Cytomegalovirus Complicating Biological Immunosuppressive Therapy in Two Patients with Psoriasis Receiving Treatment with Etanercept or Efalizumab

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Sir,
Cytomegalovirus (CMV) is a herpes virus with life-long persistence following primary infection. Forty percent of the population carry the virus by the age of 20 years and sixty percent by the age of 60 years. CMV infections are usually asymptomatic, but in the immuno-compromised patient reactivation or a primary infection may cause severe disease, with retinitis, colitis, hepatitis or pneumonia.

TNF-α mediates host-resistance against microorganisms and inhibits CMV replication and serum TNF-α is elevated during acute CMV-infections (1). TNF-α blocking agents (infliximab, etanercept and adalimumab) block the pivotal role of TNF-α in the inflammatory response. Efalizumab is a monoclonal antibody directed against the CD11a subunit of LFA 1 on lymphocytes, thereby blocking lymphocyte to antigen-presenting cells interaction and diapedesis. We describe here 2 cases of CMV infection in patients receiving biological treatment.

CASE REPORTS

Case 1
A 37-year-old man with psoriasis since the age of 16 years and psoriatic arthritis since the age of 36 years was treated with etanercept 50 mg twice weekly with excellent clinical response.

After one month of treatment, fever and ear pains raised the suspicion of otitis media in the patient; he was treated with penicillin and recovered. Two months later he developed fever, productive cough and malaise. Pneumonia was suspected and etanercept treatment was stopped. Biochemical analysis showed no signs of infection and chest X-ray was normal. His symptoms were persistent and he was admitted to hospital with fever of unknown origin (FUO). He was fatigued and confined to bed. Biochemistry: liver function tests (LFT) were raised with alanin-aminotransferase 135 U/l (10–70), aspartat-aminotransferase 167 U/l (15–45), gamma-glutamyltransferase 196 U/l (10–80) and alkaline phosphatase 143 U/l (35–105). Serum-screening for a large array of infections was positive for IgG and IgM anti-CMV, indicating either a reactivation or a primary infection in a late phase. He received no antiviral treatment and slowly recovered over a 2–3-month period.

DISCUSSION

In any patient receiving biological therapy it is important to be aware of infections, because there is a risk of a long and aggressive course. The 2 patients described here, who were treated with etanercept and efalizumab, respectively, both had a longstanding infection.

CMV retinitis has been described in a female patient with rheumatoid arthritis treated with infliximab, Imurel (azathioprine) and cyclophosphamide. An additive aggravating effect of the combined immuno-suppressive regimen cannot be excluded (1). Torre-Cisneros et al. (2) prospectively (week 0–6 of treatment) followed 15 patients with rheumatoid arthritis treated with infliximab (3 mg/kg) for reactivation of CMV, Epstein-Barr virus (EBV) and human herpes virus (HHV) 6, 7, and 8. No signs of reactivation and no primary infections were detected.

It is well known from patients with AIDS, that immunosuppression may cause reactivation of CMV and increased susceptibility to primary infections, with potentially debilitating outcomes (e.g. CMV retinitis) (3).

In conclusion, TNF-α blocking agents and perhaps efalizumab may reactivate CMV or make the patient more susceptible to a primary infection. Our patients did not show asymptomatic infections, but were severely and prolonged fatigued.
Therefore in patients receiving biological treatment, who develop FUO, CMV should be considered. CMV may be identified immediately after infection or reactivation by PCR-analysis, but repeated analyses of antibodies against CMV are often necessary.

Our patients recovered without antiviral therapy in approximately 2 months, but treatment should be considered in each case.

Conflict of interest: Dr Lorentzen work at the Advisory Board of Wyeth and has a teaching task at Abbot.

REFERENCES