Sarcoidosis complicating treatment with natalizumab for Crohn’s disease

Case report

C A Parisinos,1 C W Lees,1 W A H Wallace,2 J Satsangi1

ABSTRACT

Natalizumab is a humanised monoclonal antibody targeting the lymphocyte adhesion molecule α4 integrin, with proven efficacy in multiple sclerosis (MS) and Crohn’s disease (CD). The development of sarcoidosis with extrapulmonary involvement is reported in two patients with refractory CD who had received maintenance therapy with natalizumab. This complication has not been previously reported. It is hypothesised that the effect of natalizumab in altering lymphocyte mucosal trafficking may underlie the development of sarcoidosis in these patients.

CASE REPORTS

Case 1

A 38-year-old man with Crohn’s disease (CD) was referred into a phase II clinical trial of natalizumab. His past medical history included 20 years of colonic CD and pancreatitis secondary to azathioprine. Following initial infusions of natalizumab (6 mg/kg) in December 2002 and January 2003, the patient entered the maintenance arm (300 mg natalizumab monthly).

During the study the patient developed a dry cough. A chest x-ray in May 2004 revealed peripheral infiltrates and hilar lymphadenopathy; carbon monoxide transfer factor (Tco) was 75% predicted and serum ACE was increased (95 U/l). A high-resolution CT (HRCT) scan of the thorax showed lung nodules with left lower lobe conglomeration.

A transbronchial biopsy demonstrated several epithelioid non-caseating granulomas consistent with sarcoidosis (figure 1C). 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CWL has a consultancy with Abbott, payment for lectures by Abbott, MSD, Ferring and Shire and a patent pending with Genentech. JS declares one paid consultancy (Elan Biotech) and financial support for the natalizumab trial from Elan, grants with Novartis and Genentech and research funding by Schering Plough. CAP and WAHW have no conflicts of interest.

Patient consent
Obtained.

Contributors
CAP: literature search, writing, figures, editing. CWL: writing, editing. WAHW: pathology images. JS: initial hypothesis, main editor of manuscript and writing.

Provenance and peer review
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REFERENCES

Figure 1
Case 1. (A) Chest x-ray in 2006 showing new widespread nodular opacification, suspicious of a progressive interstitial process. (B) High-resolution CT scan in 2006 showing extensive bilateral symmetrical fine pulmonary nodularity involving all lobes of the lung. (C) Histological section taken from a transbronchial biopsy specimen in 2004 showing the presence of epithelioid non-caseating granulomas consistent with sarcoidosis. Stains for fungus (DPAS and Grocott) and acid-fast bacilli (ZN) were negative (H&E, ×200). Case 2. (D) Chest x-ray in 2008 showing bilateral hilar lymphadenopathy. (E) High-resolution CT scan in 2009 showing prominent hilar and mediastinal lymph nodes (arrow). (F) Histological section from a mediastinoscopy in 2009 showing non-necrotising granulomas (arrows) replacing the predominant part of the lymph node tissue, consistent with sarcoidosis. DPAS, Grocott and ZN stains were negative (H&E, ×25).
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