Correspondence

Response to Zizzo et al.

As two of us (I. S. and S. P.) were also the coauthors of the first published paper suggesting similarity of symptomatology between Fabry’s disease (FD) and familial Mediterranean fever (FMF) (1), we read the study by Zizzo et al. with great interest (2). The researchers identified three cases of previously unrecognized FD among their cohort of 42 FMF patients, which corresponds to a quite high prevalence considering the rarity of the disease among the general population.

We couldn’t agree more with the authors that FD should be considered in all patients presenting with vague symptomatological patterns of FMF. Indeed, such an approach might have an outmost importance, particularly in ethnic groups (Turks, Jews, Arabs, and Armenians) in whom the FMF is more prevalent. However, the essential question in this context is how to define the vagueness of symptomatology. In other words, are all the symptoms related with FMF equal in their potential to mimic FD, or is there any special pattern observed in such cases?

Following our first encounter with a patient with FD about a decade ago (1), we have recently diagnosed one more case of FD in our department. We would like to briefly share our observation, which might help to answer above-mentioned question. The patient was a 20-year-old male whose major complaint was distal extremity (both upper and lower) pain. While the patient described periods of increased intensity in his extremity pain, he did not define any period for the last 5 years without this complaint. He had various diagnoses (venous insufficiency, rheumatoid arthritis, neuropathy, anemia, etc.) and received several treatments with little relief in his symptoms if any. Two years following the onset of extremity pain, he started to experience recurrent attacks of abdominal pain, which was accompanied by fever most of the time. The recurrent nature of his abdominal pain and the existence of fever have led us to consider FMF as the likely diagnosis. The analysis of the MEƒV gene disclosed one mutation in heterozygosis, M694V. We experienced a kind of relief with the positive result of the genetic testing, despite knowing (and almost all physicians dealing frequently with FMF patients) that extremity pain of this kind is not the feature of FMF. Myalgia and most of his complaint was confined to his upper extremities. While his abdominal attacks and fever relieved substantially under the treatment with colchicine, he continued to experience extremity pain. At one of the follow-up visits, the patient started his conversation, as ‘I want to tell you something which you may think it is weird and impossible’ and described his lifetime lack of sweating. It was a kind of eureka moment, which led us to check for (and find) angiookeratomas over the buttocks. It then became clear that the patient had reported the symptom of anhydrosis several times to almost all the physicians he was seen and received no attention about it. The enzyme activity of alpha-galactosidase was found to be significantly decreased and the analysis of GLA revealed c.803_806del p. L268fs mutation on exon 6.

If we get back to our question of whether there are any symptoms more indicative of FD (even if other features suggest FMF), we think there are. Neither extremity pain nor decreased sweating is a recognized feature of FMF. In both of the cases we reported and two of three patients reported by Zizzo et al., acroparesthesia was among the cardinal features. Likewise, hypo- or anhydrosis is a well-known feature of FD and the list of differential diagnosis for this symptom is very limited. Therefore, questioning the patient regarding the absence of sweating might be highly valuable in those cases with a presumptive diagnosis of FD. However, it should be kept in mind that, some patients may not plainly describe this symptom, and thorough questioning regarding the heat intolerance (usually associated with exercise intolerance and avoidance of outdoors in summer months) may be more rewarding in such cases.

In conclusion, similarities between the symptoms of FMF and FD might possess diagnostic dilemma for the physician, specifically in countries where the FMF is frequent. Moreover, this study and our limited experience show that FMF and FD can be seen concurrently, which makes the diagnostic challenge more complicated. Therefore, we suggest that FD should be investigated in FMF patients presenting with unusual clinical features even if the patient carries MEƒV mutation in genetic testing.

I Simsek
S Yilmaz
M Cinar
H Erdem
S Pay
Division of Rheumatology,
Gulhane School of Medicine,
Ankara, Turkey

References

Correspondence:
Dr Ismail Simsek
GATA Romatoloji BD
06018 Etlik
Ankara
Turkey
Tel.: +90-312-3043965
Fax: +90-312-3043960
e-mail: drisimsek@gmail.com