

Research Article

Periodic Fever, Aphthous Stomatitis, Pharyngitis and Cervical Adenitis - (PFAPA) Syndrome Clinical Cases

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ABSTRACT

The periodic fever, aphthous stomatitis, pharyngitis and cervical adenitis (PFAPA) syndrome was originally described by Marshall et al in 1987 and the acronym, PFAPA, was coined two years later together with the diagnostic criteria. PFAPA syndrome is regarded as a non-hereditary disease of unknown etiology although in a small proportion of cases, one of the parents or a more distant relative had similar symptoms in childhood. The onset is generally before the age of 5 years, with attacks lasting 3-6 days, recurring every 3-8 weeks. Patients are asymptomatic between episodes. For now the syndrome is considered as a sporadic disease.

Keywords: aphthous stomatitis, pharyngitis and cervical adenitis.

INTRODUCTION

The extremely low frequency of the disease combined with its nonspecific symptoms, usually create diagnostic difficulties during the process of the discovery the infants with PFAPA syndrome. In most of the cases children have been treated by their general practitioners with for diseases like acute viral infections, recurrent angina, recurrent pharyngitis, aphthous stomatitis etc., and for the insufficient treatment results is accused the low immune status of the child. Usually PFAPA is diagnosed during the serial exam by a specialist pediatrician, after rejecting the previous diagnoses. The aim of this study is to provoke the pediatricians to think about PFAPA in all cases with periodic fever, aphthous stomatitis, pharyngitis and cervical adenitis because it's on time diagnosis may save the child a lot of unnecessary tests, consultations, hospitalizations and antibiotic courses

Clinical criteria for diagnosis

In spite of the absence of strictly specific diagnostic markers, the clinical signs the diagnosis depends on are:

Periodic fever – every 3-4 weeks;

Tonsillitis with exudation and negative microbiological findings;

Cervical adenitis;

Aphthous changes in the oral cavity;

Absolute health between the disease attacks;

Quick effect from steroids – one shot dose;

PFAPA is diagnosed after exclusion of: respiratory infections; recurrent neutropenia, monogenic essential fevers and immune system deficit conditions, Behcet and

Crone diseases. The procalcitonin exploration may reject bacterial infection^{8,9}.

Laboratory tests

Laboratory tests of the children who suffered from PFAPA are absolutely normal between the attacks of the disease. By the time of the attacks laboratory results changes as follows:

Increased inflammatory markers - accelerated ESR, CRP - up to 196 mg/l.

Microbiological tests do not show any pathogenic microorganisms from throat, urine and blood.

Aminotransferases and all others biochemical parameters are normal.

Immunological tests

normal immunoglobulin quantity.

PFAPA Treatment

After PFAPA is been diagnosed, the treatment is carried out with:

Steroids – 1-2 mg/kg one shot dose.

Cimetidin – suppresses CD8-Ly – unclear mechanism, effectiveness under 30%.

Colchicine – 0, 5 - 1mg. per day – partial remission with fever episodes frequency reduction if it is taken for a long period.

Anakinra – prevents the interleukin-1 connection with its receptor.

Тонзилектомия – invasive but effective method in cases with steroid therapy failure.

N.B. However surgical treatment of PFAPA cases is not 100% effective too – in some cases fever episodes peculiar to PFAPA continue to emerge, but even in that cases lowering the fever episodes frequency and their burden is detected.

Clinical Cases

We present two clinical cases of PFAPA diagnosed in our hospital.

Clinical case No 1- We present a five year old girl, with periodic fever episodes since 2 years of age, with recurrences every 2-3 weeks and duration 3-5 days, accompanied by clinical manifestation of stomatitis, cervical adenitis and pharyngitis. The child had been taken multiple times into different hospitals with similar complains. The multiple antibiotic treatments which had been carried out had no effect upon the normal course of the disease.

Clinical findings

I. Episodes- Recurrent fever episodes – temperature up to 39 – 40° C since 2 years of age, with recurrences every 3 weeks with duration 3–6 days;

Aphthous changes in the oral cavity;

Pharyngitis and tonsillitis with exudation often with coatings;

Cervical lymph nodes extension during the fever episodes; Sometimes fever episode is accompanied with vomiting and pain in the stomach;

Between episodes – healthy child.

Laboratory tests

During the fever episodes

Increased inflammatory markers – accelerated ESR, CRP-up to 196 mg/l.

