



## The challenge of periodic fevers in children

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A five-year-old boy is seen in your office having experienced four days of high fever. What makes him different from the other children with fevers in your waiting room is that this is his sixth such episode in as many months, each occurring with a similar predictable pattern. His parents can recognize when his fever is about to start because he begins to look tired, and soon after his temperature measures 39°C. Ibuprofen has given him partial relief; however, the fever still returns. During your prior assessments, he has been found to have a mild pharyngitis and enlarged cervical lymph nodes. A course of penicillin during his first episode was stopped as the throat swab was negative, and they were told that he 'probably had a virus'. His parents comment on how predictable the fevers seem to be. By keeping a diary, they have demonstrated that the fevers occur approximately every 28 days and last five to six days before resolving.

This child's past medical and family histories are unremarkable. There is no one in the family with recurring fevers or concerning rheumatological illnesses.

On examination, the boy's vital signs are stable with a temperature of 38.8 °C. He appears fatigued but not toxic. There is mild erythema of the posterior pharynx without exudate, and enlarged lymph nodes in the anterior cervical chain, but not elsewhere. He does not have a rash. The remainder of a complete physical examination is unremarkable.

Laboratory tests show leukocytosis (leukocyte count of  $15 \times 10^9/L$ ), with mild neutrophilia, an elevated erythrocyte sedimentation rate (ESR) of 25 mm/h, and C-reactive protein (CRP) levels at 44 mg/L. Routine chemistry and urinalysis are normal. Throat swab, antistreptolysin-O titer (ASOT) and a monospot test were normal. Complete blood count (CBC) and ESR had also been checked two weeks earlier when he was well, and they were normal at that time.

His parents are reassured that these episodes resolve on their own, and understand that he is otherwise a healthy boy when he does not have these fevers. Nevertheless, frustration is setting in, as his schooling is repeatedly interrupted and both parents have missed time from work. They are beginning to believe that they will need to plan the time of their vacation so as to avoid the next fever event.

The overall presentation is felt to be consistent with periodic fever, aphthous stomatitis, pharyngitis and adenitis (PFAPA). A single dose of 1 mg/kg prednisone given at the onset of his next episode aborts the fever.

### LEARNING POINTS

- Autoinflammatory diseases are characterized by recurring episodes of fever and inflammation in the absence of infection or autoantibody formation (1). Periodic fever syndromes (PFS) (2) represent a group of autoinflammatory diseases, of which PFAPA is the most common.
- PFAPA onset typically occurs before five years of age with children experiencing episodes of high fever lasting three to six days and recurring every three to eight weeks. At least one condition of aphthous stomatitis, pharyngitis, and cervical adenitis accompanies the fevers. Children remain well between the fever episodes and continue to thrive (3).
- The diagnosis of PFAPA requires the exclusion of other possible causes of fever in children, such as infection, malignancy, cyclic neutropenia, autoimmune disease and consideration of the other forms of PFS (1,4).
- Laboratory testing during the fever episode shows mild to moderate leukocytosis and an elevation of the ESR or CRP. These tests normalize between episodes when the child is well.
- Beyond supportive care, no specific treatment is required for all fevers, and parents can be reassured that the condition is benign and usually resolves by adolescence (4).
- A single dose of 1 mg/kg prednisone at the onset of an episode can usually abort the fever. Other treatment options include prophylaxis with daily cimetidine and tonsillectomy (4,5).
- Presently, there are very little data regarding the different types of PFS among Canadian children. Additional research must be performed to better describe the burden of illness among these patients, such as the ongoing Canadian Paediatric Surveillance Program study regarding PFS (2).

### REFERENCES

1. Frenkel J, Wietse K. Overt and occult rheumatic diseases: The child with chronic fever. *Best Pract Res Clin Rheumatol* 2002;16:443-69
2. Periodic fever syndromes. <<http://www.cps.ca/English/surveillance/cpsp/studies/PFS.pdf>>.
3. Thomas KT, Feder HM Jr, Lawton AR, Edwards KM. Periodic fever syndrome in children. *J Pediatr* 1999;13:15-21.
4. Cassidy JT, Petty RE, Laxer RM, Lindsley CB. *Textbook of Pediatric Rheumatology*, 6th edn. Elsevier Inc, 2011.
5. Garavello W, Pignataro L, Gaini L, Torretta S, Somigliana E, Gaini R. Tonsillectomy in children with periodic fever with aphthous stomatitis, pharyngitis, and adenitis syndrome. *J Pediatr* 2011;159(1):138-42.

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