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Kaposi's sarcoma associated with tumour necrosis factor α neutralising therapy

C D Cohen, S Horster, C A Sander, J R Bogner

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Inhibition of tumour necrosis factor α (TNFα) by antibodies or soluble receptors has developed as a potent treatment of chronic inflammatory diseases like rheumatoid arthritis (RA) or Crohn's disease. Because TNFα is an important mediator in the inflammatory response, this blockade led to the concern of increased risk of severe infections or malignancies. Despite reassuring data from clinical trials, an association between TNFα inhibition and tuberculosis has been shown, and several cases of serious infections and malignant complications have been described.[1–3]

We report the case of Kaposi's sarcoma (KS), a malignancy with infectious pathogenesis,[4] associated with the initiation of TNFα blockade by the humanised, mouse derived monoclonal antibody infliximab.

CASE REPORT

A 69 year old Turkish woman with a 25 year history of severe RA presented with multiple firm, purple-reddish plaques and nodules covering her left lower leg. The lesions had started to develop a few weeks after initiation of infliximab and had progressed during the past 18 months. In this time she had received 12 doses of 3 mg/kg infliximab. The first six doses were given during concurrent methotrexate treatment until she developed a pneumonitis. Subsequently, she had three infusions in combination with leflunomide. This was discontinued owing to increased liver enzymes. Before infliximab, several treatments were stopped owing to adverse reactions or lack of efficacy.

At the time of presentation she received methylprednisolone (12 mg/day) and rofecoxib (25 mg/day) concomitantly with the TNFα inhibition. A biopsy of one of the lesions revealed KS. Histopathological examination showed expansion of spindle cell vascular processes and the tissue was stained positive for human herpes virus 8 (HHV8). The patient tested serologically positive for HHV8, but negative for HIV. Her total lymphocytes were 871 cells/μl with an absolute CD4+ cell count of 391 cells/μl (45%). The patient did not report any family history of endemic KS. Her husband tested negative for HHV8. Screening for antinuclear or antineutrophil cytoplasmic antibodies was negative. *Mycobacteria* or *Bartonella* were excluded by microbiological and serological tests, and a negative tuberculin skin test. Investigations for metastasis disclosed no abnormal findings.

DISCUSSION

Iatrogenic KS has been described in immunosuppressed patients.[4] It occurs mainly in recipients of organ transplant but has also been reported in other patients with chronic immunosuppressive treatment.[5] The patient reported here originated from Turkey, a region with an increased risk for iatrogenic KS.[6]

As far as we know, KS in coincidence with initiation of TNFα neutralising therapy has not been reported previously. Therefore, a causal connection between TNFα inhibition and KS is unclear. None the less, monitoring patients for skin tumours might be advisable during treatment with TNFα antagonists, and special care may be needed in patients with increased risk for iatrogenic KS.[6]

Authors' affiliations

C D Cohen, S Horster, C A Sander, J R Bogner, University of Munich, Germany

Correspondence to: Dr C D Cohen, Medizinische Poliklinik, University of Munich, Pettenkoferstr 8a, 80336 Munich, Germany; c.cohen@web.de

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