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REVIEW ARTICLE

A clinical review of 105 patients with PFAPA (a periodic fever syndrome)

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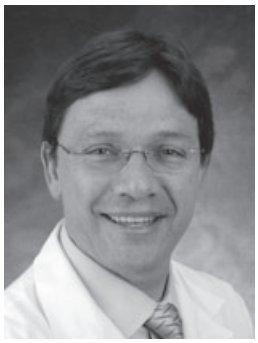

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Abstract

Aims: We describe the presentations and clinical outcomes of pediatric patients diagnosed with PFAPA (Periodic Fever, Aphthous lesions, Pharyngitis, and cervical Adenitis).

Materials and methods: The medical records of children with recurrent fever and referred between 1998 and 2007 to a tertiary pediatric care hospital were reviewed. Children who met clinical criteria for PFAPA were then asked to participate in a follow-up study.

Results: One hundred and five children met study criteria for PFAPA which included at least six episodes of periodic fever. Most (62%) were males, the mean age at onset of PFAPA was 39.6 months (80% were <5 years at onset), the mean duration of individual fever episodes was 4.1 days, and the mean interval between episodes was 29.8 days. Accompanying signs and symptoms included aphthous stomatitis (38%), pharyngitis (85%), cervical adenitis (62%), headache (44%), vomiting with fever spikes (27%) and mild abdominal pain (41%). A prodrome (usually fatigue) preceded the fever in 62% of patients. Parents noted that when their child with PFAPA had fever, other family members remained well. Laboratory tests in patients with PFAPA were nonspecific. Individual episodes of fever usually resolved with a single oral dose (~1 mg/kg) of prednisilone. The interval between fever episodes shortened in 50% of patients who used prednisilone. PFAPA resolved spontaneously (mean length 33.2 months) in 211105 (20%) patients. PFAF'A episodes continued (mean length 23 months) at the end of this study in 661105 (63%) patients. Cimetidine therapy was associated with the resolution of the fevers in 7/26 (27%) patients; tonsillectomy was associated with the resolution of the fevers in 11/11 (100%) patients.

Conclusion: PFAPA can usually be defined by its clinical characteristics. Individual febrile episodes usually resolve dramatically with oral prednisilone. The cause of PFAPA is unknown and research is needed to define its etiology. The overall prognosis for children with PFAPA is excellent.

Abbreviations

FCAS, familial cold autoinflammatory syndrome; FMF, familial Mediterranean fever; HIDS, hyper immunoglobulin D with periodic syndrome; JIA, juvenile idiopathic (rheumatoid) arthritis; NOMID, neonatal onset multisystem inflammatory disease; PFAPA, Periodic Fever, Aphthous, Pharyngitis and cervical Adenitis; TRAPS, tumour necrosis factor receptor-associated periodic syndrome.

INTRODUCTION

In 1987, Marshall et al. (1) reported a new periodic fever syndrome in 12 otherwise healthy paediatric patients. Similar reports were subsequently published by us and others, and the acronym PFAPA (**P**eriodic **F**ever, **A**phthous, **P**haryngitis and cervical **A**denitis) was coined (2–4). PFAPA could resolve spontaneously over time, or in some cases, it resolved with the use of oral cimetidine or with tonsillectomy (3,5,6).

A subset of the PFAPA patients who were previously reported in the literature had been evaluated at our institution (3,5,7). In the late 1980s, we evaluated a new PFAPA patient every 6–12 months; then in the mid 1990s to the early 2000s, we were seeing a new case (referred from within Connecticut) every 1–2 months. We now see more than one new patient per month. In this report, we present a retrospective review of the clinical manifestations and outcomes of 105 PFAPA patients evaluated and followed at the Connecticut Children's Medical Center (CCMC) over a 10-year period.

METHODS

Human subjects

This study was approved by CCMC's Institutional Review Board (IRB). We reviewed the medical records of all children referred to the paediatric infectious disease division at CCMC, between January 1, 1998 and June 30, 2007, for evaluation of recurrent fevers. Subjects met our case definition of PFAPA (i) if they had at least six episodes of documented fever (T > 38.9°C), (ii) if each febrile episode lasted no more than 10 days, (iii) if the fevers recurred at regular intervals of 2–8 weeks, (iv) if they were well between febrile episodes, (v) if they did not have arthritis or a distinctive rash or documented neutropenia and (vi) if they did not have a clinical explanation for the fever other than PFAPA. In addition to fever, patients needed to have at least one of the three major clinical findings associated with PFAPA – aphthous stomatitis, pharyngitis or cervical adenitis [Our case definition differs from the original (1,7) in that ours required at least six episodes of fever versus >1 year of periodic fevers, our episodes were no more than 10 days versus 3–6 days and our episodes recurred every 2–8 weeks versus 3–6 weeks in the original].