Microbiological tests do not show any pathogenic microorganisms from throat, urine and blood.

Aminotransferases and all others biochemical parameters are normal.

Immunological tests – normal immunoglobulin quantity, without distinguished deviations in the lymphocyte subpopulations.

Between episodes – normal test results.

Before the right diagnose discovery a lot of tests and consultations with various specialists had been carried out and a treatment with antibiotics had been applied along with symptomatic treatment.

Treatment after PFAPA had been diagnosed

Steroids 1-2 mg/kg – one shot dose, and if it is necessary additional applications – they have quick effect upon the fever but the frequency of the fever episodes is detected.

Colchicine 2 x 0, 25mg. daily dose – no significant therapeutic effect.

After consultation with pediatrician, ENT specialist and anesthesiologist considering the insufficient conservative treatment effect a decision for surgical treatment was taken. At 28 04 2015 year in the ENT Department of UMHAT “St. George” Plovdiv, under general anesthesia tonsillectomy and adenoidectomy was carried out. The surgery proceeded with no complications. Smooth postoperative period. The child was discharged at the third day after surgery with no fever in a good condition. Fifty days after surgery the child had a fever episode again

which was treated successfully with antipyretics only and the temperature levels do not reached more than 38,5°C. The fever episode was with two days duration. The next few postoperative months showed slight decrease of the frequency of episodes with fever, stomatitis, cervical adenitis and pharyngitis, with vastly decrease of their burden, easily treated with antipyretics only.

Clinical case No2: We present a five year old boy, with complains started 6 months after birth – episodes of high fever (up to 41°C), accompanied by severe redness of the oral cavity and throat, purulent coatings at the tonsils and cervical lymph nodes extension. The complains duration is about three days and they fade away spontaneously, no matter if antibiotic treatment is administrated or not. The child had been taken multiple times into different pediatric departments and treated for pneumonia and angina.

Clinical findings

Episodes

Recurrent fever episodes with temperature up to 41°C since 6 months of age, with recurrences every 30-40 days and duration 2-3 days;

Discreet aphthous changes in the oral cavity;

Pharyngitis and tonsillitis with exudation often with coatings;

Bilateral cervical lymph nodes extension during the fever episodes;

Between episodes – healthy child.

Laboratory tests

I. During the fever episodes

Increased inflammatory markers – accelerated ESR, CRP, Leucocytosis.

Microbiological tests – during the hospitalizations from the patient's throat *Pseudomonas Aeruginosa* and *Str. Pneumoniae* was isolated;

Aminotransferases and all others biochemical parameters are normal.

Immunological tests – normal immunoglobulin quantity, without distinguished deviations in the lymphocyte subpopulations.

Between episodes – normal test results.

Treatment after PFAPA had been diagnosed

In two fever episodes an antibiotic treatment had been administrated, because the main disease (PFAPA) was accompanied by additional bacterial infection which caused worsening the patient's condition and prolonged fever episode and pharyngeal complains. All other fever episodes were easily treated with antipyretics only, with no need of steroid or any other therapy. After consultation with pediatrician and ENT specialist decided in that case to undertake wit and see behavior because of the mildness fever episodes and the tendency of spontaneous recovery. Through the last three months the child had just one mild fever episode with two days duration, treated successfully with only three administrated doses of antipyretics.

DISCUSSION

PFAPA is described as a representative of the auto inflammatory diseases group, but until now the exact etiology of the syndrome remains mystery. Some genetic disorders are discussed but which genes or proteins are part

of the cell signals and metabolite path of the disease activation remains unclear. The immune deregulation of the congenital immunity is possible to be provoked by an infection - high levels of gamma interferon are found, TNF, IL6, IL 1,18^{9,10}. The vast differential diagnosis of the disease leading to many interdisciplinary consultations, as well as large number of tests necessary for the rejection of similar diagnoses lay at the bottom of the late syndrome diagnosing. The interdisciplinary approach is necessary not only for diagnosing but also for treating the patients especially in cases when decision for changing the conservative therapy with surgery must be made. The comparison between the different treatment methods showed that adenoidectomy and tonsillectomy is more effective method than antibiotic and cimetidine therapy, and is as effective as steroid therapy¹¹.

CONCLUSION

Knowing the symptom and it's on time diagnosis may save the child a lot of unnecessary tests, consultations, hospitalizations and antibiotic courses and may make the life of the whole family better.

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