Reumatol Clin. 2021;17(8):489–490

Sociedad Española de Reumatología - Colegio Mexicano de Reumatología

Reumatología Clínica

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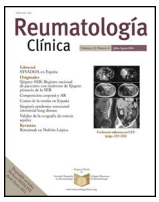

Letter to the Editor

Atypical familial Mediterranean fever with PFAPA-Like symptoms and psoriasis☆

Variante atípica PFAPA-like de la fiebre mediterránea familiar asociada a psoriasis

Dear Editor,

Autoinflammatory syndrome covers a set of disorders (the majority of which are hereditary) characterised by recurring and self-limiting episodes of inflammation, the result of inflammatory process control dysregulation. Clinically it is not easy to differentiate one entity from another, and atypical forms that simulate other processes also exist within clearly defined entities. Genetic diagnostic techniques will help us to improve our knowledge of these entities.

Within this context we describe the case of a 70 year-old woman who was referred to study recurring episodes of pharyngeal angioedema and fever. The first symptoms appeared at the age of 4 years, with recurring and self-limiting episodes of fever, pharyngitis, adenopathies and crises of abdominal pain. These symptoms were attributed to viral infections. The pharyngeal symptoms improved in adolescence, although the fever and abdominal crises persisted, with the addition of joint symptoms. At 58 years old she was diagnosed with cutaneous psoriasis and psoriatic oligoarthritis, without signs in MR imaging of spondyloarthritis or sacroiliitis, with negative HLA-B27. Treatment commenced with leflunomide. Symptoms have worsened in recent years, with weekly episodes.

There was no sign of eosinophilia in the haemogram. Routine biochemical analyses were normal. Electrophoresis, immunoglobulins A, G, M, D and E, complement levels, ANA, cryoglobulins, tryptase, HIV, HBV and HCV were normal or negative. Given the suspicion of an autoinflammatory syndrome a genetic study was requested, focussing on 109 genes involved in autoinflammatory processes. Heterzygotic alterations were only found in the germ line that involved the MEFV E148Q gene (exon 2)/P369S and R408Q (exon 3). Based on these data the diagnosis of atypical variant familial Mediterranean fever (FMF) was established, Aphthous stomatitis, Pharyngitis and Adenopathy (PFAPA)-like.

A typical attack of FMF is defined as an episode lasting from 12 h to 3 days, with fever accompanied by peritonitis, pleuritis or monoarthritis. Nevertheless, atypical variants have been described, one of which is similar to PFAPA syndrome. The 8 cases published in the literature on this variant,[1–3] like our case, describe episodes of fever associated with pharyngitis, cervical lymphadenopathy and tonsillitis. In 7 of these 8 cases it is associated with the E148Q/P369S/R408Q variant, while in the other case it is associated with P369S/R408Q. Only one previously published case of this FMF variant had abdominal pain and, as in our case, it was associated with the E148/P369S/R408Q variant of the MEFV gene.

The second point to be considered is superimposition with other autoinflammatory syndromes. An increase in the frequency of psoriasis in patients with FMF has been described in this context, especially in the adult population (OR of 16.34, and an incidence of 3.7% in comparison with 0.42% of the general population).[4] The mechanism shared by both processes would be the action of IL-1. The purine produced in FMF causes an increase in the levels of IL-1, which plays an essential role in the early signalling of Th17 lymphocytes. Ashida et al.[5] have demonstrated that active Th17 lymphocytes are present in the dermis of FMF patients with similar lesions to those present in cutaneous psoriasis. These lymphocytes stimulate keratinocytes.

In the few studies that exist, the presence of psoriasis has chiefly been associated with the M694V and 680I variants in homozygosis and heterozygosis, and there is only one case of an E148Q variant in heterozygosis, this being the variant of our patient.[6] Respecting oligoarthritis, Kaşifoğlu et al. describe this in 27% of patients with clinical musculoskeletal FMF, although only 7% of the total number of patients have sacroiliitis, which in 94% of cases is associated with the M694V mutation, and in 47% of cases with HLA-B27^{+}. Thus sacroiliitis is not the usual form of joint involvement in FMF, while oligoarthritis is with negative HLA-B27.[7]

Treatment with colchicine and corticoids is only partially beneficial, so that treatment with anakinra is proposed for this variant, a human IL-1 receptor antagonist. After 2 months of treatment the patient has progressed from suffering a crisis every week to not having any crises.

