Recurrent limb and facial oedema with R92Q mutation: A non-febrile late-onset tumour necrosis factor receptor-associated periodic syndrome (TRAPS)?

Œdèmes récurrents et mutation R92Q : TRAPS sans fièvre ?

Tumor necrosis factor receptor-associated periodic syndrome (TRAPS) is an autosomal dominant auto-inflammatory disorder characterized by recurrent episodes of fever, periorbital oedema, abdominal pain and musculoskeletal and/or skin manifestations, resulting from mutations in the tumour necrosis factor receptor superfamily 1A (TNFRSF 1A) gene [1]. The median age at onset is about 10 years [2]. We report a patient with recurrent limb and facial oedema, biological inflammatory syndrome and R92Q mutation in TNFRSF 1A gene, suspected of non-febrile late-onset TRAPS and responding well to etanercept with a 5-year follow-up period.

Case report

A 49-year-old man presented with a one-year history of recurrent episodes of segmental oedema affecting the limbs and face (figure 1). He had not suffered from recurrent fever or other systemic symptom, had no other relevant medical or familial history. Attacks occurred at intervals of 1 to 3 months and usually lasted 3 to 5 days. Laboratory tests were normal between attacks but during attacks showed increased C-reactive protein (CRP) levels of between 20 and 60 mg/L (normal < 3 mg/L) with a white blood cell count of 11,000 to 15,000/mm³. After excluding complement abnormalities (especially C1 inhibitor), infections, allergy, auto-immune disease or vasculitis, an auto-inflammatory syndrome was hypothesized. An R92Q TNFRSF 1A gene mutation was identified, suggesting to the diagnosis of TRAPS. As oral corticosteroids were not effective, etanercept 25 mg was administered twice a week with complete resolution of attacks; it was well-tolerated. After 4 months, the patient spontaneously stopped etanercept but quickly experienced a relapse. Etanercept was resumed with a 50 mg injection administered at the start of each attack, resulting in a dramatic reduction in their severity and duration. The patient required about 1 injection per month. CRP levels and white blood cell count were normal during the follow-up period of 5 years.

Discussion

We describe a case of recurrent limb and facial oedema with biological inflammatory syndrome and R92Q TNFRSF 1A heterozygous mutation, disclosing probable non-febrile late-onset TRAPS. TRAPS usually begins during the first two decades [1]. Some cases of late-onset TRAPS have been described, with a median age of 32 years [2]. However, only few patients with an onset after 45 years have been described [2,3]. These phenotype variations, which increase the difficulty of diagnosis, could be due to the different TNFRSF 1A gene mutations. R92Q is one of 60 different mutations currently described. R92Q is associated with an atypical or incomplete phenotype: later onset, shorter duration of attacks and less frequent abdominal pain [4,5]. This mutation has a low penetrance thus accounting for the sporadic
cases. Recently, R92Q raises a lot of discussion about its direct pathogenicity as it is its frequency in the general population range from 1 to 8% [6-9]. Others authors consider than R92Q mutation can be regarded as a low-penetrance variant with a mild and broad contribution to auto-inflammatory disease, most likely depending on other modifying genes or environmental factors [10]. As our patient presented with recurrent episodes of inflammatory symptoms spanning a period of more than 6 months and a TNFRSF 1A mutation, we disclosed auto-inflammatory disorder and probable TRAPS. Corticosteroids were not effective so etanercept (TNFRSF 1B fusion protein) was prescribed. Actually, etanercept appears to be effective in decreasing the severity, duration and frequency of attacks [11] as in our patient. Anakinra has been suggested as an alternative in the event of etanercept failure [12]. Preventing attacks in TRAPS patients is particularly important in order to avoid the occurrence of AA amyloidosis. In cases of recurrent attacks of limb and facial oedema with an inflammatory syndrome, TRAPS should be considered after other possible causes have been excluded as etanercept could be an effective treatment.

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References


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Hyperkaliémie secondaire à l’activité physique intense : une complication rare de l’anorexie mentale

Hyperkalemia linked to intense physical activity: A rare complication in anorexia nervosa

L’hyperkaliémie est un trouble hydro-électrolytique défini par un taux plasmatique de potassium supérieur à 5 mmol/L. C’est une affection potentiellement mortelle en raison des troubles de la conduction et du rythme cardiaque qu’elle entraine. Les grandes causes d’hyperkaliémie sont la lyse cellulaire, l’insuffisance rénale, l’insuffisance surrénalienne, l’acidose métabolique, l’excès d’apport, les prises médicamenteuses (diurétiques, inhibiteurs de l’enzyme de conversion) et l’exercice physique intense. Des cas d’hyperkaliémie ont été décrits chez les patients anorexiques grands consommateurs de banane et de fruits.