Acute Inflammatory Syndrome with Elevated Procalcitonin Induced by Mycophenolate Sodium

JAN LOOCK, PETER LAMPRECHT and WOLFGANG L. GROSS

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To the Editor:

Mycophenolate is one of the mainstays of immunosuppressive therapy after organ transplantation and has also been increasingly used in the treatment of rheumatic diseases. It is applied either as mycophenolate mofetil (MMF) or its enteric coated formulation (mycophenolate sodium; MPS). The immunosuppressive action of mycophenolate is mainly based on the inhibition of the de novo purine biosynthesis required for the proliferation of T and B lymphocytes.

We describe a 72-year-old man with a 35-year history of seropositive rheumatoid arthritis (RA). During his disease course he had received multiple disease-modifying antirheumatic treatments (DMARD), which were either ineffective (chloroquine, sulfasalazine, gold) or discontinued because of adverse effects or contraindications (methotrexate, leflunomide). In 2007, the course had been complicated by an infected hip replacement with sepsis and secondary aortic valve endocarditis. A steady decline of his renal function (creatinine clearance 20 ml/min) was attributed to systemic amyloidosis. In September 2010, DMARD treatment with azathioprine was switched to MPS because of toxic bone marrow damage. Shortly thereafter, he developed severe migrating pains in rapidly altering locations together with a severe decline of general status. An increase of the daily glucocorticoid dose (from 5 to 10 mg prednisolone daily) did not alter the symptoms. He was finally admitted to our service in a severely compromised general state and complaining of severe, immobilizing pain and marked tenderness to palpation at multiple discrete periarticular points very atypical of a synovitic cause and without clinical or sonographic signs of synovitis.

Laboratory values showed an increased erythrocyte sedimentation rate (ESR) of 110 mm/h and C-reactive protein (CRP) 57 mg/l (normal < 5 mg/l). An elevated serum procalcitonin (PCT) and subfebrile temperatures to 38°C were present. Intensive investigations including blood and urine cultures, transesophageal echocardiography, endoscopy of the upper gastrointestinal tract, skeletal scintigraphy, ear-nose-throat and dentistry contributed to systemic amyloidosis. In 2010, DMDH treatment with azathioprine was switched to MPS because of toxic bone marrow damage. Shortly thereafter, he developed severe migrating pains in rapidly altering locations together with a severe decline of general status. An increase of the daily glucocorticoid dose (from 5 to 10 mg prednisolone daily) did not alter the symptoms. He was finally admitted to our service in a severely compromised general state and complaining of severe, immobilizing pain and marked tenderness to palpation at multiple discrete periarticular points very atypical of a synovitic cause and without clinical or sonographic signs of synovitis.

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relates with serum IL-6 levels. Thus it can be speculated that mycophenolate metabolite-mediated IL-6 production induces elevated PCT serum levels in the acute inflammatory syndrome. Interestingly, increased PCT serum levels have also been described recently in patients with idiosyncratic inflammatory drug reactions to azathioprine and carbamazepine, and in the neuroluptic malignant syndrome. Therefore, drug reactions should be considered in the differential diagnosis of inflammatory states with elevated PCT in rheumatic diseases.

The ability of mycophenolate to induce an acute inflammatory response appears to be rare and less appreciated than the similar systemic inflammatory reaction to azathioprine. However, awareness of the syndrome is important in routine clinical care, since discontinuation of the responsible agent results in prompt resolution of the symptoms.

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