

ANSWER TO PHOTO QUIZ (ON PAGE 119)

TWO PATIENTS WITH RECURRENT FEVER AND
WINE RED DISCOLOURATION OF THE EYELIDS

DIAGNOSIS

At the time of presentation the recurrent febrile attacks had been present for several decades in both patients. Such a long duration makes an infectious or neoplastic disorder unlikely.¹ The attacks tend to recur after an asymptomatic period and have a predictable course, with a similar set of symptoms and time course during each attack. This suggests a form of periodic fever. Onset of the first attack in early childhood with lifelong persistence and the fact that more family members are affected suggests a congenital or hereditary form of periodic fever. Because women as well as men are affected an autosomal inheritance pattern is likely. Two of the four main subtypes of hereditary periodic fever syndromes show an autosomal recessive inheritance pattern: familial Mediterranean fever (FMF) and the hyper-IgD syndrome (HIDS). TNF-receptor associated periodic syndrome (TRAPS) and the cryopyrin-associated periodic syndromes (such as the Muckle-Wells syndrome) show an autosomal dominant inheritance pattern.^{1,2} In this family, an autosomal dominant inheritance is likely. Because none of the family members have experienced urticaria (a distinctive feature of the cryopyrin-associated syndromes), the most likely diagnosis would be TRAPS. TRAPS is caused by mutations in the gene encoding for the TNF type 1 receptor (TNFRSF1A). These mutations are thought to cause increased signalling of TNF- β , thus inducing cytokine secretion, activation of leucocytes, fever and cachexia. The attacks in TRAPS are characterised by spiking fever, skin lesions, myalgia, arthralgia, abdominal distress and ocular symptoms including peri-orbital oedema as shown by the picture (*figure 1*).^{1,2} In this family we found a missense mutation (C29F) of the gene encoding for the TNF type 1 receptor in all affected family members, confirming the diagnosis of TRAPS. After the diagnosis was confirmed both patients were treated with etanercept, a recombinant form of the TNF type 2 receptor, which blocks TNF signalling. With this treatment both intensity and duration of the symptoms were reduced.

REFERENCES

1. Drenth JPH, Meer JWM van der. Hereditary periodic fever. *N Engl J Med* 2001;345:1748-57.
2. Simon A, Deuren M van, Tighe PJ, Meer JWM van der, Drenth JPH. Genetical analysis as a valuable key to diagnosis and treatment of periodic fever. *Arch Intern Med* 2001;161:2491-3.

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