Correspondence

INSTRUCTIONS FOR LETTERS TO THE EDITOR

Editorial comment in the form of a Letter to the Editor is invited. The length of a letter should not exceed 800 words, with a maximum of 10 references and no more than 2 figures or tables; and no subdivision for an abstract, methods, or results. Letters should have no more than 4 authors. Financial associations or other possible conflicts of interest should be disclosed.

Letters should be submitted via our online submission system, available at the Manuscript Central website: http://mc.manuscriptcentral.com/jrheum For additional information, contact the Managing Editor, The Journal of Rheumatology, E-mail: jrheum@jrheum.com

Septic Abscess in a Child with Juvenile Idiopathic Arthritis Receiving Anti-Tumor Necrosis Factor-α Therapy

To the Editor:

We read with interest the case report by Kaur and colleagues[1] of septic arthritis and abscess formation caused by *Actinobacillus urea* in a patient with rheumatoid arthritis receiving etanercept and methotrexate (MTX). There are many reports of infection associated with tumor necrosis factor-α (TNF-α) blocking agents, including those of the superficial skin[2] and abscess[3-6]. There have been post-market reports of etanercept-associated abscesses in the pediatric population with chronic arthritis[7]. However, none of these cases have been documented in the literature. This includes not even a single case reported in the open-label extension study[8] of etanercept for treatment of juvenile idiopathic arthritis (JIA), now through 4 years of followup[9]. Recently, we cared for a child who developed a deep abscess while on treatment with etanercept and MTX.

An 11-year-old African-American girl was diagnosed with polyarticular JIA 4 months prior to presentation to the emergency department with a fever to 102°F and an 8 × 10 cm area of erythema and tenderness over the left flank. She reported an insect bite to the area occurring the day before. Her current therapy consisted of etanercept 25 mg subcutaneously twice a week (started 2 months before), MTX 25 mg subcutaneously weekly (started 4 months before), prednisone 10 mg orally daily, and naproxen 500 mg orally twice a day. In the emergency department she was given intravenous clindamycin, but within several hours of admission the area of tenderness and erythema spread rapidly. A magnetic resonance scan showed heterogeneous abnormal low signal in the subcutaneous flank in T1-weighted images and heterogeneous high signal in T2 (Figure 1). This is consistent with necrotizing fasciitis, and extended from the inferior liver to the iliac crest, roughly 16 cm in total length. She was taken to surgery, where the area was dissected down to the fascia. A localized area of pus in the soft tissue was debrided and a penrose drain was placed. A biopsy of the fascia showed evidence of inflammation but not necrosis. She remained hospitalized over the next 5 days with continued serosanguinous drainage from the wound, undergoing antibiotic therapy with vancomycin and clindamycin. The abscess culture grew methicillin-resistant *Staphylococcus aureus* sensitive to clindamycin, vancomycin, and trimethoprim-sulfamethoxazole. She was discharged on a 14-day course of trimethoprim-sulfamethoxazole. Etanercept and MTX were stopped during the phase of active infection. After antibiotic therapy was completed, MTX was restarted and etanercept was changed to adalimumab, 40 mg subcutaneously every 2 weeks.

Etanercept appears to be an effective therapy for polyarticular JIA unresponsive to more traditional therapy of intraarticular corticosteroid injections and MTX[8,10]. However, as noted by Kaur and colleagues, 21% of adverse events attributable to etanercept are infection-related, and physicians must be vigilant in screening for early evidence of infection[1]. Additionally, Song, *et al* reported that infliximab, a TNF-α inhibitor not currently approved for treatment of pediatric arthritis, delayed the onset and reduced the incidence and severity of abscess formation induced with *S. aureus* in a primate model[11]. Conversely, in the same study, etanercept caused a modest increase in the incidence and severity of abscess formation[11]. Thus, not all TNF-α inhibitors may share the same risks for infections [e.g., monoclonal antibodies (infliximab and adalimumab) versus soluble TNF-receptor fusion proteins (etanercept)]. Our case of a deep tissue abscess occurring during TNF-α inhibition highlights the importance of close attention to the safety profiles of biologic agents used to treat JIA.

