CLINICAL VIGNETTE

PFAPA (Periodic Fever, Aphthous Ulcer, Pharyngitis and Adenopathies) Syndrome: A Case of Periodic Fever

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Introduction

PFAPA (Periodic Fever, Aphthous ulcer, Pharyngitis and Adenopathies) is considered the most common cause of periodic fever syndromes in pediatrics. Yet it is still commonly missed which leads to misuse and overuse of antibiotics. PFAPA is diagnosed on clinical criteria after excluding other potential causes of periodic fever. It is considered an auto-inflammatory condition that is characterized by attacks of unprovoked inflammation.

Case Presentation

A six-year-old male presents to clinic with recurrent episodes of high fever associated with sore throat, cervical adenopathy and occasionally oral ulcers. The episodes started at age 5 years with monthly episodes of fever to 39-40°C for 3-4 days associated with pharyngitis and cervical adenopathy. Some episodes included aphthous ulcers. He was treated with anti-biotics multiple times for presumed bacterial infections. Each of the episodes resolved after 4 days regardless whether or not antibiotics had been given. He was free of skin rash and arthralgia's he meets all developmental milestones. He is also fully vaccinated with unremarkable prenatal records. Physical exam during an episode was remarkable for temperature of 38.6°C small < 1 cm cervical lymphadenopathy, no mucous membrane ulcers and absence of splenomegaly. Laboratory tests include Hbg 12.g/dL, hematocrit of 38.4%, white blood cell count 12,700/mm3 and platelet count was 380,000/mm3. Inflammatory markers were elevated with C-reactive protein 3.8 mg/dL and erythrocyte sedimentation rate of 51 mm/h. Serum electrolytes, renal, and liver function tests were normal as were several cultures of blood, urine, and throat. Immune testing panels all returned within normal limits. After careful review of his history and exclusion of other diagnoses, he met clinical criteria for PFAPA syndrome. Oral prednisolone 1 mg/kg/day was prescribed for febrile episodes, with dramatic resolution of his symptoms.

Discussion

PFAPA Syndrome is a clinical diagnosis that is based on certain clinical criteria and exclusion of other diagnoses as described in Table 1.

Regularly recurring fevers with an early age of onset (<5 years of age)
Symptoms in the absence of upper respiratory tract infection with at least one of the following clinical signs: 1) aphthous stomatitis 2) cervical lymphadenitis 3) pharyngitis
Exclusion of cyclic neutropenia
Completely asymptomatic interval between episodes
Normal growth and development

Table 1.

The episodes in our case were usually associated with high fever, pharyngitis, cervical lymphadenopathy and occasionally oral ulcers. Labs during the episodes showed significant inflammatory marker elevation with negative blood, urine and throat cultures. Differential diagnoses include cyclic neutro-penia, familial Mediterranean fever, hyperglobulinemia D syndrome, and juvenile rheumatoid arthritis.[1] Cyclic neutro-penia in general begins during the first year and is characterized by an episode of fever, oral ulcers, pharyngitis, and lymphadenopathy associated with neutropenia (less than 500/mm3) occurring every 3 weeks.[2] Neutropenia has never been reported in PFAPA syndrome.[2,3] Our patient had periodic episodes of fever, pharyngitis, and lymphadenopathy, but did not have neutropenia on repeated testing. Familial Mediter-ranean fever is an autosomal recessive disease that differenti-ated from PFAPA syndrome by the familial history.[4] It is characterized by periodic fever of short time intervals, usually 2 days, and is associated with arthritis, peritonitis, pleuritis, and rash. Patients are usually of Mediterranean descent and patients usually do not respond to steroids.[4] Our patient did not have a family history of recurrent fevers, nor arthritis, peritonitis, pleuritis or skin rash. Hyperglobulinemia D syndrome is characterized by self-limiting febrile episodes with variable frequency.[5] The febrile periods usually begin in infancy and may be associated with arthritis, cervical adenitis, rash, and splenomegaly.[5] Our patient presented later in age, and did not have arthritis, rash or splenomegaly. PFAPA Syndrome is generally considered a benign condition because the affected children have no long-term sequelae. It usually resolves

spontaneously as the child get older with less frequent, less severe episodes. In conclusion, PFAPA syndrome can be diagnosed by careful history taking and the clinical findings during the febrile episodes. Therefore, it is important to recognize this clinical entity to avoid unnecessary antibiotic use and to improve control of symptoms.

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