MARSHALL'S SYNDROME OR PFAPA. CASE REPORT

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Abstract: *PFAPA is a chronic condition, typically starting after 2 years old, in which fever occurs periodically (lasts for 3-7 days), accompanied by aphthous-like ulcers, pharyngitis and/or cervical adenitis (cervical lymfadenopathy).The patients have no clinical symptoms between episodes and it is required to exclude all other diseases (a Streptococcus infection) before confirming the diagnosis. The dramatic response to the treatment helps diagnosing PFAPA. We are presenting the case of a 17-month-old male patient, with the personal history of recurrent episodes of fever (onset at the age of one), who constantly received antibiotherapy. On the first examination of the patient in our service (at the age of 17 months) he presented hyperpyrexia and dysphonia; physical examination showed pharyngeal tonsils congested with hyperemia, white patches on the bilateral tonsils. Laboratory investigations performed at that time revealed leukocytosis with lymphomonocytosis. Suspicion was raised on infectious mononucleosis, but it was without serological confirmation. The child received only antipyretic treatment with favourable outcome (the patient had no fever after three days of evolution). Subsequently, the patient presented other 5 episodes of fever which disappeared after one dose of steroids. After 4-5 hours the fever disappeared. Physical examination showed pharyngeal congestion, the throat swab being constantly negative. The particularity of the case lies on the onset of the syndrome PFAPA onto a very small patient.*

Cuvinte cheie: *sindrom Marshall, febră recurentă, copil*

Rezumat: *PFAPA este o boală cronică cu debut după vârsta de 2 ani, manifestându-se cu febră periodică (durata 3-7 zile) acompaniată de afte, faringită şi adenopatie. Pacienţii sunt asimptomatici între pusee, impunându-se excluderea altor afecţiuni (infecţia streptococică) înainte de confirmarea diagnosticului. Răspunsul la tratament confirmă diagnosticul. Prezentăm cazul unui băieţel în vârstă de 17 luni cu febră recurentă (debut la 1 an) primind constant antibiotice. La prima evaluare în serviciul nostru (17 luni) acesta prezenta hiperpirexie şi disfonie; examenul obiectiv a evidenţiat congestie faringiană cu depozite albicioase amigdaliene; investigaţiile au relevat leucocitoză cu limfo-monocitoză. S-a suspectat mononucleoza infecţioasă, fără confirmare serologică. Sub antitermice evoluţia a fost favorabilă (afebrilizare după trei zile). În evoluţie pacientul a prezentat 5 episoade de febră ce a remis prompt după steroizi po doză unică. Examenul obiectiv a evidenţiat congestie faringiană, exudatul faringian fiind constant negativ. Particularitatea cazului: vârsta mică de debut a bolii.*

INTRODUCTION

PFAPA is a syndrome that consists of recurrent episodes of fever, sore throat, mouth sores and swelling of the glands in the neck.(1) Occasionally, there also may be exudates (white patches on the tonsils).(2) The frequency of PFAPA is not known, but the disease appears to be the most common recurrent fever syndrome that does not come from an infection.(3) Both males and females and all ethnic groups can develop PFAPA. PFAPA usually starts in early childhood between the ages of 2 to 5 years old.(4) No gene defect has been found in PFAPA yet, although sometimes more than one family member has the disease.(5) No infection has been found in PFAPA and it is not a contagious disease (6), although fever episodes are associated with elevated erythrocyte sedimentation rate, C reactive protein and leukocytosis.(7) It is an autoinflammatory disease.(8) In cases without classic presentation it may be necessary to exclude other cases of recurrent fever (9) (recurrent tonsillitis, a number of infectious diseases, juvenile idiopathic arthritis, Behçet's disease, cyclic neutropenia, familial Mediterranean fever (FMF), and, finally hyperglobulinemia D syndrome.(10) The disease may last for several years but it usually resolves by itself in the second decade of life. In time, the period between the episodes will increase. Children with PFAFA continue to grow and develop normally. The use of the steroids at the start of an episode might stop it and it might shorten the time till the next episode, too.(11) The fever usually does not respond well to acetaminofen or nonsteroidal antiinflammatory drugs ibuprofen.(12) Medication like cimetidine and colchicine, when used regularly, may prevent future episodes to about a third of the children.(13) Several studies have found that a tonsillectomy might cure PFAPA.(14) The episodes may affect the quality of the child's life and their family by being absent from school.(15)

CASE REPORT

The authors present the case of a-17-month old patient, urban, who was admitted in Polisano Medical Centre Sibiu (Tălmaciu) with fever and moderate dysphonia (his mother said that the boy was dysphonic almost all the time).