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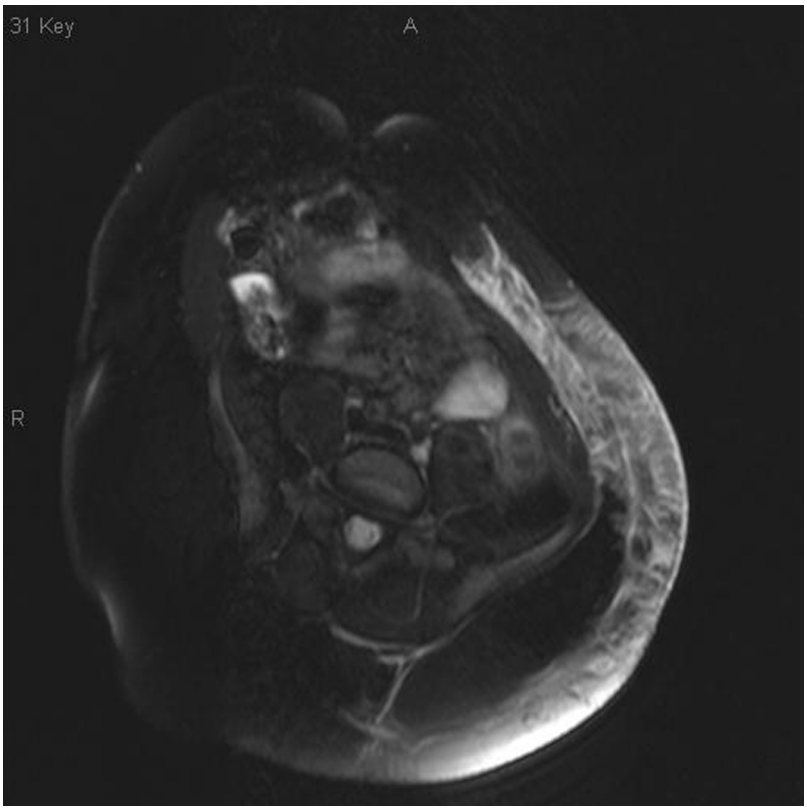

Figure 1. Necrotizing fasciitis appears on a T2-weighted MRI scan of the mid-abdomen.

Dr. Kaur, *et al* reply

To the Editor:

Drs. Fitch and Cron describe a case of abscess formation in a child with juvenile idiopathic arthritis who was being treated with prednisone, methotrexate (MTX), and etanercept. Our patient had rheumatoid arthritis with overlap features and developed septic arthritis and abscess formation with *Actinobacillus ureae* while on treatment with MTX and etanercept. We agree with their conclusion to pay close attention to safety profiles of all biologic agents. However, Fitch and Cron raise the possibility that all TNF-α inhibitors do not share the same risks for infections, based on a study of a primate model by Song, *et al*[1]. The study showed that administration of anti-TNF-α monoclonal antibody to *S. aureus*-challenged monkeys results in both a delay in the onset and a reduction in the incidence and severity of abscess formation, compared with saline administration[1]. They also administered etanercept using the same regimen, which resulted in a modest increase in the incidence of abscess formation and no improvement in the severity of abscess formation, compared with saline administration[1].

It is hard to predict how these findings will translate to clinical significance in humans, since abscess formation has been reported in patients being treated with all TNF-α inhibitors[2-5]. Septic arthritis[6,7] and osteomyelitis[8] have been reported in patients treated with infliximab. Therefore physicians should be vigilant to discern the earliest signs of infections in all patients treated with any of the biologic agents.

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Hypothyroidism Contributes to Increased Triglyceride Levels Among Patients with Systemic Sclerosis

To the Editor:

We read with interest the article by Kodera and colleagues[1] on anti-lipoprotein lipase antibody-mediated lipid metabolism abnormalities in patients with systemic sclerosis (SSc). The report provides new insight into the pathogenesis of dyslipidemia in SSc and probably in other connective tissue disorders. The findings are of special importance in light of the increased prevalence of macrovascular disease observed in this group of patients[2]. However, according to the results obtained in the study, only one-third of patients with increased triglyceride levels had anti-lipoprotein lipase antibody, which suggests the involvement of other factors. A lipid profile is the result of complex metabolic processes involving dietary habits, environmental influences, race, and endocrine system function. Among the latter, thyroid function is of great interest, with its influence on lipoprotein metabolism.

We describe our experience in lipid metabolism among patients with diffuse SSc. In a cohort of 49 patients with diffuse SSc we observed clinical and laboratory features of hypothyroidism in 13 patients (27%) and increased triglyceride levels in more than 55%. Unexpectedly, no differences were observed between hypothyroid and euthyroid SSc patients with regard to their total cholesterol or HDL and LDL-cholesterol levels. Moreover, the patients with hypothyroidism had statistically significantly higher levels of triglycerides than euthyroid patients with SSc[3].

Hypothyroidism is a common finding in patients with SSc. It is estimated that about half of SSc patients experience overt or latent hypothyroidism[4]. In contrast to previous reports[2,5], patients with SSc showed marked lipid metabolism abnormalities, which may predispose them to early development of macrovascular disease and serious cardiovascular complications. SSc has a very strong influence on triglyceride metabolism in all subgroups of patients, since all SSc patients had higher triglyceride levels. Thus, hypothyroidism may partially explain the elevation of triglyceride levels in the patients with SSc. Kodera, *et al* have provided more information on lipid metabolism in SSc, supporting the effect of autoimmune mediation upon lipoprotein-lipase, a key enzyme in lipid metabolism. Consistent with this finding, hypothyroidism may be responsible for triglyceride elevation in patients who had no anti-lipoprotein lipase autoantibodies. On the other hand, immune-mediated lipoprotein lipase dysfunction could be responsible for increased triglyceride levels in euthyroid patients with SSc. The findings of these 2 studies might offer a way to verify the hypothesis on overlapping anti-lipoprotein lipase antibody and hypothyroidism, and the influence of both conditions on lipid metabolism in patients with SSc.

