Ulcerative Colitis in a Renal Transplant Patient on Azathioprine

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Dear Sir,

Ulcerative colitis is a disease of unknown etiology with an intermittent clinical course and irregular response to the therapy. In the last few years, some authors have suggested that ulcerative colitis should be considered as an autoimmune disease. In fact, immunosuppressive therapy has been used as treatment although without definitive results [1, 2].

We present a patient with a cadaveric renal allograft taking azathioprine and prednisone to prevent kidney rejection in whom ulcerative colitis developed. To our knowledge this is the first described case of development of ulcerative colitis after kidney transplantation while taking azathioprine.

A 27-year-old patient with end-stage renal disease of uncertain etiology received a cadaveric renal allograft in 1979. The recipient HLA type was A2 Aw23/Bw52/4a/DRw7 and shared 4 antigens with the donor (2 A and 2 B). The postoperative period was troublesome. On the 3rd postoperative day the patient became anuric due to urinary extravasation through ureterovesical suture and required reoperation, after which the surgical wound was infected by *Staphylococcus aureus* and he also developed a duodenal stress ulcer. Immunosuppressive therapy consisted of azathioprine (2.5 mg/kg/ day) and prednisone (1 mg/kg/day). The patient recovered from all complications and was discharged from the hospital after 53 days. At this time the serum creatinine was 1.2 mg/dl. One month later he suffered from an acute rejection episode which was treated with 3 intravenous boluses of 1 g of methylprednisolone and the renal function returned to basal level. Sixteen months later he was again admitted to the hospital. He referred to have rectal bleeding, abdominal cramps and tenesmus with frequent liquid mucous stools. *Shigella*, *Salmonella*, *Campylobacter*, *Clostridium difficile* and parasites were absent in stool cultures. The barium enemas revealed characteristic features of ulcerative colitis involving the whole circumference of the colon. Endoscopic examination and histological picture of the colon confirmed the diagnosis. At this time the patient was taking prednisone (10 mg/day) and azathioprine (2.5 mg/kg/ day). Treatment was instituted with oral sulfasalazine, steroid enemas and an increase of the maintenance doses of prednisone.

Remission was achieved after 4 weeks. Since then, the patient has suffered four other attacks of similar characteristics in 6 years of follow-up. He has always been on azathioprine and low prednisone. During the four attacks the clinical symptoms were controlled with the treatment described above. Renal function was maintained at normal range throughout the observation period (fig. 1).

The etiology and pathogenesis of ulcerative colitis is far from being understood. It was thought to have a genetic basis as it was universally recognized as tending to occur in families, but the study of histocompatibility antigens in different individuals of families with the disease have yielded contradictory results [3, 4], and it is not known why some people develop the disease. Some authors considered it to be an autoimmune disease and based on this assumption, patients were treated with antimetabolic drugs (6 mercaptopurine) as an alternative to conventional therapy, consisting of sulfasalazine and steroids. In 1972, Jeweld and Truelove [5, 6] reported the first clinical control study. In the final report, they were unable to conclude that azathioprine produces a significant benefit administered together with steroids in an acute attack or as a maintenance treatment, although it may be possible that it reduces the frequency of relapses. Rosenberg et al. [7] think that the clinical course of ulcerative colitis is not modified by azathioprine but it could help to decrease the steroid dosage. Nowadays, azathioprine has been recommended in patients that lack response or intolerance to conventional therapy (steroids and sulfasalazine) or in the event that they do not accept a colectomy, which is the definitive treatment for ulcerative colitis.

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Fig. 1. Clinical evolution of the patient (J.-A. G.F., ♂, 27 years old).

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1980 1981 1982 1983 1984 1985 1986 1987 15

The presentation of the disease in our patient on chronic treatment with azathioprine would not support the usefulness of this drug, either as treatment for the first attack or reducing the appearance of relapses. As the dose administered was similar to that reported in other studies its uneffectiveness can not be attributed to the utilization of low doses. On the other hand, it is important to point out that the disease was always controlled by increasing steroid dosage and by adding sulfasalazine. Although no conclusions can be drawn from a single case, it questions once again the role of the azathioprine in the treatment of ulcerative colitis.

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