

# Periodic Fever, Aphthous Stomatitis, Pharyngitis, and Adenitis (PFAPA)

dr. leila ghasemi  
pediatric rheumatologist  
Qazvin medical university



[www.shutterstock.com](http://www.shutterstock.com) · 242568938

- ✓ Onset before 5 year old
- ✓ Male
- ✓ Autoinflammatory
- ✓ Familial predominance
- ✓ Poly genetic
- ✓ Innate immune system
- ✓ Familial cluster
- ✓ Association with FMF

# pathogenesis

- ✓ Proinflammatory cytokines
- ✓ Inflammasome-related pathway
- ✓ Tonsillar microbiome
- ✓ IL-6
- ✓ IFN- $\gamma$
- ✓ TNF- $\alpha$
- ✓ IL-12p70
- ✓ Lower IL-4

# Clinical Manifestations

- ✓ Onset before 5 year old
- ✓ clock-like
- ✓ every 28 days
- ✓ lasting around 5 days
- ✓ healthy between episodes
- ✓ normal growth
- ✓ Malaise
- ✓ chills
- ✓ fatigue

# Clinical Manifestations

- ✓ Fever
- ✓ Cervical adenitis
- ✓ Pharyngitis
- ✓ Aphtous ulcers
- ✓ Gastrointestinal symptoms
- ✓ Arthralgia
- ✓ Myalgia
- ✓ Skin rashes
- ✓ Neurologic symptoms
- ✓ Cough
- ✓ Coryza



# Adults with PFAPA

- ✓ Onset approximately at 20 year old
- ✓ Intervals between episodes 5 w
- ✓ longer period of fever
- ✓ Arthritis
- ✓ Ocular symptoms
- ✓ Headache
- ✓ Myalgia
- ✓ Overlap with other periodic fever syndromes

# Laboratory tests

- ✓ Not spesefic diagnostic test
- ✓ Lokocytosis
- ✓ ESR
- ✓ CRP

# diagnosis

- ✓ Regularly recurring fever (  $>38.3$  )
- ✓ Early age of onset
- ✓ Constitutional symptoms
- ✓ Aphthous stomatitis
- ✓ Cervical adenitis
- ✓ Pharyngitis
- ✓ Exclude :
  - ✓ Cyclic neutropenia
  - ✓ Other periodic fevers