Clinical evaluation and follow-up

All PFAPA patients had a complete history and physical examination completed by a member of the division of infectious diseases at CCMC. Patients had a complete blood count (CBC) and erythrocyte sedimentation rate (ESR) performed at the onset of a febrile episode. Quantitative assay of immunoglobulins (IgA, IgG, IgM, IgE and IgD) was carried out at CCMC for half the patients. Clinical follow-up of all eligible PFAPA patients was attempted during 2007 (July 1–December 31), either by a clinic visit or by a telephone interview.

RESULTS

Patient characteristics

In the 10-year study period (1998–2007), 124 patients fulfilled the case definition for PFAPA. In addition, two subjects were excluded because other possible causes of periodic fever were identified: One patient was diagnosed with Sjogren's syndrome and another was diagnosed with Behcet's disease. These two subjects initially appeared to have PFAPA. A total of 19 patients were lost to follow-up and could not be contacted at the time of follow-up (July 1, 2007–December 31, 2007). Table 1 lists the demographics and clinical characteristics of the remaining 105 PFAPA patients reviewed in this study. All patients were well between febrile episodes and none had a history of being chronically ill. Episodes of fever began before age 5 years in 87/105 (83%) patients. The mean interval between episodes of fever was 29.8 days. It was not unusual for patients to intermittently skip an episode of fever. The longest intervals between fevers were 6 months in two patients and 1 year in one patient. Some parents (15/105) noticed a pattern of their child skipping episodes of fever during the summer.

The geographical ancestry of the 105 PFAPA patients was diverse and included Western Europe 39%, England/Scotland/Ireland 17%, Eastern Europe 15%, South/Central America 9%, Russia (old geography) 5%, China 3%, Scandinavia 3%, Greece 2%, India/Pakistan 2%, Africa 2% and others 2%.

Associated signs and symptoms

Table 2 lists the frequency of the three major signs and symptoms associated with the febrile episodes. When aphthous stomatitis was present, it was usually limited to 1–4 aphthae (<1 cm or less) or less frequently by a cluster of very small aphthae. Patients presented with either tonsilar (pharyngeal) erythema or white patches on the tonsils. In a few patients, the white patches were Gram stained and cultured, which revealed rare polymorphonuclear leucocytes with normal respiratory flora. Maximum temperature during fever episodes ranged from 39.2 to 42.1°C. During febrile episodes, most patients were described by their parents as listless but not toxic. When the patients were seen by their physicians for fevers (before PFAPA was suspected), parents were frequently told that their child 'had recurrent viral infections'. Other symptoms associated with the febrile episodes included headache 46/105 (44%), vomiting 28/105 (27%) especially with fever spikes and mild abdominal pain 43/105 (41%). Of the parents, 46% (48/105) reported that their children with PFAPA were less prone to the usual viral

Table 1 Demographics and clinical characteristics of PFAPA patients

Total number of patients	105 patients
Male/female	65/40 (62% males)
Mean/median age at onset (range)	39.6/30 months (3–144 months)
Mean duration per febrile episode (range)	4.1 days (2–7 days)
Mean interval between episodes (range)	29.8 days (14–50 days)

Table 2 Signs and symptoms in 105 patients who were associated with PFAPA febrile episodes

	Not present	Sometimes present	Usually present
Aphthous stomatitis	65/105 (62%)	18/105 (17%)	22/105 (21%)
Pharyngitis	16/105 (15%)	25/105 (24%)	64/105 (61%)
Cervical adenitis	40/105 (38%)	17*/105 (16%)	48*/105 (46%)

*Of the 65 patients with cervical adenitis, the adenitis of 42 (65%) were usually tender and 18 (28%) were usually enlarged to the point of being visible.
Sometimes present = <50% of the episodes.
Usually present = >50% of the episodes.

respiratory and gastrointestinal infectious diseases circulating through their homes and communities. A prodrome preceded fever in 65/105 (62%) patients. The prodrome included fatigue, headache, abdominal pain or irritability, which began a mean of 20 h (4–48 h) before the onset of fever. A defining characteristic of the PFAPA (versus recurrent viral infections) was that when a PFAPA patient had many episodes of fever, his/her siblings and parents remained well.

