PARTICULARITIES IN THE CHILD CHRONIC RHINOSINUSITIS

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ABSTRACT

Chronic rhinosinusitis is a rare pathology in pediatric pathology versus adult patients. Clinical manifestations are related, on the one hand, with the anatomical particularities and, on the other hand, with the immune response correlated with the age of the child. Allergy is the main cause in 50% of child rhinitis, 40% of them debuting early until the age of 6 years. The clinical expression of allergic rhinosinusitis in children can sometimes be accompanied by comorbidity manifestations or complications. Impaired mucociliary clearance can be induced by other rare pathological situations that produce mucus rheology modification, as in cystic fibrosis (CF). Through, the clinical heterogenicity of expression is in relation, on the one hand, with immunogenic response and anatomical particularities relative to age of the child, and secondly with the diversity of inducing factors (from very frequent like allergy to the least frequent, CF). It requires a correct diagnosis, early and appropriate treatment by a multidisciplinary team collaboration.

Keywords: rhinosinusitis, child, cystic fibrosis, allergy

Chronic rhinosinusitis, defined as chronic inflammation of nasal mucosa and paranasal sinuses lasting more than 3 months is a rare pathology in pediatric pathology versus adult patients, but recognizes a variety of causes that can sometimes constitute diagnostic pitfalls. In the US, 30 million adults are diagnosed annually with rhinosinusitis, but only 15% develop chronic rhinosinusitis vs. 0.5-5% of children who are diagnosed with acute rhinosinusitis, and of these only a small part will develop chronic rhinosinusitis (1). The most commonly affected in small children and infants are the ethmoidal sinuses and maxillar sinuses, and after 6 years of age- sphenoidal and frontal sinuses. In fact, the clinical manifestations are related, on the one hand, with anatomical particularities and, on the other hand, the immune response correlated with the age of the child. Infants frequently express the aspect of persistent rhinorrhea or recurrent disease after upper respiratory tract infections (most often otitis, nasopharyngitis, laryngitis), with or without purulent conjunctival secretion as an expression of ethmoidal injury. The clinical picture is slightly contoured in preschool children (3-6 years) with chronic nasal obstruction and persistent runny nose that draws attention, with or without tonsillar hypertrophy, lymph node swelling and/or serous otitis sometimes. At older ages, the patient may present somewhat more frequently nonspecific symptoms such as chronic frontal headache, sleep disorders (obstructive sleep apnea) associated with irritability and/or daytime sleepiness, hyposmia, chronic cough, breathing on the mouth, dry mouth sensation, dysphagia, nocturnal snoring and nasal secretion. The core of the pathogenic mechanism triggered by a variety of factors is essentially the altered mucociliary clearance by inflammation of the sinuses. Consequently, there will be blocking in

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sinus ostium and drainage alteration with secondary respiratory secretions and stasis. Injuried ciliary epithelium has the effect of inducing secretion retention, bacterial superinfection – an aspect that creates the conditions and persistence of inflammation, thereby closing a vicious circle.

Etiological palette involved in chronic rhinosinusitis of the child are from the most common (infection, allergy, gastro-oesophageal reflux), to the rarest, as well as anatomical defects (velo-pallatine cleft, deviated septum etc.) or systemic causes (cystic fibrosis, ciliary dyskinesia, immune deficiencies etc.). Allergy is the main cause in 50% of child rhinitis, 40% of them debuting early until the age of 6 years. The incidence of chronic rhinosinusitis appreciated in a group of 4,044 children aged 8-9 years consulted in ENT department of Children's Hospital Boston (USA) in 10 years was 53.8%, of which 26.9% were associated allergic rhinitis (2). Allergic sinusitis is rarely described in children vs. adult, a small percentage (5-10%) of children aged less than 5 years being diagnosed with fungal sensitization (Bipolaris, Drechstera, Helminthosporium, Fusarium, Aspergillus spp) (3). Consequently, the child frequently has the expression of allergic rhinosinusitis, more often than a simple sinusitis. The risk for atopy is appreciated up to 40% if one parent is allergic, and up to 80% if both parents are affected. Although so far no genetic variant showed a constant association with allergic rhinosinusitis, involving genetic polymorphism, however, they have been described in relation to some HLA genes triggering pollen allergy. Regarding the pathogenic activation of TH2 via immune signals with specific cytokines (IL-4, IL-5, Il9, IL13), and the switch from Th1 to Th2 in certain immunogenic circumstances, allowed the identification of other trigger factors, in addition to those already known, as the allergy (allergens, drugs, foods) as well as viral or bacterial infection, exercise, endocrine factors (4). Therefore, the clinical expression of allergic rhinosinusitis in children (sneezing, rhinorrhea, itching and nasal obstruction) can sometimes be accompanied by comorbidities of allergic asthma (40-50% of cases), allergic conjunctivitis, gastroesophageal reflux, atopic dermatitis or complications in upper respiratory tract situses (serous otitis media, tubal dysfunction, adenoid hypertrophy, chronic tonsillitis, laryngitis, nasal polyposis) (5).

