NOTES & COMMENTS

Hidradenitis suppurativa and Mediterranean fever gene mutations

To the Editor: We read with great interest the report by Iannone et al[1] and would like to make a contribution to the discussion in the light of the recent findings in the field.

Hidradenitis suppurativa (HS) itself is a disease with prominent autoinflammatory features.[2] HS may also be a component of systemic autoinflammatory syndromes like pyoderma gangrenosum, acne, pyogenic arthritis, and suppurative hidradenitis (PAPASH) and pyoderma gangrenosum, acne, and suppurative hidradenitis (PASH), which are associated with mutations in proline-serine-threonine phosphatase interacting protein 1 gene (*PSTPIP1*).[3] In patients with familial Mediterranean fever (FMF), the most common hereditary autoinflammatory disease, HS may present with a severe phenotype and overlapping PAPASH-like features.[4] Moreover, the rates of FMF and heterozygous Mediterranean fever gene (*MEFV*) mutations were found to be increased in a cohort of patients with severe HS compared with the normal population.[5] Notably, in 2 of the 4 patients with HS and pyoderma gangrenosum, double pathogenic mutations in *MEFV* without clinical FMF and promoter elongation in *PSTPIP1* coexisted.[5] A molecular link between FMF and PASH/PAPASH was proposed in patients with complex HS, especially when accompanied by pyoderma gangrenosum, as the products of *MEFV* and *PSTPIP1* interact with each other.[4,5] *MEFV* mutations were also found to be more frequent than those in the normal population, associated with disease severity, and of prognostic importance in many inflammatory diseases other than HS, such as rheumatoid arthritis, spondyloarthropathies, vasculitis, Behçet syndrome, inflammatory bowel diseases, multiple sclerosis, and glomerulonephritis.[6] So, it is not surprising to encounter *MEFV* mutations in patients with chronic inflammatory diseases and secondary amyloidosis, especially in geographic regions and races with a high frequency of FMF. *MEFV* mutations without clinical FMF may occasionally be found in whites, in whom FMF is not a prevalent disease, with rheumatic disease–related secondary amyloidosis.[7] In brief, mutations in *MEFV* and potentially other genes related to autoinflammatory diseases may augment systemic inflammation in various chronic inflammatory diseases including HS. Supporting this hypothesis, we found a heterozygous pathogenic mutation (M680I) in *MEFV* in our previously reported patient with HS-related systemic amyloid A amyloidosis.[8] Notably, 3 of the previosly reported 8 cases of HS-related systemic amyloid A amyloidosis summarized by Iannone et al[1] were from Turkey, an endemic region for FMF. But *MEFV* mutation analyses were not available for the 2 other than ours.

Serum amyloid A, the elevation of which was a clue for a tenacious investigation for amyloidosis in the presented case, is also more than an acute phase reactant in the field of autoinflammatory diseases. It may predict amyloidosis and reflect subclinical inflammation and amyloid burden, and persistently elevated levels are associated with poor disease outcome and even increased mortality.[9] The role of serum amyloid A in predicting amyloidosis and monitorization of therapy should be investigated in HS cohorts.[1] In the era of the biological and targeted therapies, immunogenetic background of HS needs more extensive research.

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