Laboratory values

Patients had a variety of laboratory tests performed prior to being referred to CCMC for evaluation. These tests included normal CBC's and ESR's when afebrile, and/or elevated white blood cell (WBC) counts, sterile blood and urine cultures, normal chest radiographs and normal liver function tests during fevers. In addition many patients had negative rheumatoid factor and ANA values and normal quantitative immunoglobulins. Our testing included at least a CBC at the onset of a febrile episode (mean WBCs 14 600 cells/mm^3, range 5100–30 500 cells/mm^3) with a preponderance of neutrophils. No patient had neutropenia. At the very onset of fever, PFAPA patients may have normal ESRs and an elevated CRP. Markedly elevated CRPs were not uncommon. Within a few days after the onset of fever, the patients' ESRs increased (mean 28 mm/h, range 5–80 mm/h). Quantitative immunoglobulin levels were normal or close to normal – IgG mean 961 mg/dL (623–1421 mg/dL), IgM mean 123 mg/dL (30–162 mg/dL) and IgA mean 105 mg/dL (50–280 mg/dL). IgD levels were normal in the 49 patients we tested (one patient initially had a slightly elevated IgD, which was normal when retested).

Treatments and outcomes

Of the 105 PFAPA patients, 72 (69%) were treated with prednisolone for at least one febrile episode. All but two patients reported that their fever resolved within 2–24 h of taking the prednisolone. The prednisolone dose was usually 1 mg/kg (range 0.25–1.4 mg/kg) and patients were instructed that if fever did not resolve, they could repeat the dose two more times at 12-h intervals. Fifty-eight patients used one dose, 13 patients used two doses and one patient used three doses. The two patients whose fever did not resolve with prednisolone used only one dose and did not want to try it again. In addition, one parent initially stated that prednisolone was ineffective; however, their child had vomited immediately after receiving the medication. At the next fever episode, prednisolone was given in small increments without vomiting and the fever resolved. Of the 70 patients who successfully used prednisolone, 50 patients used the drug routinely. In 25/50 (50%) patients, the interval between febrile episodes was shortened by 7–14 days when prednisolone was used.

A total of 26 patients were treated with cimetidine at a dose of 150 mg twice daily for a total of 6–12 months (four patients did not tolerate cimetidine because of taste). Of the 26 patients treated with cimetidine, seven (27%) reported that the fever permanently stopped following prophylactic use of cimetidine. After discontinuing cimetidine, fever recurred in one child but resolved after a second 6-month course of the drug. An additional two patients were treated with cimetidine for 6 months and had no fever while on therapy; however, fever episodes recurred when the medication was stopped and they did not respond to a second cimetidine course. Among the seven patients who responded permanently to cimetidine, PFAPA had been present for a mean of 52 months (range 14–136 months) before apparent resolution with cimetidine.

Tonsillectomy was performed (at a mean age of 56 months) in 11 patients and PFAPA resolved in all 11 of these patients (100%). There were no relapses in the group within 18 months of tonsillectomy. The mean duration of symptoms before tonsillectomy was 40.6 months (range 16–87 months). We did not refer patients for tonsillectomy, rather they were referred by their paediatricians or they were self-referred. Parents chose tonsillectomy hoping that it would resolve the PFAPA syndrome and/or because of severe recurrent tonsillitis was the prominent PFAPA symptom.

Table 3 lists the outcomes for the 105 PFAPA patients. In 21/105 (20%) patients, the PFAPA syndrome had resolved spontaneously. The mean time to spontaneous resolution of the illness was 33.2 months (range 8–92 months). In 66/105 (63%) of the PFAPA patients, the episodes were continuing when the families were contacted in the latter half of 2007. The mean duration of PFAPA in this group was 22.5 months (range 5–120 months).

