Cogan's syndrome in a patient with familial Mediterranean fever

Sirs,

Familial Mediterranean fever (FMF) is an autoinflammatory disease caused by mutations in the Mediterranean fever (*MEFV*) gene. Flares of inflammation occur, with fever and abdominal or chest pain indicating serositis. Symptoms indicating muscle and joint inflammatory are common during or between flares (1).

A 54-year-old man was admitted in 2009 for polyarthitis of the wrists, knees, and metacarpo-phalangeal joints. One year prior to this presentation, the patient had a history of progressive bilateral sensorineural hearing loss. Cerebral and auditory conducts MRI was normal. The patient was of armenian origin. A diagnosis of FMF was made in 1982 (recurrent fever and pleurisy); and was confirmed in 2002: identification of mutations in the *MEFV* gene (*M680I / V726A*). Colchicine was effective in prevention of flare of inflammation and amyloidosis.

Upon admission, he complained of polyarthralgia, weight loss and fatigue, without fever. The otolaryngeal examination confirmed a bilateral sensorineural hearing loss. The ophthalmologic examination showed signs of posterior uveitis, with retinal vasculitis on the left eye. Laboratory tests showed normal complete blood count, liver function, and renal function. ESR was 58 mm/hour and CRP was 39 mg/l. Treponemic pallidum, rheumatoid factors, anti-citrullinated protein antibodies, anti-nuclear antibodies, anti-phospholipid antibodies, and anti-neutrophil cytoplasm antibodies were all negative. The chest x-ray, ECG, transthoracic cardiac echography, thoracic and abdominal scan were all normal. Radiography of the joints disclosed no joint destruction. An increased fluorodeoxyglucose (FDG) uptake of the aortic wall was demonstrated on (18)F-FDG PET. The diagnosis of Cogan's syndrome was established upon the association of vestibuloauditory, ocular and systemic manifestations. Treatment with prednisone 1mg/kg/day was started, which resulted in an improvement in the polyarthritis and asthenia but without improvement in the audiogram. The ophthalmologic examination showed a favourable outcome. Prednisone was slowly tapered. After 4 months of treatment, (18)F-FDG PET was normal; ESR was 10 mm/h and CRP 9 mg/l.

Cogan's syndrome is a rare, chronic vasculitis. The diagnosis is made upon the association of eye disease and vestibuloauditory dysfunction, with or without systemic features (2-4). In our case, the diagnosis of atypical Cogan's syndrome was established upon the association of vestibuloauditory, ocular and systemic manifestations (polyarthritis, asthenia, weight loss, aortitis), according to the criteria described by Grasland *et al*. (3). Deafness is not a manifestation of FMF but is a manifestation of another group of autoinflammatory disorders; cryopyrin-associated periodic syndromes (CAPS) and particularly Muckle-Wells syndrome. These diseases are related to *CIAS1*-gene mutations. Coexistent *MEFV* and *CIAS1* mutations manifesting as FMF with deafness has been reported in children (5). In our case, there was no argument in favour of CAPS; so the *CIAS1* gene was been sequenced.

Cogan's syndrome and FMF are systemic inflammatory disorders with seemingly distinct genetic and pathophysiologic mechanisms. Obviously, it can not be excluded that the two disorders are associated by chance. However, certain vasculitis have an increased prevalence among patients with FMF (6). For instance, the occurrence of Henoch-Schönlein and polyarteritis nodosa in patients with FMF has been noted in isolated reports (7). A multicenter study in patients with FMF showed that polyarteritis nodosa, Henoch-Schönlein purpura, Behçet's disease, seronegative spondyloarthritis, and chronic inflammatory arthritis had a higher frequency as expected in the normal population (8). More recently, descriptions of cases of relapsing polychondritis and FMF have highlighted the relationship between these seemingly separate disorders (9). To the best of our knowledge, no other case of Cogan's syndrome in patients with FMF has been described in the literature.

Since the identification of the *MEFV* gene, considerable progress has been made in the understanding of FMF, although the pathogenic effects of the mutations remain unclear (1). It was noticed that patients with certain rheumatic diseases had an increased carrier rate for mutations in the *MEFV* gene including seronegative spondyloarthropathies, Henoch-Schönlein purpura, polyarteritis nodosa and some forms of juvenile idiopathic arthritis (6). Furthermore, certain polymorphisms have been associated with a severe inflammatory complication in arthritis. It may be suggested that mutations and polymorphisms in the *MEFV* gene might be susceptibility factors for the disease or a more severe course of the disease for a number of rheumatic diseases (6).

T. Zenone *MD*
M. Puget *MD*

Department of Internal Medicine, Centre Hospitalier, Valence, France.

Address correspondence to:
T. Zenone, MD, Department of Internal Medicine, Centre Hospitalier, 26953 Valence, Cedex 9, France.
E-mail: tzenone@ch-valence.fr

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References

1. KONÉ-PAUT I, HENTGEN V, TOUITOU I: Current data on familial Mediterranean fever. *Joint Bone Spine* 2011; 78: 111-4.
2. MAZLUMZADEH M. MATTESON EL: Cogan's syndrome: an audiovastibular, ocular, and systemic autoimmune disease. *Rheum Dis Clin North Am* 2007; 33: 855-74.
3. GRASLAND A, POUCHOT J, HACHULLA E, BLÉTRY O, PAPO T, VINCENEUX P, FOR THE STUDY GROUP FOR COGAN'S SYNDROME: Typical and atypical Cogan's syndrome: 32 cases and review of the literature. *Rheumatology* 2004; 43: 1007-15.
4. GLUTH MB, BARATZ KH, MATTESON EL, SRISCOLL CLW: Cogan syndrome: a retrospective review of 60 patients throughout a half century. *Mayo Clin Proc* 2006; 81: 483-8.
6. OZEN S: Mutations/polymorphisms in a monogenetic autoinflammatory disease may be susceptibility markers for certain rheumatic diseases: lessons from the bedside for the benchside. *Clin Exp Rheumatol* 2009; 27 (Suppl. 53): S29-S31.
5. SINGH-GREWAL D, CHAITOW J, AKSENTIJEVICH I, CHRISTODOULOU J: Coexistent *MEFV* and *CIAS1* mutations manifesting as familial mediterranean fever plus deafness. *Ann Rheum Dis* 2007; 66: 1541.
7. OZDOGAN H, ARISOY N, KASAPÇAPUR O *et al*.: Vasculitis in familial Mediterranean fever. *J Rheumatol* 1997; 24: 323-7.
8. TUNCA M, AKAR S, ONEN F *et al*.: Familial Mediterranean fever (FMF) in Turkey: results of a nationwide multicenter study. *Medicine* (Baltimore) 2005; 84: 1-11.
9. MILLER EB, FRIEDMAN JA, LAHAV Y, LANDAU Z: Relapsing polychondritis and familial Mediterranean fever – an association. *Clin Rheumatol* 2011; 30: 711-3.