To conclude, there are atypical forms of FMF. In patients with recurring episodes of pharyngitis, stomatitis and lymphadenopathies, the possibility of an autoinflammatory syndrome should be taken into account, especially if they are accompanied by abdominal pain or monoarthritis.

References

1. Ryan JG, Master SL, Booty MG, Habal N, Alexander JD, et al. Clinical features and functional significance of the P369s/R408Q variant in pyrin, the familial Mediterranean fever protein. Ann Rheuma Dis. 2010;69:1383–8.
2. TajiKa M, Aral M, Kobayashi K, Fujimaki K, Agematsu K, Umeda Y. Famial mediterraena fever E/148Q/P369S/R408Q exon 3 variant with severe abdominal pain and PFAPA-like symptoms. J Clin Case Rep. 2015;6:790–2.
3. Yamagami K, Nakamura R, Hanioka Y, Agamatsu K. Familial Mediterranean fever with P369S/R408Q variant in pyrin presenting as symtons of PFAPA. Moderm Rheuma. 2017;27:356–9.
4. Cakir N, Pamuk ON, Dervis E, Imeryüz N, Uslu H, Beian Ö, et al. The prevalence of some rheumatic diseases in western Turkey: Havsa study. Rheumatol Int. 2012;32:895–908.
5. Ashida M, kolke Y, Kuwatsuka S, Ichinose K, Migita K, Sano S, et al. Psoriais-like lesions in a patient with familial Mediterranean fever. J Dermatol. 2016;43:314–7.
6. Erden A, Batu E, Syhoglu E, Sari A, Sönmez H, Armagn B, et al. Increased psoriasis frequency in patients with familial Mediterranean fever. Ups J Med Sci. 2018;123:57–61.

☆ Please cite this article as: Blasco F, García A Á, Martos MD, Muñoz S. Variante atípica PFAPA-*like* de la fiebre mediterránea familiar asociada a psoriasis. Reumatol Clin. 2021;17:489–490.

7. Kaşifoğlu T, Çalışır C, Cansu DÜ, et al. The frequency of sacroileitis in familial Mediterranean fever and the role of HLA-B27 and MEFV mutations in the development of sacroileitis. Clin Rheumatol. 2009;28:41–6.

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https://doi.org/10.1016/j.reumae.2020.02.005

Systemic sclerosis related interstitial lung disease: What is the recommended treatment?

Enfermedad pulmonar intersticial relacionada con la esclerosis sistémica: ¿cuál es el tratamiento recomendado?

Sr. Editor:

We have read the article by Sobolewski et al.[1] with great interest and we sincerely congratulate them for highlighting the current developments in the management of systemic sclerosis (SSc). Although they wanted to gather the newest data about the aetiology, pathophysiology and management, the part regarding the management of SSc related interstitial lung disease (SSc-ILD) has some clerical error. Firstly, they specified that patients with SSc-ILD have stable or slowly progressive disease and only 25–30% of them need immunosuppressive treatment. This statement creates an impression that ILD in SSc is not a serious complication. However, in the previous part of the same manuscript, it is stated that SSc-ILD is one of the major causes of morbidity and mortality and we know that SSc-ILD is not a benign complication of the disease. Secondly, they reported that mycophenolate mofetil (MMF) is the preferred first line agent for the treatment of SSc-ILD. On the other hand, in the following paragraph, it is written that intravenous cyclophosphamide (CYC) is the recommended first line therapy for SSc-ILD and MMF is a good alternative treatment. In this regard, European League Against Rheumatism (EULAR) also recommends CYC for SSc-ILD in the first line, but not MMF.[2]

In conclusion, as complications in SSc is still characterized by a severe course and high risk of early death, the importance and severity of ILD in SSc patients should be highlighted and the recommended first line treatment for SSc-ILD should be clarified.

References

1. Sobolewski P, Maślińska M, Wieczorek M, Łagun Z, Malewska A, Roszkiewicz M, et al. Systemic sclerosis – multidisciplinary disease: clinical features and treatment. Reumatologia. 2019;57:221–33.
2. Kowal-Bielecka O, Fransen J, Avouac J, Becker M, Kulak A, Allanore Y, et al. Update of EULAR recommendations for the treatment of systemic sclerosis. Ann Rheum Dis. 2017;76:1327–39.

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