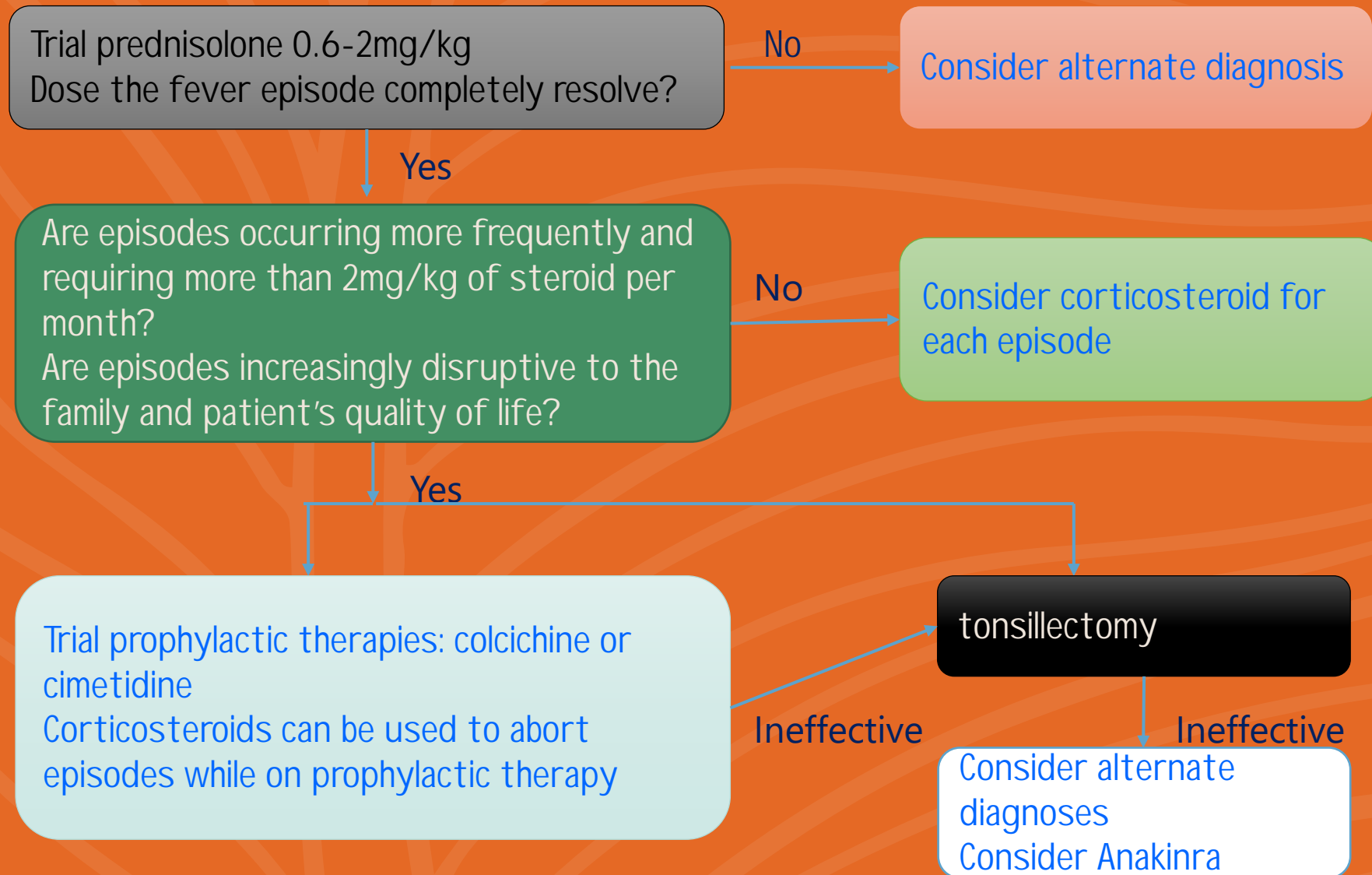
# Differential diagnosis

- ✓ Recurrent infections
- ✓ Early onset IBD
- ✓ Malignancy
- ✓ Cyclic neutropenia
- ✓ Monogenic fever syndromes

# treatment

- ✓ Corticosteroids
- ✓ Cimetidine
- ✓ Colchicine
- ✓ Montelukast
- ✓ IL-1 blocking agents
- ✓ Tonsillectomy

# Algorithm for treatment



# Outcome / prognosis

Episodes resolved after 6-10 years

**Pyogenic arthritis  
Pyoderma gangrenosum  
and Acne ( PAPA)**



- ✓ Autosomal dominant autoinflammatory
- ✓ PSTPIP1
- ✓ Overproduction of IL-1 $\beta$
- ✓ Male = female
- ✓ Onset in early childhood



# Clinical manifestations

- ✓ Constitutional symptoms
  - ✓ Pain
  - ✓ Fever not typical
- ✓ Sterile pyogenic arthritis
- ✓ Multifocal sterile osteomyelitis
- ✓ Pathergy
- ✓ Putule formation
- ✓ Sterile abscess
- ✓ Recurrent episodes of pyoderma gangrenosum
- ✓ Nodules / papules / pustules
- ✓ Cystic acne
- ✓ Psoriasis / rosacea / hidradenitis



# Laboratory tests

- ✓ Anemia
- ✓ High ESR
- ✓ Normal WBC
- ✓ Absent of autoantibodies
- ✓ Synovial fluid :
  - ✓ Cloudy
  - ✓ Seropurulent or purulent
  - ✓ High neutrophil count
  - ✓ Without microorganism
- ✓ Synovial biopsy : polymorphonuclear infiltrate
- ✓ Pyoderma gangrenosum :
  - ✓ pan-dermal neutrophilic infiltrates
  - ✓ Abscess formation
  - ✓ Matrix degeneration
  - ✓ Necrotic areas





# Laboratory tests

- ✓ Leucocytoclastic vasculitis
- ✓ Cystic acne :
  - ✓ Distended follicles
  - ✓ Cystic spaces and follicular opening filled
  - ✓ Keratinaceous debris
  - ✓ Abundant bacteria



# diagnosis

- ✓ Pathergy
- ✓ Pyoderma gangrenosum
- ✓ Severe acne
- ✓ Family history
- ✓ Genetic test



# Differential diagnosis

- ✓ Septic arthritis
- ✓ CNO
- ✓ SAPHO syndrome
- ✓ IBD
- ✓ PAAND



# treatment

- ✓ Prompt therapy
- ✓ Intraarticular steroid injection
- ✓ Corticosteroid
- ✓ Retinoid
- ✓ Anakinra
- ✓ Canakinumab
- ✓ Etanercept
- ✓ Infliximab
- ✓ Adalimumab
- ✓ Golimumab



# Prognosis

- ✓ Joint contracture / reduced mobility
- ✓ Ankylosis
- ✓ Joint destruction
- ✓ Cutaneous manifestation
- ✓ Scarring
- ✓ Pain
- ✓ Growth retardation
- ✓ Psychosocial impairment
- ✓ Depression



