

Cimetidine and tonsillectomy as treatment for PFAPA syndrome: A case report

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Introduction

Periodic fever, aphthous stomatitis, pharyngitis, and cervical adenitis (PFAPA) syndrome is characterized by periodic high fever lasting 3 to 6 days and recurring regularly every 2 or 8 weeks. The fever is also associated with aphthous stomatitis, pharyngitis, and cervical adenitis. The etiology of PFAPA syndrome remains unclear. Although various treatments, such as tonsillectomy and the use of cimetidine, prednisolone, colchicine, thalidomide, anakinra, and non-steroidal anti-inflammatory drug, have been reported, the effectiveness of these treatments is still controversial. We here show 3 thought-provoking cases.

The cases

All procedures were in accordance with the ethical standards of the responsible committee on human experimentation (Tara Town Hospital, Japan) and with the Helsinki Declaration of 1975, as revised in 2013. Written informed consent for inclusion in this study was obtained from the parents of children. Table 1 shows characteristics of our 3 patients. These patients in the present were diagnosed with PFAPA syndrome in accordance with the diagnostic criteria shown in Table 2.

Case 1:

A 1-year-old girl suffered from periodic febrile attacks every 4 to 8 weeks. She was diagnosed with PFAPA syndrome at the age of 1 year. She was started on oral cimetidine treatment (20 mg/kg, twice daily). She has not suffered from a febrile attack for more than 12 months. No side effect was detected due to cimetidine treatment.

Case 2:

A 6-year-old boy suffered from periodic febrile attacks every 2 to 8 weeks. He was diagnosed with PFAPA syndrome at the age of 3 years although onset was at the age of 1 year. He underwent tonsillectomy at the age of 6 years. He has not suffered from a febrile attack for more than 11 months since having tonsillectomy.

Case 3:

A 3-year-old girl suffered from periodic febrile attacks every 2 to 7 weeks. She was diagnosed with PFAPA syndrome at the age of 1 year. She underwent tonsillectomy at the age of 3 years. She has not suffered from a febrile attack for more than 9 months since having tonsillectomy.

Table 1: Characteristics of Three Patients with PFAPA Syndrome

Case	Sex	Symptoms	Leukocytes Count (/mm ³)	Treatment
1	F	High Fever, pharyngitis, aphthous stomatitis	10,930 – 18,800	Cimetidine
2	M	High Fever, cough pharyngitis, aphthous stomatitis	11,130 – 19,730	Tonsillectomy
3	F	High Fever, cough pharyngitis, aphthous stomatitis	12,550 – 23,160	Tonsillectomy

F: female, M: male

Table 2: The Diagnostic Criteria Advocated by Thomas et al.

- I Regularly recurring fevers with an early age of onset (<5 years of age)
- II Constitutional symptoms in the absence of upper respiratory infection with at least 1 of the following clinical signs:
 - a) Aphthous stomatitis
 - b) Cervical lymphadenitis
 - c) Pharyngitis
- III Exclusion of cyclic neutropenia
- IV Completely asymptomatic interval between episodes
- V Normal growth and development

Conclusion

Our experience shows that oral cimetidine treatment and tonsillectomy are effective against PFAPA syndrome although the mechanism is unclear.

We suggest that tonsillectomy be considered as early as possible in patients with PFAPA syndrome. We also propose the use of cimetidine to reduce the febrile attacks of PFAPA syndrome until the age of 3 years.

< Recommendation >

- at the age of 3 years and older -----> tonsillectomy
- under 3 years of age -----> oral cimetidine treatment



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