even greater long-term toxicity. A large well controlled prospective trial is needed.

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A case of familial Mediterranean fever, Behcet's disease and polyarteritis nodosa complicated by perirenal haematoma

Sirs,

Familial Mediterranean fever (FMF) is characterized by attacks of fever, accompanied by abdominal, chest or joint pain (1).

The most serious complication is the development of amyloidosis, causing chronic renal failure. There are also a number of reports of individuals who have vasculitis associated with FMF (2, 3).

We describe a case of FMF associated with the features of Behçet's disease (BD) and probable polyarteritis nodosa complicated by spontaneous perirenal and retroperitoneal haematoma.

A 37-year old man was admitted to our hospital with a two-week history of malaise, high fever, severe myalgia and severe abdominal and right flank pain in the last four days. He had a history of recurrent abdominal attacks and fever since the age of 8. He also reported periodic arthritis independent of the abdominal attacks. He had been diagnosed as having FMF at the age of 20 and colchicine was administered, which he admitted not to take it regularly. In addition, he also reported recurrent oral and genital ulcerations, and papulo-pustular skin lesions in the last two years.

On admission, he had a temperature of 39°C, blood pressure 160/100 mm/Hg, and the heart rate 98/min. Physical examination revealed abdominal tenderness, rebound and a mass in the right flank. Two ulcerations on the tongue and six genital ulcerations scars were also found. On funduscopic examination, grade II hypertensive retinopathy was found. Pathergy test was positive.

Laboratory findings were as follows: haemoglobin 7 gr/dl, white blood cell count 24,700 mm^3 and platelet count 645,000 mm^3, the erythrocyte sedimentation rate (ESR) was 129 mm/h, C-reactive protein 5.35 mg/dl, antistreptolysin O titre 583 IU/ml (normal = 0-200), urea 45 mg/dl (n = 5-20), creatinine 1.9 mg/dl (n=0.5-1.4). Urine analysis revealed proteinuria (0.9 g/day) and microscopic haematuria (5-8 red blood cell/ per high-power field). ANA, anti-DNA, c-ANCA, p-ANCA, C3, C4, ACA IgG and M, HBs Ag, anti-HBs, anti-HCV were negative or within normal limits. Abdominal computed tomography (CT) revealed right perirenal and retroperitoneal haematoma (Fig. 1). Renal angiography revealed microaneurysms and a cortical infarct. Rectal biopsy for amyloidosis was negative. The patient refused renal biopsy. Screening for mutations of the MEFV gene showed that he was heterozygote for the M694V mutation.

He was commenced on i.v. cyclophosphamide (1 gr/month) and colchicine (2 mg/day). He was discharged fit, but failed to visit for the next 4 months. In July 2000 the patient was readmitted to hospital for recurrent oral ulcerations and uncontrolled hypertension (200/120 mm/Hg). Abdominal CT showed significant regression of the right perirenal haematoma. His blood pressure stabilised with antihypertensive drugs and, in addition to colchicine 1.5 mg/day, cyclophosphamide 2 mg/kg/day was administered orally this time. No further attack has been observed during the follow-up period since he was discharged from hospital.

The presented patient fullfils the described criteria for FMF by Livneh *et al.* (4). BD was diagnosed on the basis of diagnostic criteria proposed by the International Study Group of Behçet's disease (5).

Reports exist showing the association between FMF and PAN (3), FMF and Henoch-Schönlein purpura (2). FMF and

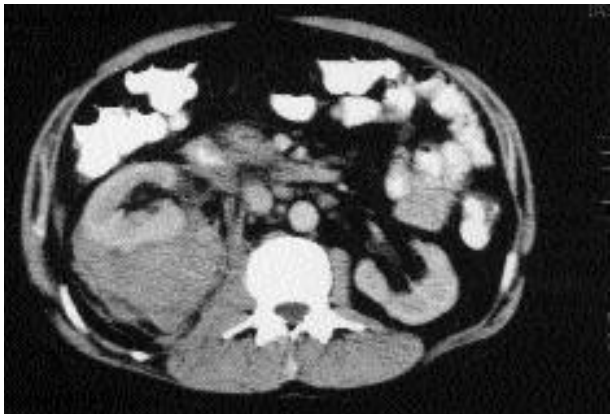

Fig. 1. Abdominal computed tomography revealing a right perirenal and retroperitoneal haematoma.

BD have also been described in the same patients (6). Whether there is an association between these two diseases or the occurrence is due to the high prevalence of these 2 diseases in the same area is not clear. Recently, Touitou *et al.* (7) screened MEFV mutations in a panel of BD patients and found that the M694V, V726A, and E148Q mutations tended to be more frequent in definite BD (2.6%, 2.6% and 5.2% respectively) than in controls (0%, 0% and 2.2% respectively),and suggested that they may act as additional susceptibility factor in BD. Schwartz *et al.* (6) showed that the prevalence of BD was higher in FMF than in populations rich in BD (*e.g.*, 16 per 4000 in FMF compared with 1 per 10^4 in Japan).

In our case, it may be difficult to make a diagnosis of PAN, as perirenal and retroperitoneal haematoma secondary to renal arterial aneurysm has been reported in two patients with BD to date (8, 9). Therefore, angiographic findings and retroperitoneal haematoma may be due to BD in this case. However, thrombophlebitis and venous thrombosis are often seen at or around the same time as arterial aneurysms in patients with BD (10,11), and since our patient neither had any history of these nor was observed to have such manifestations during the follow-up period, we can conclude that the angiographic findings and retroperitoneal haematoma may also be due to PAN. Our case met the ACR criteria (12) and the criteria suggested by us (13) for the classification of PAN. Furthermore, the prevalence of PAN in FMF is 1% (3), and perirenal haematoma is seen in almost half the patients with FMF who develop PAN (14). The relationship between these diseases requires further investigation. There are some clinical and laboratory similarities between them (6). Additional genetic and/or environmental factors may predispose an FMF patient to a more persistent inflammation in the relevant pathway, which may manifest itself in the form of vasculitis. Further studies will enlighten the association of these diseases and shed light on the pathogenesis of inflammation.

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Reporting a desensitization protocol for colchicine treatment

Sirs,

The development of toxicity and hypersensitivity to colchicine therapy is a well known entity in patients with familial Mediterranean fever (FMF) and Behcet's disease (BD) (1, 2). On the other hand amyloidosis is a known sequel of untreated patients affecting mainly patients with FMF, and therefore there is a need to treat such patients with colchicine to prevent this complication.

We recently examined a 47-year old female with FMF in whom the diagnosis of BD manifesting as recurrent oral and vaginal ulcers, pyoderma ganrenosum, erythema nodosum and arthralgias was established 20 years ago. The treatment regiment prescribed for BD as well as FMF included methotrexate, cyclophosphamide and colchicine which led to partial remission of both diseases.

The patient developed an allergic skin reaction to colchicine, proven by an oral challenge test. Despite the allergic reaction that erupted as a maculopapular rash evident on the lower limbs, it was necessary to continue the colchicine therapy because of its prominent role in preventing the development of amyloidosis.

Desensitization was achieved with the oral administration of increasing doses of colchicine. Colchicine 0.5 mg was dissolved in 500 cc of glucose 5%. On the first day of treatment 0.5 cc was administered, and the dose was doubled each day until a dose of 250 cc (0.25 mg colchicine) was reached on the tenth and last day of treatment. No adverse effects were observed during the 10 day desensitization period. At the present time, two months after the desensitization process, the patient is receiving 1 mg colchicine/day, with no evidence of an allergic reaction.

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