DISCUSSION

We report the largest cohort of children diagnosed with PFAPA and followed in a single institution. In 1999, Thomas et al. (7) reported the clinical manifestations of PFAPA in a multicentre cohort of 94 paediatric patients. A slight majority of patients were boys (55%) and all were younger than 5 years of age at the onset of fever. Episodes of recurrent fever began at a mean age of 33 months, with each episode lasting a mean of 4.8 days. The average interval between episodes was 28 days. Associated clinical features included aphthous stomatitis (70%), pharyngitis (72%) and cervical adenitis (88%). Laboratory abnormalities, if present, were nonspecific and included leucocytosis (with a preponderance of neutrophils) and increases of the ESR during febrile episodes. Patients were reported to be healthy between episodes of fever. PFAPA resolved spontaneously

Table 3 Outcomes of 105 patients with PFAPA

	N	Mean/median length (range)
Spontaneous resolution	21/105	33/24 months (8–92)
Resolved with cimetidine	7/26	52/30 months (14–146)
Resolved with tonsillectomy	11/11	41/22 months (16–87)
Continuing PFAPA episodes	66/105	23/15 months (5–120)

in 41% of the patients after a mean duration of 54 months. Six months of cimetidine therapy was associated with resolution of PFAPA in 8/28 (29%) patients. Lastly, the syndrome resolved in 9/11 (82%) patients who underwent tonsillectomy (7). The characteristics of the patients from the original PFAPA study by Thomas et al. are similar to the characteristics of the patients in this study, except that aphthous stomatitis was less common in this study (38% vs. 70%) and that spontaneous recovery occurred earlier in this study (33 months vs. 54 months).

Differential diagnosis

PFAPA is defined by both the clinical history and physical findings. Other periodic/intermittent fever syndromes must be ruled out by history, physical findings and/or laboratory testing. The differential diagnosis of PFAPA (Table 4) includes cyclic neutropenia (8), autoimmune or inflammatory diseases (including systemic onset juvenile idiopathic (rheumatoid) arthritis (JIA) (9), Behcet's disease (10), familial Mediterranean fever (FMF) (11), hyperimmunoglobulin D with periodic syndrome (HIDS) (12), tumour necrosis factor receptor-associated periodic syndrome (TRAPS) (13), and cryopyrin-associated periodic fever syndromes (CAPS) (14–19). Two of our patients were initially thought to have PFAPA and, in both, their clinical sign/symptoms changed. One was later diagnosed with Sjogren's syndrome and the other with Behcet's disease.

PFAPA can be distinguished from cyclic neutropenia because – (i) the onset of fever in cyclic neutropenia occurs predictably every 18–24 days, but the fever cycles of PFAPA are not precise and are usually longer than 21 days; (ii) oral involvement in cyclic neutropenia may include severe stomatitis and multiple aphthous ulcers, whereas PFAPA usually has only a few lesions; (iii) neutropenia does not occur in PFAPA; and (iv) the fever in cyclic neutropenia is unlikely to resolve dramatically with 1–3 doses of prednisolone (20). HIDS is a very rare, recessively inherited disease that was first reported in children of Dutch or French descent. Disease onset usually occurs in children less than 1 year of age. Fever episodes usually last 4–6 days and may recur periodically every 4–6 weeks or in some cases sporadically. Episodes can be provoked by minor trauma or stress. Cervical adenopathy, aphthous stomatitis, abdominal pain, diarrhoea, arthralgias and/or rash (erythematous macules and papules) may occur during the febrile episodes. There is no uniformly successful treatment for

Table 4 Characteristics of periodic/intermittent fever syndromes

	Clinical characteristics	Length of febrile episodes	Periodic vs. intermittent fever(interval)	Treatment	Tests to confirm diagnosis
PFAPA	Fever with at least 1 of the following: aphthous stomatitis, pharyngitis, cervical adenitis. Well between episodes	3–6 days	Periodic every 2–8 weeks	Dramatic resolution of fever episodes with 1–3 doses of prednisone	None
Cyclic neutropenia	Fevers with recurrent bacterial infections. Cycles usually exact	3 days	Periodic every 18–24 days	Granulocyte colony-stimulating factor	Neutrophil counts and ELA2 gene mutations (genetic)
Systemic JIA	Systemically sick with prolonged fever. Rash with fever spikes	Weeks	Intermittent weeks to months apart	Respond gradually to prednisone	Usually anaemic with high ferritin
Behcet	Aphthous stomatitis without fever may be the initial sign. Systemic disease with arthritis, meningitis and iritis may be associated with fever.	Variable	Intermittent months to years apart	Specific manifestations may respond gradually to prednisone	HLA B51 in Asia (genetic) not specific
TRAPS	Fever with localized muscle pain, conjunctivitis, periorbital oedema and rash	1–2 weeks	Intermittent weeks to months apart	Gradual response to prednisone or etanercept	TNFRSF1A gene mutations (genetic)
HIDS	Fever (may follow vaccines or trauma) cervical adenitis, abdominal pain, vomiting and diarrhoea	4–6 days	Periodic every 4–6 weeks	None	Increased IgD and MVK gene mutations (genetic)
FMF	Fever usually associated with serositis (peritonitis, pleuritis or arthritis)	12–72 h	Intermittent months apart	Colchicine prophylaxis	MEFV gene mutations (genetic)
FCAS	Urticaria, arthralgias and conjunctivitis after cold exposure. Daily symptoms	12–24 h	Intermittent	None	NOD2/CARD15 gene mutations (genetic)
Muckle-Wells syndrome	Urticaria, arthralgias and conjunctivitis not associated with cold. Deafness. Daily symptoms	Days	Intermittent	None	NOD2/CARD15 gene mutations (genetic)
NOMID	Rash, meningitis and arthropathy with fever. Progressive CNS impairment. Daily symptoms	Days	Intermittent	IL-1 antagonist anakinra	NOD2/CARD15 gene mutations (genetic)