The correct diagnosis of allergic rhinosinusitis suggested by eosinophils in the nasal secretion, and eosinophils/PMN percentage, supported by allergy tests (specific IgE, total IgE, skin prick test) in conjunction with the examination of ENT (rinomanometry) and imagistic investigations (radiography or, ideally, tomography of the sinuses). Usually, the nasal biopsy is not a routine procedure, but immunohistochemical determination of eosinophilic cationic protein along with neutrophilic elastase dosage may clarify the type of inflammation. On the other hand, histopathology associated with bacterial tests can objectify allergic fungal mucin (Mucor mycosis), useful for the diagnosis of allergic fungal sinusitis (6). Framing the correct diagnosis, taking into account ARIA guide for allergic rhinitis enables individualized treatment, that minimizes complications which may arise in the evolution of these patients-obstructive sleep apnea, chronic nasal obstruction, anosmia, headache, pharingeal chronic irrittation or severe risk evolutive complications, as a consequence of secondary bacterial infection – orbital cellulitis, cavernous sinus thrombosis, brain abscess, osteomyelitis, meningitis, sepsis. Allergic rhinosinusitis treatment is actually the same with allergic rhinitis and has its aims like the control of the symptoms, improving the child quality of life, without altering the functional skills, as well as preventing complications. The means to treat these patients are represented by associating optimal therapeutic efficacy with control over the patient's living environment, and pharmaceutical specific immunotherapy (modulating immune response through IL10 to IgG4 synthesis). Controller pharmacological treatment is based on topical corticosteroid nasal administratrion, with or without antihistaminic agents (nasal or oral), leukotriene modifiers and/or nasal chromone therapy (7).

However, alteration of mucociliary clearance can be induced by other rare pathological conditions which cause the modification of the rheological properties of mucus, making it difficult to eliminate, such as in cystic fibrosis (the viscosity of mucin is 30-60 times greater by altering the transport of Na and Cl ions and water), or alteration of kinetics of cils, in primary ciliary dyskinesia or Kartagener syndrome. Cystic fibrosis (CF), although it is cited as the most frequent abnormality monogenic autosomal recessive transmitted in the Caucasian population in Central Europe (1/2,000-1/2,500 births), yet it is rarely mentioned in the etiology of chronic rhinosinusitis of the child, if not associating specific and systemic symptoms or superinfection (pseudomonas aeruginosa). Segal et al (8) estimated that CF was diagnosed in 1/16 patients examined for nasal polyposis. In fact, it appears that only 10% of children with CF express clinical signs of chronic rhinosinusitis, raising the

