

A COINCIDENCE OF FMF AND VITILIGO. A CASE REPORT

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Dear Editor,

Familial Mediterranean Fever (FMF), the best known of the recurrent hereditary autoinflammatory diseases, is characterized by typical clinical signs one of which could be cutaneous manifestations. As one of the most commonly seen pigmentary disorders, vitiligo appears to have strong supports for an autoimmune origin.

A 24 year-old woman suffering since childhood from attacks of ankle arthritis accompanied by fever and abdominal pain was referred to our department. She was diagnosed as FMF due to these typical symptoms. In the physical examination, in addition to ankle arthritis signs, there were also depigmented lesions in the form of generalized vitiligo which progressively appeared for 10 years. Because vitiligo is perhaps the most common pigmentary disorder and FMF predominantly affects our population, these two distinct entities can be present coincidentally in our patient. However, it has been reported that aside from its classic symptoms, cutaneous manifestations with a wide range of polymorphism can be seen approximately in one thirds of the cases with FME¹

FMF is an autosomal recessive autoinflammatory disorder, which is the most prevalent periodic fever syndrome, affecting more than 10,000 patients worldwide. It predominantly affects people from the Mediterranean basin, including Sephardic Jews, Arabs, Turks, and Armenians.² This condition is characterized by short attacks of serositis (peritonitis, pleuritis, or arthritis) and fever and in most cases and the first episodes appear before the age of 20 years.³ There are no specific diagnostic laboratory tests for FME, although genetical analysis may be helpful for such a patient. Its gene, MEFV, is located on chromosome 16 and has autosomal

recessive transmission, with incomplete penetrance. It codes for a protein called pyrin or marenos-trin, which is probably involved in the inflammatory process.³ The FMF diagnosis is usually made on clinical grounds only, when recurrent attacks of abdominal pain, fever, and arthritis are observed in a patient with an appropriate ethnic background and family history. The abdomen is the classic site of FMF and acute abdominal flares masquerade as abdominal emergencies. Musculoskeletal involvement is revealed by episodes of arthritis (more often mono- than oligoarthritis) and muscle pain. Chest pain due to unilateral pleuritis is reported in 30 percent of the patients, whereas pericarditis occurs in less than 1 percent.²

Besides these clinical signs, cutaneous involvement occurs in 7 to 46% of cases and mainly consists in erysipela-like erythema.⁴ These lesions characterized by tender erythematous plaques on the shins or feet have been considered to be a specific clinical finding for the disease. Histological examination of these findings have been found to be in accordance with those in the peritoneum of patients with FMF and it has been also suggested that erysipela-like erythema belongs to the spectrum of neutrophilic dermatoses and supports a pathogenesis that involves abnormal inhibition of the inflammatory cascade.⁵ There are also some studies reporting FMF patients who developed several cutaneous lesions other than erysipela-like skin lesions. In a previous study, a high rate of cutaneous manifestations (47% of 91 patients) were observed in patients with FMF and erythema, oedema and recurrent oral ulcers were reported as the most frequent findings.⁶ Also in another six-year observation study, it has been indicated that 43% of 46 children with FMF developed cutaneous manifestations most of them were erysipela-like erythema; the other cutaneous manifestations included episodes of non-specific purpuric rash, Henoch-Schönlein purpura, diffuse erythema of the face and/or trunk, angioneurotic oedema, diffuse erythema of the palms, Raynaud's phenomenon and

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a subcutaneous nodule. Also it has been concluded that the high incidence of these manifestations and their response to colchicine strongly suggested that skin involvement is an integral part FMF.⁷ In patients with FMF, some unusual cutaneous lesions of FMF such as pseudo-erysipela, Sweet's syndrome-like lesions, long lasting panniculitis, persistent and lichenified erysipela-like plaque⁴ and severe recurrent pyoderma⁸ were also reported. Similar to our case, progressively appeared vitiligo over years in a patient with FMF was also indicated in a case presentation.¹ These reports illustrate the polymorphism of cutaneous manifestations of FMF.

On the other hand, vitiligo, as one of the most common pigmentary disorder, involves complex interactions of several factors that ultimately contribute to melanocyte destruction, resulting in the characteristic depigmented lesions. It has been considered that generalized vitiligo appears to be an autoimmune disease of multifactorial origin that results from a combination of multiple inherited genetic risk factors and environmental stimuli.⁹ Studies on generalized vitiligo have led to the recognition that vitiligo is part of a broader, genetically-determined, autoimmune/autoinflammatory diathesis. Vitiligo has been found to be associated with some disorders including autoimmune thyroid disease, pernicious anemia, Addison's disease, and lupus; these same disorders occur at increased frequency in patients' first-degree relatives. Affected members of the vitiligo families have been shown having elevated frequencies of autoimmune thyroid disease, rheumatoid arthritis, psoriasis, adult-onset insulin-dependent diabetes mellitus, pernicious anemia, and Addison's disease.¹⁰ Several candidate genes and genetic linkages have been identified that could mediate susceptibility to both generalized vitiligo and to a specific group of other autoimmune/autoinflammatory disorders with which vitiligo is epidemiologically associated and additional genes may mediate susceptibility to vitiligo itself.⁹

The case we have presented has demonstrated a possible coincidence of FMF and vitiligo. These observations might contribute to illustrate the polymorphism of cutaneous manifestations in FMF, and FMF might be involved in autoimmune/autoinflammatory disorders that could be associated with vitiligo. Further documentations of these kind of observations of possible coincidences are needed to yield results that shed light on bio-

logical pathways of cutaneous as well as systemic inflammation.

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References

1. Devaux J, Belaube P, Garcin G et al. Cutaneous manifestations of mediterranean periodic disease. Concerning an observation. Review of the literature. *Sem Hop* 1980;56:2041-2044.
2. Drenth JP, van der Meer JW. Hereditary periodic fever. *N Engl J Med* 2001;345:1748-1757.
3. Vinceneux P, Pouchot J. Familial Mediterranean fever, clinical and laboratory findings. *Presse Medicale* 2005;34:938-946
4. Bafounta ML, Doumat-Batch F, Vasseur E et al. Unusual cutaneous lesions of familial Mediterranean fever *Ann Dermatol Venereol* 2004;131:183-186
5. Barzilai A, Langevitz P, Goldberg I et al. Erysipelas-like erythema of familial Mediterranean fever: Clinicopathologic correlation. *J Am Acad Dermatol* 2000; 42:791-795
6. Paut IK, Dubuc M, Sportouch J et al. Phenotype-genotype correlation in 91 patients with familial Mediterranean fever reveals a high frequency of cutaneous-mucous features. *Rheumatology* 2000;39:1275-1279.
7. Majeed HA, Quabazard Z, Hijazi Z et al. The cutaneous manifestations in children with familial Mediterranean fever (recurrent hereditary polyserositis). A six-year study. *Q J Med* 1990;75:607-16.
8. Lugassy G, Ronnen M. Severe Pyoderma Associated with Familial Mediterranean Fever - Favorable Response To Colchicine In 3 Patients. *Am J Med Sci* 1992;304:29-31
9. Spritz RA. The genetics of generalized vitiligo and associated autoimmune diseases. *Pigment Cell Res* 2007;20:271-278.
10. Laberge G, Mailloux CM, Gowan K et al. Early disease onset and increased risk of other autoimmune diseases in familial generalized vitiligo. *Pigment Cell Res* 2005;18:300-305