HIDS episodes (12). PFAPA can be distinguished from HIDS by the rapid a batement of fever in response to prednisone/prednisolone.

The FMF should be considered as part of the differential diagnosis of PFAPA. Padeh et al. (21) studied a group of Israeli children with recurrent fever and noted that FMF could potentially be misdiagnosed as PFAPA. This is particularly true in regions of the world where FMF is common. However, FMF can be differentiated from PFAPA because FMF patients do not respond to prednisone/prednisolone (21). Genetic testing for FMF would be diagnostic in this setting of frequent FMF.

Treatment alternatives for PFAPA

The fever episodes in patients with PFAPA usually resolve dramatically with 1–3 doses of prednisone/prednisolone (~1 mg/kg per dose). The accompanying aphthous, pharyngitis and/or adenitis may take longer to resolve. We know of no febrile syndrome other than PFAPA where fever resolves predictably with one to three doses of prednisolone. This prednisolone response is usually maintained throughout the course of the PFAPA syndrome. Families may report the length between febrile episodes becoming shorter (e.g. a 28-day cycle decreasing to a 21- to 14-day cycle). Over time with continued prednisone/prednisolone use, the shortened cycles, in our experience, may lengthen. Tasher et al. (22) reported that a single small dose of approximately 0.6 mg/kg of prednisolone usually aborts individual febrile PFAPA episodes. The same group reported that the prednisone was well tolerated, although it caused transient hyperactivity, in 16/48 (33%) children tested.

Cimetidine, an H2 blocker used to decrease stomach acid secretion, has mild immunomodulating properties. These properties include suppressing cytotoxic T cells (CD8), increasing interferon gamma production, increasing chemotaxis of neutrophils and eosinophils, increasing lysosomal enzyme release and increasing migratory inhibitory factor production (15,23). There is anecdotal experience of using cimetidine (like that of prednisone) to decrease the symptoms associated with mononucleosis (24). We previously reported three patients whose PFAPA syndrome resolved with cimetidine therapy. The cimetidine prophylaxis was prescribed for 6 months and the PFAPA syndrome did not recur when the drug was discontinued (3,5). In our collaborative study of 94 patients, PFAPA resolved in 8/28 (29%) patients who received prophylactic cimetidine (7). In this study, PFAPA resolved in 7/26 (27%) patients prophylaxed with cimetidine. It is important to point out that PFAPA may resolve spontaneously; thus, possible syndrome-ending therapies such as cimetidine may be given undue credit for ending the PFAPA syndrome.

In 1989, Abramson et al. (6) reported that four children with probable PFAPA had their illnesses resolved following tonsillectomy. In our collaborative study (7) of 94 patients, PFAPA resolved in 9/11 (82%) patients following tonsillectomy with or without adenoidectomy. Adenoidectomy alone was not effective. Tonsillectomy was performed because of severe recurrent pharyngitis associated with PFAPA. Following these initial reports (6,7), additional otolaryngology groups reported that tonsillectomy cured the PFAPA syndrome (25–29). Renko and colleagues (27) randomized 14 PFAPA patients to tonsillectomy and 12 PFAPA patients to observation without tonsillectomy. PFAPA resolved immediately in all 14 patients randomized to tonsillectomy; however, PFAPA resolved spontaneously within 6 months in the six of 12 patients who did not receive a tonsillectomy. Of the six patients with persistent PFAPA symptoms (after more than 6 months of observation), five underwent tonsillectomy and their PFAPA signs and symptoms resolved. In the present study, tonsillectomy was successful in 11/11 (100%) PFAPA patients.

