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%

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: 11.0
8.4 209
32.9
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 – 104°F)
- 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

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


QUESTIONS?