

Case Report

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Periodic Fever, Aphthous Stomatitis, Pharyngitis, and Cervical Adenitis (PFAPA) Misdiagnosed as Recurrent Urinary Tract Infection

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Recurrent fever is common in children and specific infections account for the fever in most cases. PFAPA is not an uncommon cause of periodic fever during childhood. On the other hand, in patients with vesicoureteral reflux (VUR), urinary tract infection usually presents with fever.

Here, we report two PFAPA cases in patients with VUR in whom recurrent episodes of fever were misdiagnosed as UTI.

Keywords: PFAPA Syndrome; Periodic Fever Syndrome; Vesico-Ureteral Reflux; Urinary Tract Infections; Child.

Running Title: PFAPA Misdiagnosed as Recurrent UTI

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Introduction

In 1987, Marshall GS et al. described a chronic syndrome characterized by periodic episodes of high fever (>39°C) lasting 3 to 6 days and recurring every 3 to 8 weeks accompanied by aphthous stomatitis, pharyngitis, and cervical adenitis. Although the details of its pathogenesis are unclear, periodic abnormalities involving the mechanisms regulating cytokine secretion have been suggested [1]. After this initial article, others reported patients with this syndrome [2-4]. In 1989, they coined the acronym PFAPA (Periodic Fever, Aphthous stomatitis, Pharyngitis, and cervical Adenitis) to describe this entity [5].

No specific diagnostic test is available for PFAPA and the diagnosis is based on published diagnostic criteria [5].

The exact prevalence of this syndrome is not known but PFAPA seems to be far more frequent than other auto-inflammatory diseases [6,7].

Recurrent fevers are common in children and specific infections account for the fever in most cases. In children with a history of VUR who complain about fever, UTI is the first diagnosis.

Thus, in these patients, treatment for UTI starts empirically before a diagnosis of urinary tract infection is established.

We describe two children who had a periodic fever syndrome associated with VUR and were wrongly diagnosed as UTI.

Case Report

Case 1

A 19-month boy experienced repeated episodes of fever exceeding 39° C. He had bilateral VUR in his past medical history so he was treated as breakthrough UTI each time he was admitted to the hospital. He was born with bilateral neonatal hydronephrosis, VCUG was performed at the age of 14 days that revealed bilateral VUR grade 3-4 in the left kidney and grade 2 in the right kidney. Because of the repeated episodes of fever and bilateral VUR, he was treated with antibiotics. At the age of 2 months, DMSA scan was performed that revealed a small-sized dysfunctional left kidney; however, the right kidney was intact. He was admitted to the hospital several times because of periodic fever and a diagnosis of breakthrough UTI was made wrongly despite negative or equivocal urine cultures. The signs of upper respiratory tract infection and exudative pharyngitis were reported frequently during admissions. The negative U/C tests and clinical symptoms led us to a diagnosis of PFAPA for the patient and short-term treatment with prednisolone was started. The patient was discharged after three days.

Case 2

Since the age of 6 months, a 9-year-old girl was frequently admitted to the hospital with a diagnosis of UTI. VCUG was performed showing bilateral VUR grade 3-4 in the left kidney and grade 3 in the right one. During each admission, repeated episodes of fever with pharyngitis were reported; however, she was treated as a case of UTI. At the age of two years, anti-reflux surgery was performed but the fever persisted and pharyngitis, adenitis, and aphthous ulcers were also seen. Finally, PFAPA was diagnosed and she was treated with short-term prednisolone with a dramatic response.

Discussion

Urinary tract infection (UTI) is an acute illness usually accompanied by fever, with or without other constitutional symptoms and local symptoms of loin pain and bladder irritation [8].

In the 1950s, researchers identified a close relationship between UTI, vesicoureteral reflux (VUR), and permanent kidney damage [9].

Vesicoureteral reflux (VUR) is the most common congenital anomaly of the urinary tract [10]. Children with VUR detected after UTI are predominantly females [11]. PFAPA syndrome is an auto-inflammatory disease with recurrent fever episodes like TRAPS (tumor necrosis factor receptor-associated periodic syndrome), FMF (familial Mediterranean fever), hyper IgD syndrome, cryopyrin associated periodic syndrome. A genetic origin has been found for these diseases except for PFAPA for which no clear etiology has been found so far. PFAPA occurs before 5 years of age with aphthous stomatitis, pharyngitis, cervical adenopathy, and a dramatic response to steroids [12]. PFAPA is a disease of exclusion based primarily on clinical findings; it is essential to first rule out other causes of periodic fever, including infection, malignancy, and cyclic neutropenia, which is diagnosed with serial white blood counts. The dramatic response to a single oral dose of corticosteroids is unique to this syndrome. Successful prophylactic therapy with cimetidine has been reported [13,14]. In our patients, the clinical presentation was clear enough to confirm a diagnosis of PFAPA; however, UTI was diagnosed by mistaken.

In conclusion, this report shows that a diagnosis of PFAPA must be considered in any child with recurrent unexplained fever; however, it may be missed especially in the presence of another cause of recurrent fever such as VUR.

Increased awareness results in more frequent diagnosis, prevents unnecessary investigations, and provides considerable reassurance to patients and parents.

References

1. Marshall GS, Edwards KM, Butler J, Lawton AR. Syndrome of periodic fever, pharyngitis, and aphthous stomatitis. *J Pediatr* 1987;110:43-6.
2. Feder HM Jr, Bialecki CA. Periodic fever associated with aphthous stomatitis, pharyngitis and cervical adenitis. *Ped Infect Dis J* 1989;8:186-7.
3. Rubin LG, Kamani N. Syndrome of periodic fever and pharyngitis (letter). *J Pediatr* 1987;110:307.
4. Feder HM Jr. Cimetidine treatment for periodic fever associated with aphthous stomatitis, pharyngitis and cervical adenitis. *Ped Infect Dis J* 1992;11:318-21.
5. Marshall GS, Edwards KM. PFAPA syndrome (letter). *Ped Infect Dis J* 1989;8:658-9.
6. Thomas KT. Periodic fever syndrome in children. *J Pediatr* 1999;18:68_6.
7. Hofer MF, Mahlaoui N, Prieur AM. A child with a systemic febrile illness—differential diagnosis and

- management. *Best Pract Res Clin Rheumatol* 2006;4:627-40.
8. Spencer JD, Schwaderer A, McHugh K, Hains DS. Pediatric urinary tract infections: an analysis of hospitalizations, charges, and costs in the USA. *Pediatr Nephrol.* 2010;25(12):2469-75. PubMed PMID:20711740.
 9. Ransley PG. Vesicoureteric reflux: continuing surgical dilemma. *Urology.* 1978;12(3):246-55.
 10. Dick PT, Feldman W. Routine diagnostic imaging for childhood urinary tract infections: a systematic overview. *J Pediatr.*1996;128(1):15-22.
 11. Smellie J, et al. Vesico-ureteric reflux and renal scarring. *Kidney Int Suppl.* 1975;4:S65-72.
 12. Padeh S, Brezniak N, Zemer D, et al. Periodic fever, aphthous stomatitis, pharyngitis and adenopathy syndrome: clinical characteristics and outcome. *J Pediatr* 1999;135:98-101.
 13. Padeh S, Brezniak N, Zemer D, et al. Periodic fever, aphthous stomatitis, pharyngitis, and adenopathy syndrome: clinical characteristics and outcome. *J Pediatr* 1999;135:98-101.
 14. Feder HM Jr. Cimetidine treatment for periodic fever associated with aphthous stomatitis, pharyngitis and cervical adenitis. *Pediatr Infect Dis J*1992;11:318-21.