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PFAPA syndrome

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PFAPA syndrome (Periodic Fever, Aphtous Stomatitis, Pharyngitis and cervical adenits) is a clinical entity of inflammatory origin. It is characterized by periodic fever, with one or more of the following clinical manifestations: oral aftosis, erythematosus or exudative pharyngeal tonsillitis and latero-cervical lynphadenitis .

These episodes are different from normal recurrent infectious of early life because: they show up while in full well-being state, there is absence of clear signs of high respiratory tract infection, they are characterized by regular frequency, the relative symptoms tend to disappear and they have poor response to antibiotic therapy.

The most important hypothesis is that PFAPA is a minor disorder of inflammatory control mechanism that shows up only in the early years of life also in relation to lymphatic tissue hypertrophy.

Recently, PFAPA has been classified as an autoinflammatory syndrome but the prognosis of PFAPA SYNDROME is always good and there is no tendency to amyloidosis. The frequency of PFAPA syndrome is much more common than one can imagine. It is currently estimated that its incidence is 4 cases / 10.000 children per year. It seems like there is an underlying disorder of the immune system characterized by a continuous activation of proinflammatory cytokines with the simultaneous suppression of the anti-inflammatory response. It shows up more frequently in the early years of life mostly in men. The disease usually occurs within the first 5 years of life and it is characterized by recurrent episodes of high fever for 3-6 days, with regular inter-critical periods. Febrile episodes are generally very responsive to oral steroid therapy.

Diagnostic criteria for PFAPA syndrome (Marshall et al. 1989, mod Thomas et al.,1999)

o Feverish episodes with a debut before 5 years of life o Essential symptoms, in the absence of high respiratory infections with at last one between:

o Apthous Stomatitis (70%)
o Cervical adenits (88%)
o Pharyngitis (72%)

These features could also be added to the positive and quick (3-6 hours) fever response to a single dose of corticosteroids. From the laboratory point of view, only a rise in the index of

flogosis occurs during the fever episode that promptly become negativized during inter-critical periods (homochromous is found to be mild leucocytosis and a moderate elevation

of VES and PCR.)

Hematopoietic chemistry is therefore useless in typical forms. Only cortisone (prednisone and methylprednisone) may be used on the therapeutic side. At doses of 1 mg / kg die of metiprednisone or equivalent steroid for 1-2 days a rapid response is achieved not only on fever but also on overall well-being and baby's appetite, and in addition to these doses the metabolic side effects of corticosteroids are insignificant.

Paracetamol and ibuprofen have poor therapeutic efficacy. The administration of antibiotics is absolutely useless. There are studies on the use of cimetidine and colchicine that demonstrate the therapeutic ineffectiveness. The colchicine is used only for the Mediterranean family fever for the prevention of amyloidosis.

On the specialist Otorinolaryngologist side, in addition to medical diagnosis and therapy, tonsillectomy may be considered when it is difficult to handle, since it is effective in interrupting or drastically reducing feverish recurrence in the vast majority of cases (in recent Italian case studies tonsillectomy proved effective in about 80% of the cases). Irrespective of the absence of controlled randomized trials, Tonsillectomy may be proposed anyway, even if the National Health Guidelines Plan of the Ministry of Health does not recognize this indication. In this regard, we have outlined Recommendations II-V / D and VI / D for the PFAPA syndrome (Guideline 15 of March 2008).

In very rare cases where cortisone administration and tonsillectomy are not feasible for the coexisting serious pathologies of the young patients, the use of anakinra (commercial name Kineret ampicillin 100mg) is permitted. Anakinra is a recombinant form of IL-1Ra, an endogenous antagonist that binds to IL-1 receptors and inhibits pro-inflammatory effects of IL-1. By subcutaneous administration, anakinra has a high bioavailability (95%) and reaches maximum plasma levels in 3-7 hours.

Regarding the prevention, there are a studies on the efficacy of Pidotimod in association with bacterial ligation in the treatment of PFAPA syndrome.

The message that the ORL specialist has to communicate to the parents of afflicted young patients affected by PFAPA has to be simple and clear:

o good prognosis (does not interfere with growth and the disease is not chronic); o adequacy of immune defense against pathogens (not an immunodeficiency); o the disease is not contagious;

o treatment is only symptomatic and does not heal;
o a simple analysis of the cost-benefit ratio of therapies.

Bibliography

Atas B, Caksen H, Arslan S, et al. PFAPA syndrome mimicking familial Mediterraneanfever: report of a Turkish child. J Emerg Med 2003;25:383-5.

Caorsi R, Meini A, Cattali M, et al. Low specificity of current diagnostic criteria forPFAPA syndrome Time to change? Clin Exper Rheumatol 2008;26:214.

Dahn KA, Glode MP, Chan KH. Periodic fever and pharyngitis in young children:a new disease for the otolaryngologist? Arch Otolaryngol Head Neck Surg 2000;126:1146-9. Galanakis E, Papadakis CE, Giannoussi E, et al. PFAPA syndrome in children evaluated for tonsillectomy. Arch Dis Child 2002;86:434-5.

Gattorno M, Sormani MP, D'Osualdo A, et al. A diagnostic score for molecularanalysis of hereditary autoinflammatory syndromes with periodic fever in children.Arthritis Rheum 2008;58:1823-32. Hofer MF. Cured by tonsillectomy: was it really a PFAPA syndrome? J Pediatr2008;153:298.

Licameli G, Jeffrey J, Luz J, et al. Effect of adenotonsillectomy in PFAPA syndrome.Arch Otolaryngol Head Neck Surg 2008;134:136-40.

Parikh SR, Reiter ER, Kenna MA, et al. Utility of tonsillectomy in 2 patients with the syndrome of periodic fever, aphthous stomatitis, pharyngitis, and cervical adenitis. Arch Otolaryngol Head Neck Surg 2003;129:670-3.

Renko M, Salo E, Putto-Laurila A, et al. A randomized, controlled trial of tonsillectomy in periodic fever, aphthous stomatitis, pharyngitis, and adenitis syndrome. Tasher D, Somekh E, Dalal I. PFAPA syndrome: new clinical aspects disclosed.Arch. Dis Child 2006;91:981-4.

Tasher D, Stein M, Dalal I, et al. Colchicine prophylaxis for frequent periodic fever, aphthous stomatitis, pharyngitis and adenitis episodes. Acta Paediatr2008;97:1090-2. Wong KK, Finlay JC, Moxham JP. Role of Tonsillectomy in PFAPA Syndrome. ArchOtolaryngol Head Neck Surg 2008:134:16-9.

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