Isolated Recurrent Pleuritis Revealing Familial Mediterranean Fever in Adulthood

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Abstract

Familial Mediterranean fever (FMF) is a genetic autoimmune disease especially affecting populations of Mediterranean origin with an autosomal recessive inheritance. The cardinal manifestations consist of short febrile and painful attacks of peritonitis, arthritis and pleuritis developing during childhood. We report the case of a 26-year-old man of Tunisian descent who had febrile episodes of right-sided pleuritis without any extrathoracic complaints. Disappearance of attacks with one dose of colchicine (1 mg/day) strengthened the presumptive diagnosis of atypical FMF, which was further confirmed by genetic testing identifying the homozygous mutation M694I/M694I of the MEFV gene.

Novel Insights

- Recurrent febrile pleuritis may be the sole manifestation of FMF in adulthood.
- Serositis may occur in unpredictable sequence in a given patient with FMF during the course of disease.

Key Words

Colchicine  • Familial Mediterranean fever  • Fever  • M694I mutation  • MEFV gene  • Pleuritis

Introduction

Familial Mediterranean fever (FMF) is an autoimmune disorder of genetic origin with an autosomal recessive inheritance, characterized by recurrent episodes of fever and systemic manifestations usually developing...
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during childhood in populations of Mediterranean origin. The cardinal manifestations are febrile attacks of sterile peritonitis, monoarthritis, erysipela-like erythema and pleuritis [1]. Pleural manifestations present in 30–40% of patients with FMF may reveal the disease in <10% of patients [2, 3]. We report a case of recurrent febrile pleuritis as the sole manifestation of FMF in an adult.

**Case Report**

A 26-year-old man of Tunisian descent was referred in May 2007 for the diagnosis of recurrent right-sided chest pain with fever. Since 2001, he had experienced nine similar episodes without any extrathoracic complaint treated with antibiotics and high-dose prednisone. The resolution of symptoms occurred within 3–10 days.

Physical examination was unremarkable. Laboratory tests during the flares showed increased C-reactive protein (110–130 mg/l) and normal white blood cell counts. Urine testing did not reveal microscopic hematuria or proteinuria. Serologies for human immunodeficiency virus and antinuclear antibodies were negative. A chest radiograph showed a minimal right pleural effusion; contrast-enhanced CT confirmed the right pleural effusion without parenchymal involvement and ruled out embolism (fig. 1). Pulmonary function tests, electrocardiogram and echocardiography were normal. Thoracentesis failed to retrieve pleural fluid.

We re-interviewed the patient and it became apparent that he had had several flares of arthritis of the ankles during his adolescence. A clinical diagnosis of atypical FMF was made and the patient was put on colchicine 1 mg/day in June 2007. He decided to stop colchicine in March 2008, resulting in recurrence of acute pleuritis 5 days after the interruption. Resuming colchicine treatment led to rapid regression of the pleuritis within 2 days. Molecular testing of the *MEFV* gene identified one homozygous mutation (M694I/M694I).

**Discussion**

FMF is characterized by an erratic course with patients having all forms of serositis or synovial attacks, which recur at irregular intervals and in unpredictable sequence [2]. Although the delay from onset of disease to diagnosis has shortened [3], the diagnosis of FMF may be challenged in atypical presentations, notably in case of pleuritis as the sole manifestation [4, 5].

Pleuritis is usually unilateral [1, 2, 5] and resolves within hours to several days [4], similarly to other serositis attacks. Pleural rub and transient minimal pleural effusion may be present [4]. The pleural fluid was described as containing mainly polymorphonuclear cells, but predominance of lymphocytes was also reported [2, 5]. The pleura usually appears entirely normal on histopathologic examination [2]. However, recurrent chest attacks may eventually be associated with pleural thickening [2, 4]. Other chest manifestations include pericarditis in <1% of patients and rarely amyloid A amyloidosis or vasculitis of the lungs [4].

Despite the cloning of the *MEFV* gene causing FMF and the ongoing identification of new mutations, diagnosis of FMF remains clinical. In fact, identifiable mutations may be lacking in at least 20% of cases with clinically defined FMF [3, 6]. Mutation testing confirms the diagnosis especially in patients with atypical manifestations of FMF and may identify asymptomatic siblings susceptible to develop amyloidosis [2]. In addition, detection of the homozygous M694V/M694V mutation provides accurate information about an elevated risk for secondary amyloidosis [7].

Colchicine at a dose of 1–2 mg·kg⁻¹ per day dramatically improves the course of FMF, but 10% of patients are resistant to the drug. This treatment is mandatory as it almost completely prevents the development of secondary amyloidosis [6].

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**Fig. 1.** Contrast-enhanced chest computed tomography showing right-sided pleural effusion.
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