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Patient history: he was born after a normal pregnancy that lasted 9 months; he is the only child of their family, he weights=3995 g, 57 cm birth length, Apgar=9, physiologic jaundice, discharged at 3 days from the maternity hospital. He was breast fed for 5 months, the diversification was correctly made at 5 months, the baby feed on breast was stopped at 13 months and now, he eats with adults sitting at table.

Family history: maternal grandfather with diabetes type II (without episodes of recurrent fever in his family). Personal history: the patient was admitted at 6 months old for diarrheal, he had bronchiolitis at 11 months old and 5 episodes of pharingolaringitis (each episode at 4-5 weeks starting at when he was 1 year old). For these episodes of pharingolaringitis, the boy received dexamethasoneteraphy i.m. and antibiotheraphy. It is interesting to notice that, after 3-4 hours of corticoteraphy administration, the fever disappeared even before the patient received antibiotic. Immunoprophylaxis was complete (the last vaccine at 15 month-ROR). Prevention of rickets: was correct: 2 drops/day Vigantol Oel. Motor and mental skills according to age. Weight development was good: 2995g (birth), 7400g (6 month), 11000g (now). The consulting in our service was occasioned by the fever recurrence at the end of 7 days of oral Keflex therapy associated with antitermics and steroids. The physical examination shows good general condition, the state of consciousness preserved, hiperpirexia, normal nutritional status (weight=11Kg), pale skin and mucouses, rash disseminated at the neck and upper chest, normal subcutaneous tissue, no lymph nodes enlargement, skull bossing, punctuate bregmatic fontanelle, tachycardia (hyperpyrexia), the examination of the respiratory apparatus, cardiovascular urogenital tracts and central nervous system were normal (exception: moderate disphonia), gastro-intestinal tract: congestion of pharynx with white spots on the tonsils bilateral, no hepatomegaly, no splenomegaly.

Investigation was performed, as follows:

- complete blood count (CBC) revealed leukocytosis (WBC=24.810/mmc) with lymphocyte and monocyte predominant pattern (Ly=40,7%, Mo=19,8%), haemoglobin level=11,5g/dl, MCV71,1fl
- inflammatory status: moderate raise of ranges for „C" reactive protein(CRP=1,19mg/dl; normal value=0.5).
- iron blood level: low
- normal glycaemia, calcemia, and phosphate blood level
- normal transaminases
- infectious status: Ac IgM-Vca anti Epstein-Barr negative, negative results for uroculture
- from an immunological point of view: normal IgA and IgG, IgM rise at 249mg/dl.
- normal urinary status

Treatment and evolution:

The child received only antipyretic (acetaminofen and ibuprofen); the fever disappeared after 3 days. After 1 month, he came over in our service presenting fever; physical exam showed pharynx congestion. The step throat exam was negative. In the suspicion of PFAPA context, a prednisontherapy was initiated (1 mg/b.w one administration) but his mother refused to give the child this therapy (fear of adverse effects). The patient received no antibiotic (throat swab was negative), just antipiretycs (like at the former episode) and fever disappeared after 3 days. At the 3-rd episode of fever with pharynx and tonsils congestion (white patches on the tonsils), his mother accepted prednisonteraphy and, with no antipyretic, the fever disappeared 5 hours later. At the 4- and 5-th episode of fever with pharingitis, the patient received Dexametazona (0,6 mg/w.b. one administration) and the fever disappeared after 4 hours(the throat swab was negative).

CONCLUSIONS

1. In case of recurrent fever onset under 5 years old, appearing each 3-8 weeks and lasting for 3-7 days in association with at least one of the following: pharyngitis, aphtuous- like ulcers or cervical lymfadenopathy, we must take into account the possibility of PFAPA.
2. Not every febrile episode in childhood must receive antibioteraphy.
3. There is no specific laboratory test for PFAPA. Diagnosis is based primarily on history, physical examination and therapeutic trial (fever disappeared after one single dose of steroids).
4. It is important to exclude all other diseases with similar symptomatology (Specially Streptococcus infection) before confirming the diagnosis.
5. The particularity of the case lies on the onset of the syndrome in a very small patient.

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