Two cases of intestinal perforation in patients on anti-rheumatic treatment with etanercept

Sirs,

At Sacco Hospital 100 patients affected by rheumatoid arthritis (RA) are under treatment with etanercept (1) and regularly followed by rheumatologists. In the last year we observed 2 cases of sigmoid perforation requiring emergency surgical treatment (2). Both patients were middle-aged (43 and 60 years old), with a disease duration of 2 and 15 years respectively. Both started etanercept (50 mg sq) weekly and oral prednisone (5 mg) daily 2 years before. The 2 patients presented with acute abdominal pain and fever (39° and 37.9°C). Neither had a history of previous abdominal surgery. At the time of admission both patients had leucocytosis (WBC 12,440 mm^3 and 13,850 mm^3). A standard abdominal X-ray (flat and upright), abdominal ultrasound and CT scan were performed. One patient showed free intraperitoneal air and had a diagnosis of intestinal perforation; the second one had findings consistent with diverticulitis at the CT scan.

Due to the worsening of their general condition they underwent emergency operation. At the time of surgery we observed in both cases acute peritonitis due to diverticular perforation and we performed colonic segmentary resection with temporary loop colostomy. The post-operative course was uneventful and the colostomy was closed 2 months later. Pathology confirmed the presence of severe suppurative diverticulitis, peridiverticulitis and acute sierositis. There was no evidence of specific lesions due to infective agents on histological examination.

Although both the patients were under combination treatment with etanercept plus steroids and these latter drugs increase the risk of colonic perforation by 3-fold (3), it should be stressed that a 2% estimated incidence of colonic perforation is very high. The hypothesis is that anti-tumour necrosis factor α inhibits host defences and facilitates an imbalance between protective and aggressive factors at the weak mucosal barrier of the diverticules of the colon (4, 5). A second hypothesis is that anti-tumour necrosis factor α causes vasculitis (6) and necrosis of the mucosal membranes with passage of bacteria into the peritoneal cavity (7, 8).

As described by other authors the introduction of these news and promising biologic agents has evidenced the necessity for long term monitoring and for a prolonged ascertainment of safety data from such a heterogeneous group of patients (9, 10). Therefore we suggest that in patients affected by diverticular disease the benefit of treatment with etanercept should be carefully balanced against the above described potential morbidity (11).

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Comment on "Not Lucy, not the one"

Sirs,

I am writing in regard to an editorial published in your journal by Bruce Rothschild, 2002, "Not the Lucy, not the one" (1). On page 741, Dr. Rothschild refers to an article I published in 1989, "Possible case of rheumatoid arthritis from Sudanese Nubia" *American Journal of Physical Anthropology*, 79: 177-83. In this article I described lytic lesions primarily in the wrist and metacarpal-phalangeal joints of an elderly female from a medieval site in the Sudan. Dr. Rothschild has always taken exception to my interpretation and that is, of course, his right. But in the above-mentioned editorial he wrote the following: "...Kilgore subsequently deleted rheumatoid arthritis as the diagnosis, accepting that the Nubians actually had spondyloarthropathy (Kilgore, personal communication). This assertion is not true. I have never made such a statement and in fact I stand by my diagnosis of "possible rheumatoid arthritis." Dr. Rothschild has tried to convince me on one or two occasions that his views are correct, but I have never in any way suggested that I agree with him.

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Reply

Sirs,

Lynn Kilgore (personal communication) asked me to write to retract the statement that had acknowledged her acceptance of the new diagnosis for her Nubian case (1), once I made her aware of the existence of spondyloarthropathy. She now indicates no recollection of any conversation related to a change in her perspective of possible rheumatoid arthritis in a Sudanese Nubian. Please recall that her description was of limited distribution (only 5 joint groups affected), subchondral and punched out erosions with prominent remodeling and no periarticular/peri-lesional osteopenia (2).

I originally thought her perspective (2) was related to lumping erosive arthritis (and its various pseudonyms and subtypes). Spondyloarthropathy was not listed in her differential diagnosis. As limited joint group affliction, and subchondral remodeled erosions in the absence of periarticular osteopenia are part of the classic description for spondyloarthropathy and at variance with what is today recognized, rheumatoid arthritis can confidently be excluded.

However, I respectfully ask that her request to note that she does not at this time disavow her perspective that she reported a possible case of rheumatoid arthritis in a Nubian be honored. Diagnosis on the basis of a single case must be placed in the per-

spective of the character of inflammatory/erosive arthritis in the entire population (3). Such has been performed for the population from which Kilgore's example derives (4). The pattern of disease as a population phenomenon in that Nubian population is typical of spondyloarthropathy and at variance from what has been found with rheumatoid arthritis (3).

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