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Drs. Kodera and Sato reply

To the Editor:

We are interested in the letter by Dr. Kotyla and colleagues. As described in the discussion section of our article[1], we speculate that there are multiple factors that cause dyslipidemia other than anti-lipoprotein lipase antibodies in patients with systemic sclerosis (SSc). It is possible that hypothyroidism may contribute to the elevated serum levels of triglycerides, as noted by Kotyla, *et al*.

We have seen SSc patients with anti-microsome/thyroglobulin antibodies and/or hypothyroidism. However, our clinical database lacked precise information on this. Nonetheless, a previous study showed that serum antithyroid antibodies (antithyroglobulin and/or antimicrosomal antibodies) were detected in 18% and indicated an increased frequency of (sometimes previously unsuspected) clinical and subclinical hypothyroidism in patients with SSc[2].

In cases of hypothyroidism, many patients with dyslipidemia have elevations of both serum total cholesterol levels and triglyceride levels[3]. As shown by Figure 2 in our article[1], we found some patients who had both hypercholesterolemia and hypertriglyceridemia. Thus, these patients may suffer from overt or latent hypothyroidism.

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Corrections

Souza L, Machado SH, Bredemeier M, Brenol JCT, Xavier RM. Effect of inflammatory activity and glucorticoid use on nutritional variables in patients with juvenile idiopathic arthritis. J Rheumatol 2006;33:601-8. The correct title is: Effect of inflammatory activity and glucocorticoid use on nutritional variables in patients with juvenile idiopathic arthritis. We regret the error.

Tannenbaum H, Bombardier C, Davis P, Russell AS, for the Third Canadian Consensus Conference Group. An evidence-based approach to prescribing nonsteroidal antiinflammatory drugs. Third Canadian Consensus Conference. J Rheumatol 2006;33:140-57. Please note a slide rule for calculating creatinine clearance (as shown) may be obtained upon request from: creatinineclear@aol.com, not creatinineclearance@aol.com, as stated on page 145, column 2, line 5. We regret the error.

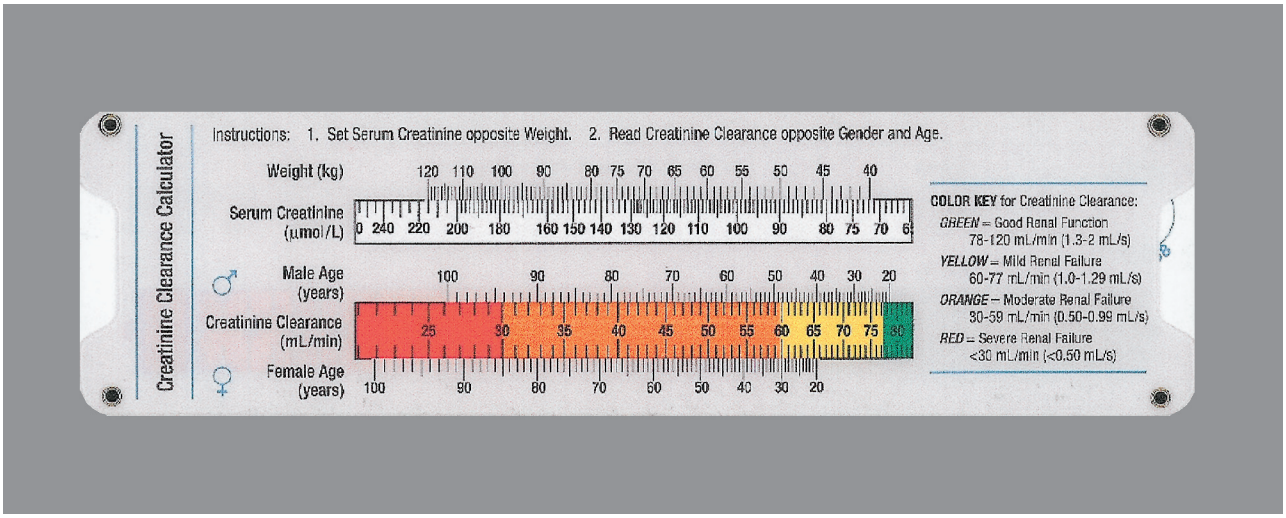

Figure 1. An easy-to-use device for calculating creatinine clearance. Available upon request from: creatinineclear@aol.com