Tab. Prednisolone 10 mg OD) along with MBMDT, Eltroxin and other supportive medications.

Discussion

Our objective of gathering diverse information available related to this case was, to explore on the issue, whether lepra bacilli could have some role in the aetiopathogenesis of sarcoidosis ? It is well established that leprosy transmitted occurs through nasal route and although AFB enters bronchial vasculature after passing through upper respiratory tract, it never produces any leprosy lesion in the bronchus or lung tissue, while on other hand, the later are the common sites of development of sarcoid granuloma.

The cutaneous manifestations of the two conditions could sometimes be difficult to differentiate and there have been several reports where the two conditions have been confused with each other (Fields and Hellreich 1969, Levy and Lantis 1971, Ramanujam 1982, Singh et al 1990, Sawhney et al 1995, Yupin and Pairaj 2007). Radiologically also, the features of pulmonary sarcoidosis and pulmonary tuberculosis are sometime difficult to differentiate. There are reports when patients of confirmed tuberculosis have developed sarcoidosis while on anti-tuberculosis treatment (ATT) (Emerson and Young 1956, Wong et al 1998). Despite various reports mentioned above describing confusing situations among sarcoidosis, tuberculosis and leprosy, there has been only one case report of coexisting leprosy and sarcoidosis, where tuberculoid leprosy was diagnosed in a known case of sarcoidosis for 13 years (Burdick and Anne 2000). In our case, the other way round, the pulmonary sarcoidosis was detected in a patient of lepromatous leprosy (BI 6+), when she had completed 2 years of MBMDT. On work up for complaints of dry cough she was found to have BHL and other features described above. It would be speculative to presume for how long before, the patient could have been having (obscure) sarcoidosis. It would also be difficult to presume, that leprosy infection was of recent development, because of the chronic course of Hansen's disease and long incubation period. To comment upon, whether the mycobacterial antigen would have triggered the immune response leading to sarcoidosis development in this case, would be debatable. In the other case report of leprosy-sarcoidosis dual affliction described above, the mycobacterial load was minimal, as shown by negative PCR findings with *M. leprae* and the dual conditions seem to be a matter of coincidence.

Isolation and/or identification of *Mycobacterium paratuberculosis* or closely related *Mycobacterium avium* complex strains has been reported from sarcoidosis lesions which provides support to the mycobacterial etiology of sarcoidosis (el Zaatari et al 1996). A similar PCR based study of tissue specimens from 25 patients of sarcoidosis and 25 control subjects, a total of 60% cases specimen were found positive for

mycobacterial species, but negative for IS*6110* (the specific for *Mycobacterium tuberculosis*) (Drake et al 2002). A study based on Restriction Fragment Length Polymorphism (RFLP) and hybridization of DNA extracted from *Mycobacterium tuberculosis*, non-tuberculous mycobacteria and nonmycobacterial species with a probe derived from IS*6110* has confirmed that IS*6110* was specific to *M. tuberculosis* complex (Willie et al 1999).

Despite many reports pointing towards mycobacterial (especially those other than tubercular) possible aetiology in its causation, all available evidence is consistent with the concept that the disease results from an exaggerated cellular immune response (acquired, inherited or both) to a limited class of persistent antigens or self-antigens. The reported efficacy of minocycline used in sarcoidosis patients was also inconclusive on the issue whether the beneficial effects were due to antimicrobial activity against some putative microbe responsible for sarcoidosis or it was the anti-inflammatory effect of the antibiotic which helped resolution of sarcoidal granuloma (Bachelez et al 2001). It may also be noted that anti-bacterial role of minocycline is well established against *Mycobacterium leprae*, however, this does not support the role of lepra bacilli in aetiopathogenesis of sarcoidosis.

Conclusion

The role of mycobacteria (tubercular, leprae or any other atypical form) in the aetiopathogenesis of sarcoidosis is far from clear at present, more so, whether it is the direct infection or some poorly understood triggering of immune mechanism leading to granuloma formation.

References

1. Bachelez H, Senet P, Cadranel J et al (2001). The use of tetracyclines for the treatment of sarcoidosis. *Arch Dermatol*. **137**:69-73.
2. Burdick A and Anne E (2000). Hansen's disease in a patient with a history of sarcoidosis. *Int J Lepr Other Mycobact Dis*. **68**: 307-311.
3. Crystal RG, Bitterman PB, Rennard SI et al (1984). Interstitial lung diseases of unknown cause. Disorders characterized by chronic inflammation of the lower respiratory tract. *New Eng J Med*. **310**:154-166.
4. Drake WP, Pei Z, Pride DT et al (2002). Molecular analysis of sarcoidosis tissues for mycobacterium species DNA. *Emerg Infect Dis*. 8: 1334-1341.
5. Emerson PA and Young FH (1956). Sarcoidosis following tuberculosis. *Tubercle*. **4**: 116-119.
6. el Zaatari FA, Naser SA, Markesich DC et al (1996). Identification of *Mycobacterium avium* complex in sarcoidosis. *J Clin Microbiol*. **34**: 2240-2245.
7. Fields JP and Hellreich PD (1969). Sarcoidosis masquerading as Hansen's disease. *Arch Dermatol*. **100**: 649-651.
8. Levy E and Lantis S (1971). Sarcoidosis ? Leprosy? *Arch Dermatol*. **103**: 349-350.
9. Ramanujam K (1982). Tuberculoid leprosy or sarcoidosis? A diagnostic dilemma. *Leprosy India*. **54**: 318-323.
10. Sawhney MP, Srinivasan S and Dey GN (1995). Leprosy and pulmonary tuberculosis or sarcoidosis? *Indian J Lepr*. **67**: 473-477.
11. Singh K, Raina V, Narula AK et al (1990). Sarcoidosis masquerading as leprosy, pulmonary tuberculosis and urolithiasis. *J Assoc Physicians India*. **38**: 657-659.
12. Willie AG, Stuart MW and Francis AD (1999). Specificity of IS*6110* - based DNA fingerprinting and diagnostic techniques for *Mycobacterium tuberculosis* complex. *J Clin Microbiol*. **37**: 1224-1226.
13. Wong CF, Yew WW, Wong PC et al (1998). A case of concomitant tuberculosis and sarcoidosis with mycobacterial DNA present in sarcoid lesion. *Chest*. **114**: 626-629.
14. Yupin T and Pairaj K (2007). Sarcoidosis mimics lepromatous leprosy: a case report. *J Med Assoc Thai*. **90**: 171-174.