Recurrent pericarditis in hyper-IgD syndrome

Sirs,

We observed a 12-year-old boy affected by hyper-IgD syndrome (HIDS) who was successfully treated with etanercept, but developed a recurrent pericarditis.

The boy suffered, since the age of three months, from recurrent attacks of fever, abdominal pain and arthritis involving small and large joints. Symptoms resolved within a few days with steroid administration but recurred every two weeks. Laboratory findings showed: IgD:1550 mg/dl; IgA: 1.010 mg/dl; ESR: 101 mm/h; CRP: 5.00 mg/dl. The boy was diagnosed as having HIDS by demonstration of an homozygous missense mutation (C367S) on exon 11 of the mevalonate kinase (MVK) gene. No mutations in *MEFV* and *TNFRSF1A* genes were detected. Because of symptomatic therapy inefficacy, etanercept, a TNF-α antagonist, 0.4 mg/kg twice weekly was started. A dramatic response was observed: attacks disappeared and no side effects were registered. Two years later, the patient developed fever, precordalgia and orthopnea. Laboratory investigations revealed elevated ESR and C-reactive protein values (58 mm/h and 15.8 mg/dl respectively) and leukocytosis (white blood cells count: 24.31 x 10^3/mm^3; neutrophils: 88%). Other tests, including hepatic and renal function, C3, C4, hydroelectric balance, anti-streptolysine O titre, were within normal range. Blood, urine, stool and throat cultures did not show any bacterial nor mycetal growth. The Mantoux test and serology for various infectious agents including coxsackievirus, echovirus and herpesviruses were all negative. Pleural and pericardial effusion were demonstrated by x-rays and echocardiogram (Fig. 1). Etanercept was interrupted and the child was started on prednisone (2 mg/kg/day) with good clinical and laboratory response. Four months later, he was admitted for a relapse of pericarditis during steroid tapering. Colchicine (1 mg/day) and ibuprofen were therefore associated to prednisone. One year later, the patient was symptom free, after prednisone tapering. Three months after prednisone interruption, the boy presented new attacks of HIDS.

HIDS is an autosomal recessive autoinflammatory syndrome characterized by recurrent attacks of fever and a serum IgD concentration >100 IU/ml. Febrile episodes are accompanied usually by lymphadenopathy, abdominal pain, diarrhea, arthralgia, arthritis and cutaneous rash (1).

Recurrent pericarditis is not a typical clinical finding of HIDS and no evidence of this association exists in the literature; pericarditis has been well described in patients with familial Mediterranean fever (FMF), another genetic fever affecting Jews, Turks, Armenians and Arabs (2).

It is difficult to understand the pathogenesis of pericarditis in this patient as no trauma or surgery, no apparent source of infection, no evidence of contiguous pneumonia could explain this complication. Sweet et al. recently described the development of purulent pericarditis in an adult patient with rheumatoid arthritis during treatment with etanercept and methotrexate (3). Conversely, Aslangul *et al.* reported a beneficial effect of etanercept in the treatment of constrictive pericarditis complicating rheumatoid arthritis in an adult (4). The hypothesis that etanercept could predispose our patient to pericardial inflammation, presumably of viral origin, is questionable for at least two reasons: firstly, pericarditis occurred after two years since etanercept was started; secondly, the interruption of anti-TNF-α treatment did not avoid pericarditis recurrence. Surely etanercept was effective in aborting attacks of HIDS in our patient. A complete resolution of symptoms was achieved with etanercept and new recurrences were observed after treatment interruption. Other recent studies suggest that anakinra (5), an IL-1 ra antagonist, and etanercept (6, 7) are effective in preventing IgD-related febrile attacks; but data about etanercept are contradictory (8, 9, 10).

In conclusion, recurrent pericarditis is a possible clinical finding in patients with HIDS. Etanercept, an anti- TNF-α drug, seems to be highly effective in the treatment of febrile attacks of HIDS. However, further studies are necessary to better understand the long-term efficacy and safety of anti-TNF-α treatment in these patients.

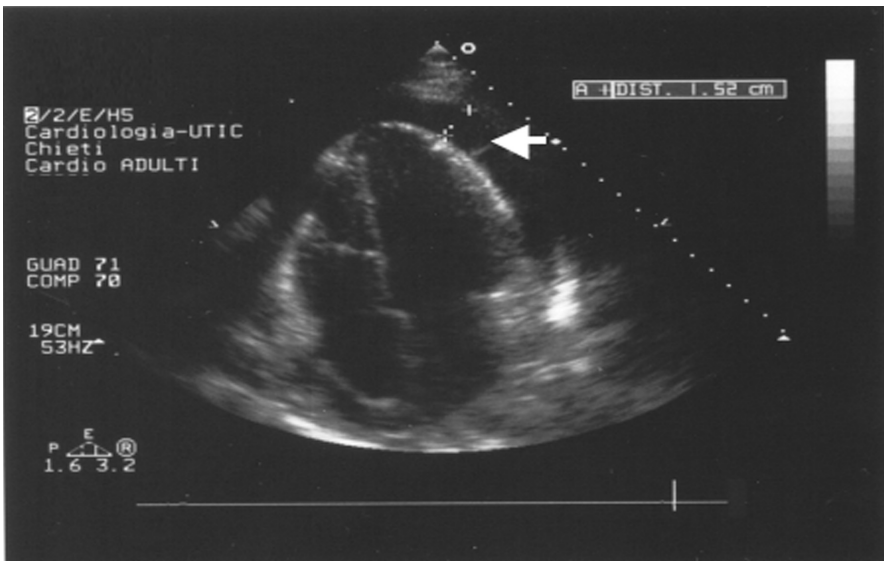

Fig. 1. Two-dimentional ecocardiogram showing large pericardial effusion (arrow).

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