## Treatment of severe ulcerative colitis during pregnancy

Sir,

We read with interest the article by Daskalakis et al (Hell. J. Gastroenterol. 1998; 11:42-44) reporting a case of a woman who underwent caesarean section and subtotal colectomy as a single procedure in the 32<sup>nd</sup> week of gestation for severe ulcerative colitis. The authors recommend a close co-operation between the obstetrician, the gastroenterologist and the surgeon, in order to determine the timing of possible surgery in this situation, although the results of surgery in pregnancy are uncertain. However, no information has been given on other alternatives in the management of severe ulcerative colitis during pregnancy.

The following recent data indicate that an alternative therapy, involving administering cyclosporine in acute steroid-refractory disease, appears to be preferable to avoid surgery in a pregnant woman: Although patients with severe, steroid-resistant (high-dose intravenously administered corticosteroids) ulcerative colitis are candidates for emergency colectomy,<sup>1</sup> recent evidence suggests that intravenous cyclosporine therapy is effective in these patients.<sup>1-6</sup> Approximately 80%-90% of the patients respond to cyclosporine and avoid urgent colectomy.<sup>7-10</sup> In particular, appropriate candidates for intravenous cyclosporine therapy may be patients with recently diagnosed ulcerative colitis who are not yet psychologically prepared for colectomy, those with left-side colitis that has previously been easily controlled, and those who are poor surgical risks.<sup>11,12</sup>

The use of cyclosporine in pregnant women with severe ulcerative colitis is limited to one published case of a woman who received cyclosporine for fulminant disease at 29 week of gestation, with good results for both the mother (no colectomy) and the baby.<sup>13</sup> However, experience with this drug in other conditions provides information about its effect on pregnancy. Cyclosporine crosses the placenta, and blood levels in the fetus are about 50% of those found in the mother.<sup>14</sup> Cyclosporine does not seem to be teratogenic in humans or animals.<sup>15</sup> In addition, data from pregnancies in transplant recipients treated with cyclosporine show that about 50% of babies are either premature or underweight.<sup>14</sup> Moreover, nephrotoxicity was been found in a series of 26 infants whose mothers had received cyclosporine for renal transplantation.<sup>16</sup> There is also no clear cyclosporine-induced immunosuppression in the neonate.<sup>14</sup> Cyclosporine is found in the milk in significant concentrations and it is better avoided during breastfeeding.<sup>14</sup>

Taken together, these data lead to the following conclusion<sup>14</sup>: The use of cyclosporine in ulcerative colitis is limited to acute steroid-refractory disease, as an alternative to surgery. It may be preferable to avoid surgery in a pregnant woman in this situation where cyclosporine does not seem to carry a prohibitory risk.<sup>14</sup>

We agree with the above mentioned conclusion by introducing cyclosporine as a first-line regimen for fulminant steroid-refractory ulcerative colitis during pregnancy. Cyclosporine is given intravenously at a dosage of 4 mg per kg per day for one to two weeks. The advantage of cyclosporine is that the usual time until response is four to seven days.<sup>17</sup> If the patient does not show improvement during that period, it is unlikely that cyclosporine will be effective and treatment can progress to surgery. In general, colectomy may be preferable to medical management in those patients with long-standing disease who are also at high risk for malignancy, and that even if remission occurs there is a high relapse rate ultimately leading to colectomy anyway. Nonetheless, the use of cyclosporine is an option for those patients hesitant to have surgery.

> J. Kountouras, D. Hatzopoulos, F. Halkidis, P. Boura

Department of Medicine 2<sup>nd</sup> Medical Unit Division of Gastroenterology, University of Thessaloniki, Ippokration Hospital, Thessaloniki, Greece

## REFERENCES

- Sanborn WJ, Tremaine WJ. Cyclosporine treatment of inflammatory bowel disease. Mayo Clin Proc 1992; 67:981-990.
- Pepprecorn MA. Advances in the drug therapy for inflammatory bowel disease. Ann Intern Med 1990; 112:50-60.
- Hirschfeld S, Clearfield HR. Pharmacologic therapy for inflammatory bowel disease. Am Fam Physisian 1995; 51:1971-1975.
- Korelitz BI. Immunosuppressive therapy of inflammatory bowel disease: a historical perspective. The Gastroenterologist 1995; 3:141-152.
- Sandborn WJ. A review of immune modifier therapy for inflammatory bowel disease: azathioprine, 6-mercaptopurine, cyclosporine, and methotrexate. Am J Gastroenterol 1996; 91:423-433.
- Baert F and Rutgeerts. Immunomodulatory therapy of inflammatory bowel disease. Acta Clin Belg 1997; 52-5:251-256.
- Lichtiger SL, Present DH, Kornbluth A, Gelernt I, Bauer J, Galler G, Michelassi F, Hanauern S. Cyclosporine in severe ulcerative colitis refractory to steroid therapy. N Engl J Med 1994; 330:1841-1845.
- 8. Rosselli M, Cas'a A, Oliva L, Orlando A, Cottone M. Treatment of acute a steroid-resistant ulcerative colitis with continuous venous infusion of cyclosporine. Recenti Prog Med 1996; 87:416-421.

- Marion JF, Present DH. The modern medical management of acute, severe ulcerative colitis. Eur J Gastroenterol Hepatol 1997; 9:831-835.
- Aranda R, Horgan K. Immunosuppressive drugs in the treatment of inflammatory bowel disease. Sem Gastrointest Dis 1998; 9:2-9.
- 11. Santor BR. Cyclosporine therapy for inflammatory bowel disease. N Engl J Med 1994; 330:1897-1898.
- Treem WR, Cohen J, Davis PM, Justinich CJ, Hyams JS. Cyclosporine for the treatment of fulminant ulcerative colitis in children. Immediate response, long-term results, and impact on surgery. Dis Colon Rectum 1995; 38:474-479.
- Bertschinger P, Himmelmann A, Risti B, et al. Cyclosporine treatment of severe ulcerative colitis during pregnancy. Am J Gastroenterol 1995; 90:330.
- Modigliani R. Drug therapy for ulcerative colitis during pregnancy. Eur J Gastroenterol Hepatol 1997; 9:854-857.
- 15. Connell WR. Safety of drug therapy for inflammatory bowel disease in pregnant and nursing women. Inflamm Bowel Dis 1996; 2:33-47.
- Shaheen FAM, Al-sulaiman MH, Al-Khader AA. Longterm nephrotoxicity after exposure to cyclosporin in utero. Transplantation 1993; 56:224-225.
- Kountouras J. Cyclosporine and inflammatory bowel disease. Postgraduate lessons Hell. Soc. Gastroenterol. University Studio Press, Thessaloniki 1999:114-129.