Noncaseating Granulomas in Lung: Think Beyond Sarcoidosis

To the Editor:

The case report by Papanikolaou and Sharma in a recent issue of CHEST (Dec 2009), whereby they reported sarcoidosis concurrently in a patient with rheumatoid arthritis, generates a lot of interest. After going through this report, I would like to raise the following issues which I feel should be addressed.

Having a close look at the high-resolution CT image, it is hard to appreciate the perivascular distribution of nodular opacities in the left lung parenchyma. Also, the absence of bilateral hilar lymph nodes makes the radiologic picture rather incompatible with that of sarcoidosis.

As far as the presence of noncaseating granulomas on histopathologic examination is concerned, Daïen et al have recently reported a series of 10 cases of sarcoid-like granulomas in patients treated with Etanercept (anti-tumor necrosis factor [TNF] therapy). It has been suggested that TNF levels may paradoxically increase on treatment with Etanercept, occasionally leading to TNF-mediated disease. Although the same effect was mentioned by the authors in this discussion, I wonder why the case is being seen as a dual pathology harboring both sarcoidosis and rheumatoid arthritis. In such cases, discontinuation of treatment with anti-TNF therapy has been suggested to help the patient recover from the illness. The delay between onset of treatment and appearance of granulomatosis has been reported to be ≥4 years, and it may take up to a year for the clinical and radiologic signs to go into remission after stopping the culprit drug. Therefore, in this particular case, the pulmonary involvement should be seen as a side effect of Etanercept treatment rather than labeling the patient as having sarcoidosis.

Alkesh Kumar Khurana, MD, DNB, FCCP
Chandigarh, India

Affiliations: From the Department of Pulmonary Medicine, the Government Medical College and Hospital.

Financial/nonfinancial disclosure: The author has reported to CHEST that no potential conflicts of interest exist with any companies/organizations whose products or services may be discussed in this article.

Correspondence to: Alkesh Kumar Khurana, MD, DNB, FCCP, Government Medical College and Hospital, Sec 32, Chandigarh, India; e-mail: lunggancer@rediffmail.com

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DOI: 10.1378/chest.09-3017

REFERENCES


Response

To the Editor:

We would like to sincerely thank Dr Khurana for her interest and her comments regarding our article published in CHEST (December 2009). Dr Khurana suggested that the patient’s current disease should be better attributed to an etanercept side effect, rather than to a second primary disease (meaning sarcoidosis) in a patient diagnosed with rheumatoid arthritis. Although the suggestions made by our colleague are reasonable, certain remarks should be made.

In the article by Daïen et al, all drug-induced granulomatous disease developed during etanercept treatment and mean delay times for disease to present (26 months for etanercept and 51 months for infliximab) were under continuous anti-tumor necrosis factor (TNF) treatment. Our patient had been off any treatment with anti-TNF for >5 years. Even if we hypothesize that her disease was present and asymptomatic all that time, it should have normally already subsided. In the article by Daïen et al, all cases resolved within 1 year of drug withdrawal. Therefore, the clinical course of this patient does not support a drug-induced reaction.

For these reasons, it is unlikely that etanercept was the cause in our patient; the option of a second primary disease (meaning sarcoidosis) seems much more reasonable. Etanercept side effects, though, are not fully elucidated. Although late development of pulmonary fibrosis may occur after chest irradiation or certain drugs, this has not been demonstrated for granulomatous lung disease and anti-TNF medication.

Ilias C. Papanikolaou, MD
On P Sharma, MD, Master FCCP
Los Angeles, CA

Affiliations: From the Division of Pulmonary and Critical Care, Keck School of Medicine (Drs Papanikolaou and Sharma), University of Southern California; and the 3rd Pulmonary Department (Dr Papanikolaou), Sismanoglio General Hospital, Athens, Greece.

Financial/nonfinancial disclosures: The authors have reported to CHEST that no potential conflicts of interest exist with any companies/organizations whose products or services may be discussed in this article.

Correspondence to: Ilias C. Papanikolaou, MD, Rm 11-900, LAC + USC Medical Center, 1200 N State St, Los Angeles, CA 90033; e-mail: iliaspapa@hotmail.com

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