question what happens to the other 90% of the patients – are they clinically asymptomatic or have adapted to their symptoms by tolerating forms of from mild or moderate rhinosinusitis (9). In particular, 6-67% of these patients can develop sino-nasal polyposis in chronic evolution of the disease. Out of these cases, 19% are diagnosed endoscopically until the age of 6 years old and 45% up to 18 years (10). Chronic polyp expansion gives a particular phenotype, with enlarged base of the nose, hypertelorism, predominance of chronic nasal obstruction, headache and facial pain. Another feature of chronic rhinosinusitis in CF are mucocel formation by deposition of thick mucus in the sinuses. If they reach a considerable size they can even affect facial area with unilateral swelling or pseudotumoral aspect. Mucocels can be objectified with specific imagistic methods, such as radiography or CT scan. About 12% of children with CF may develop medial swalling of the sinus wall, as well as secondary mucocel of the maxillary sinus (11). On the other hand, more than 90% of CF patients presented sinus imaging with opacification, especially in those F 508 homozygote individuals, as well as poor pneumatisation and hypoplasia of the sinus (12,13). Frequently, adolescents with CF dont have frontal sinus pneumatisation, which can indicate the suspicion of disease and atypical forms of CF manifestations, or as CFTR-related disease (chronic rhinosinusitis bronchopulmonary aspergillosis, idiopathic bronchiectasis). In conclusion, CF (atypical form) can be expressed as refractory chronic rhinosinusitis, with normal or slightly elevated iontophoresis values between 40-60 mmol/l, a situation which requires genetic investigation (usually 38 mutations) (14). Raman V et al (15) identified 12% carriers of a single mutation CF in a study of 58 children with rhinosinusitis. Sinus bacterial superinfection is common in chronic rhinosinusitis. The ideal microbiological diagnosis is performed in an invasive manner, considering the fact that differences between pathogens were reported in the same patients, as well as different colonisation in sinuses of the same patient. Bacterial etiology in these cases is suggestive and sometimes particular to the patient with chronic rhinosinusitis vs FC – Pseudomonas sp (65%), nontypable H. influenzae (50%), anaerobes (Peptostreptococcus, Bacteroides sp, 25%), s. Aureus, Burkholderia cepacia, Achromobacter xylosoxydans, sternotrophomonas maltophylia. However, in 33% of cases of CF associated chronic rhinosinusitis there were reported positive fungal cultures (16). Given these features, the management of CF and chronic rhinosinusitis is complex and it aims eliminating chronic obstruction by secretion drainage, airway inflammation control, effective treatment in associated infections, nutritional and immunological support. So the pathogenic treatment with alpha dornase will combine respiratory physiotherapy and antibiotics in microbiologically proven specific situations, especially local therapeutic actions. Dornase alfa (Pulmozyme, rh-DNAse) administered by nebulization improves the rheological properties of mucus by decreasing its viscosity, thereby having an anti-inflammatory effect and improving ciliary clearance, reducing the risk of infection (17). Antibiotic therapy of chronic rhinosinusitis is intensely debated today especially for the inhaled form of administration. Although there are studies that support the beneficial role of certain inhaled antibiotics as tobramycin (Tobi), Colistin, Aztreonam, yet still are not enough evidence to support their effectiveness in chronic rhinosinusitis with polyposis of FC patients (18). Consequently, systemic antibiotic therapy lasting 3-6 weeks remains the recognized treatment in these cases. Among described antibiotics, macrolides and quinolones, as well as IL8 agents mediating anti-inflammatory effect have demonstrated to decrease the size of polyps (19). Immunoprophylaxy vaccines and supporting those with immune deficiency (associated with administration of intravenous immunoglobulin) should be considered in these patients. Additional conservative therapeutic measures have improved the prognostic score. It can be used saline lavage 0.9% or hypertonic 3%, having an decongestant effect (20), with or without other nasal decongestants (oxymetazoline, xylometazoline, phenylephrine etc.) within one week (depending on risk in prolonged use), but unfortunately without direct effect on the maxillary and ethmoidal sinus. Topical nasal corticosteroid therapy (betamethasone) proved its efficiency by decreasing polyp size perhaps by having anti-inflammatory effect (21), although it remains controversial in systemic (short course) therapy in combination with antibiotics. NSAIDs (ibuprofen) appears effective in patient with compromised lung function, but at higher doses, which induce some risk of side effects (22). Dornase alfa therapy decreases the risk of recurrence after polyp surgery, sustaines anti-edematous effect and thereby decreases the necessary for invasive rhinosinusal procedures (23). Approximately 3% of patients with CF and chronic rhinosinusitis associated with polyps require surgical treatment, as 10-20% of those are non-responders to medical treatment (18). In particular, those are patients whose quality of life is

deeply disturbed by facial pain or headache, as in severe chronic rhinosinusitis directly correlated with decreased lung function, especially before lung transplantation (24). CF therapeutic perspectives are represented by the use of modulators of CFTR for targeted groups of patients selecting a particular type of mutation, possibly efficient also in chronic rhinosinusitis (Ivacaftor VX-770 for the mutation G551D, Lumacaftor VX-809, Ataluren-PTC124), currently approved by the FDA in the US for children older than 6 years (25). Gene therapy using a viral vector (adenovirus) aimes mainly the respiratory epithelium damage, but can also improve pain and reduce the incidence of ciliary chronic rhinosinusitis (26).

CONCLUSIONS

The chronic rhinosinusitis clinical heterogenity of expression in relation on the one hand, with immunogenic response and anatomical particularities of the child, and secondly the diversity of etiologic factors (from very frequent-allergy, to least frequent – FC) requires proper diagnosis, early and appropriate treatment, and a multidisciplinary team collaboration (pediatrician, ENT physician, allergist, pulmonologist).

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