There are also anecdotal reports (http://groups.yahoo.com/group/PFAPA/) of PFAPA treatment successes and failures using a variety of different immunomodulating agents, including montelukast, colchicine and thalidomide. Recent study results indicated that colchicine increased the interval between PFAPA episodes (30). No treatment modality in this group has been used extensively or studied prospectively to recommend their routine use in PFAPA.

Possible aetiologies for PFAPA

PFAPA has characteristics of both a relapsing infection and immune dysregulation (31). Patients with PFAPA do not respond to antibiotics either prophylactically or during the febrile episodes (7). Some bacterial (i.e. *Borrelia recurrentis,* brucellosis) and parasitic (i.e. malaria) infections can cause relapsing fever, but the characteristic fever cycles recur every few days, not every few weeks (as is characteristic of PFAPA). Herpes simplex virus (HSV) can cause periodic outbreaks without periodic fevers. Epstein–Barr virus (EBV) infection has, at least, on one occasion been associated with periodic fevers (32). A 13-year-old boy had 13 years of periodic fevers (maximum fever 102–104°F), lasting 2–3 days and recurring every 2–4 weeks. Accompanying the fevers were generalized adenopathy and splenomegaly. EBV was recovered from 14/15 throat cultures over the years and the patient had a persistent unusual EBV antibody response (positive VCA-IgM and negative EBNA). Ineffective therapies in this patient included acyclovir, cimetidine and Interferon-α (32). Some of our patients had received treatment with acyclovir without success. In addition, oral cultures for HSV in some PFAPA patients were negative (7,16). Testing of PFAPA patients for antibodies to HSV, CMV and EBV revealed both positive and negative results without any pattern emerging.

Results from the Thomas et al. (7) study as well as this study suggest that PFAPA is not familiar or likely to be associated with specific ethnic backgrounds. With only one exception, PFAPA did not occur in siblings of the original index cases in either study. A wide variety of geographical and ethnic groups were represented in our cohort of 105 PFAPA patients, with no particular group being overrepresented. However, children of both African–

American and Asian backgrounds were under-represented in the present study.

As stated by Long and collaborators (31), PFAPA also has features associated with immune dysregulation. Patients could have a group of cytokine-producing cells that are not always expressed but cycle based on a biorhythm (such as cyclic neutropenia) or respond abnormally to a variety of environmental exposures including common viruses.

Limitations of PFAPA studies

Our study was a clinical experience and the data were collected retrospectively. A standard panel of laboratory tests was not performed for our 105 subjects. Recurrent viral illnesses are a possible but unlikely explanation for our PFAPA patients, as six episodes or more of periodic fever with similar symptoms, and the sparing of family members, would be very unusual with recurrent viral illnesses. It could be argued that genetic testing for all the hereditary periodic fever syndromes should be performed before a diagnosis of PFAPA is made. In our study, genetically identifiable causes of periodic fever were not ruled out with testing (as genetic testing for cyclic neutropenia, TRAPS, HIDS and FMF costs more than $3000). PFAPA seems clinically distinct from the hereditary causes of periodic fever (Table 4); thus, genetic studies were part of our PFAPA case definition. A recent Italian study (33) suggests giving a diagnosis score for children with periodic fever to help determine those who need genetic testing. We are presently collaborating with the National Institutes of Health (NIH, Daniel Kastner, M.D.) and performing genetic testing, flow cytometry and cytokine determinations in a cohort of our patients with PFAPA.

CONCLUSIONS

Nonspecific viral illnesses with fever are common in childhood and may occur as often as 5–10 times per year but are not periodic. PFAPA should be considered in patients with periodic fever, when the disease is not contagious to other family members, when the patient presents with aphthous stomatitis, culture negative pharyngitis and/or cervical adenitis and when the child is well between febrile episodes. Unfortunately, no laboratory test is available to confirm the diagnosis. One to three doses of prednisone/prednisolone given at the onset of fever will generally abort the febrile episode if the patient has PFAPA. Although the aetiology of PFAPA is unknown, families with a child with PFAPA can be reassured that the fevers are not harmful and spontaneous resolution will occur over time.

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