PFAPA

Periodic Fever, Aphthous stomatitis, Pharyngitis, and Adenitis Syndrome

An Elusive Diagnosis for Common Symptoms

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DISCLOSURES

I have no disclosures to make.

OBJECTIVES

1. **Describe a case that warrants suspicion for PFAPA.**
2. **Recognize the features of PFAPA.**
3. **Prescribe appropriate treatment for patients who experience PFAPA flares.**
4. **Identify patients who might benefit from subspecialty referral.**

CASE: 10-year-old boy with fever

HPI: daily fever (102 – 104F) for 5 days

epigastric abdominal pain

oral aphthous ulcers

vomiting for 2 days (now resolved x36 hours)

saw PCP yesterday –

rapid flu and RSV negative

Rx'd amoxicillin

PMH: recurrent "fever blisters"

Meds: acyclovir; acetaminophen and ibuprofen

Social: lives with parents and 12-year-old brother

in 5th grade – doing well

CASE: 10-year-old boy with fever

Physical Exam:

Temp 102.9F

HR 135, BP 109/63

RR 18, O_2 sat 97%

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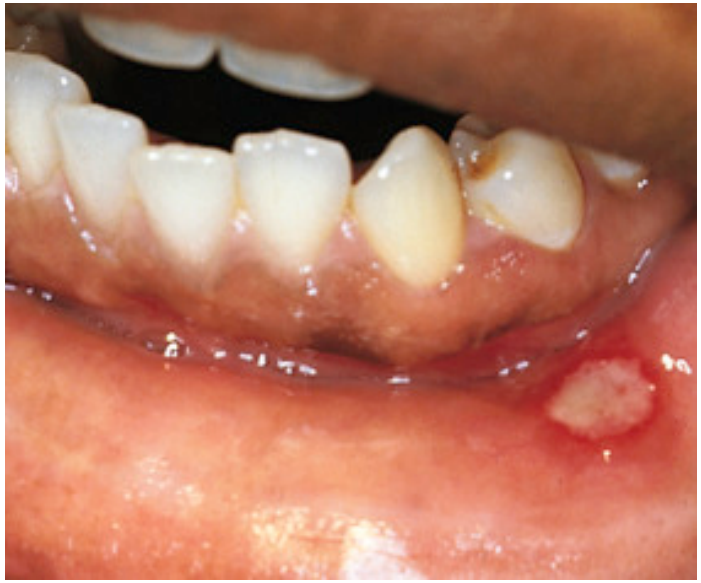
alert, nontoxic

pharyngeal erythema without exudates

oral aphthous ulcers

shotty, nontender cervical lymphadenopathy

epigastric tenderness



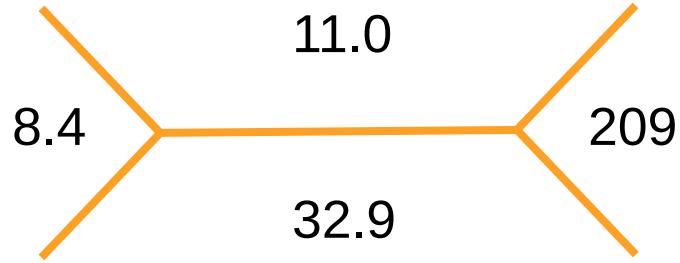
Source: *Zitelli and Davis' Atlas of Pediatric Physical Diagnosis*. 7th ed.

CASE: 10-year-old boy with fever

Rapid Strep: negative

Monospot: negative

CBC:



N 76%, L 14%, M 11%, E 0%

ESR: 58

Within normal limits: CMP, amylase, lipase, and urinalysis

DIFFERENTIAL DIAGNOSIS: Recurrent fever

- **distinct viral and/or bacterial illnesses**

- **cyclic neutropenia**
- **malignancy**
- **systemic juvenile idiopathic arthritis**
- **tick-borne relapsing fever**
- **autoinflammatory syndromes:**
  - familial Mediterranean fever
  - tumor necrosis factor receptor-associated periodic syndrome (TRAPS)
  - hyperimmunoglobulin D syndrome (HIDS)
  - cryopyrin associated periodic syndromes
  - PFAPA

PFAPA: Origins

- **first described in 1987**
- **the most common recurrent fever syndrome in children**
  - estimated 2.3 per 10,000 children under age 5 in Norway (Førsvoll, et al.)
- **autoinflammatory disorder: caused by dysregulated activation of the innate immune system**
  - antigen-independent
  - activated: neutrophils, macrophages, NK cells, TNF, IL-1, IL-12
- **no known genetic mutations**
- **no known triggers or diagnostic markers**

CLINICAL FEATURES

TIMING OF EPISODES

onset age 2 – 5 years

lasting 3 – 5 days

recurrence every 3 – 6 weeks

less frequent and less severe with age

resolution in 5 – 7 years

SIGNS/SYMPTOMS

fever (102 – 104F)

malaise

tonsillitis with exudates (but negative cultures)

cervical lymphadenopathy

oral aphthae

less common:

- headache
- abdominal pain
- arthralgia

DIAGNOSTIC CRITERIA (1999)

I. **Regularly recurring fevers with an early age of onset (<5 years)**

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**

Source: Thomas KT, et al. Periodic fever syndrome in children. *J Pediatr* 1999;135:15-21.

TREATMENT

- **prednisone 0.6 – 2 mg/kg PO x1 dose**
  - improves symptoms of each episode
  - “very effective” in 84% of patients (Wurster, et al.)
- **cimetidine 20 – 40 mg/kg/day PO divided BID**
  - symptoms less severe, but episodes more frequent
  - effective in 30 – 40% of patients (Thomas, et al.)
- **tonsillectomy**
  - resolved fevers in 98% of Finnish patients (n = 108) (Lantto, et al.)
  - less effective in other studies
- **anakinra 1 mg/kg subcutaneous**

WHEN TO REFER

- **to Immunology, Rheumatology, or Infectious Diseases:**
  - atypical symptomatology
  - family history of recurrent fevers
  - genetic testing desired

- **to ENT for tonsillectomy:**
  - 5 or more characteristic episodes of fever with no other symptoms

REFERENCES

Førsvoll J, Kristoffersen EK, Øymar K. Incidence, clinical characteristics and outcome in norwegian children with periodic fever, aphthous stomatitis, pharyngitis and cervical adenitis syndrome: a population-based study. *Acta Paediatr* 2013;102:187-92.

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QUESTIONS?