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PEDIATRIC ALLERGY AND IMMUNOLOGY

Cytology in the diagnosis of rhinosinusitis

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Nasal cytology is a diagnostic tool currently used in rhinology, with the aim of assessing cell changes in the nasal epithelium exposed to irritant or inflammatory agents. Its rationale is based on the knowledge that nasal mucosa of healthy individuals is constituted by four cytotypes (*ciliata*, *mucipara*, *striata,* and *basalis*) and does not show other cells except, rarely, neutrophils and, very rarely, bacteria. In this view, the detection of a given cell type different from these is a sign of possible pathology. The advantage and the diffusion of nasal cytology were increased by a number of factors such as the easiness of performance, the non-invasiveness allowing repetition (which is often needed in the efficacy monitoring of medical or surgical treatment of nasal diseases), and the low cost. This makes nasal cytology particularly feasible for application in children. The cytological feature characterizing infectious inflammation is the presence of abundant bacteria, which may be found in extracellular tissue and also inside neutrophils as a result of phagocytosis. In such clinical condition it is important to monitor the disease with cytological controls to verify the significant decrease, or the disappearance of inflammatory cells, which indicates the resolution of the pathology.

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Nasal cytology is a diagnostic tool currently used in rhinology, with the aim of assessing cell changes in the nasal epithelium exposed to acute or chronic exposure to irritant (physico-chemical) or inflammatory agents, the latter including bacteria, viruses, fungi or parasites. Nasal cytology has been a subject of clinical and scientific interest for the past century (1–3) and in particular it has provided an important contribute to the definition and understanding of the pathophysiologic mechanisms of allergic and non-allergic rhinitis and to the identification of new pathological entities, such as the non-allergic eosinophilic rhinitis (NARES) or mast cell mediated nasal inflammation (4–7).

The rationale of this method is based on the knowledge that the nasal mucosa of healthy individuals is constituted by four cytotypes (*ciliata*, *mucipara*, *striata* and *basalis*) and does not show other cells except, rarely, neutrophils and, very rarely, bacteria (Fig. 1). In this view, the detection of a given cell type different from these is a sign of possible pathology.

In 1889 Hollash suggested that the numerous eosinophils present in nasal secretions of a patient suffering from bronchial asthma were important in the pathogenesis of such disease, and the importance of eosinophils at both nasal and bronchial level was confirmed recently (8,9). However, the real drive to the development of nasal cytodiagnostic was given in 1927 by the report of Eyermanna, who detected eosinophils in nasal secretions from allergic patients and underlined their diagnostic. Since then, many researchers (including Hansel, Dean, Lindsay and Semenov), have attributed an increasing importance to the detection of the various inflammatory cell types in the different nasal pathologies and this has led to a rising usefulness of nasal cytology in the study of allergic and non-allergic rhinitis as well as of acute and chronic rhinosinusitis.

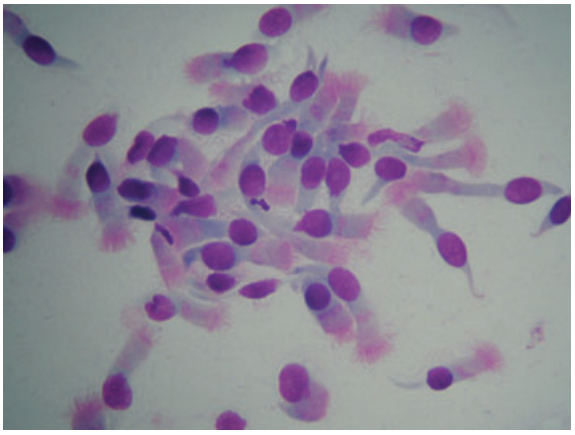

Fig. 1. Normal nasal cytology, showing a prevalence of ciliated cells and the lack of inflammatory cells, bacteria and mould spores.

The advantage of nasal cytology and its diffusion were further increased by a number of factors, such as the ease of performance, the non-invasiveness allowing repetition (which is often needed in the efficacy monitoring of medical or surgical treatment of nasal diseases), and the low cost. This makes nasal cytology a simple and safe technique, which can be performed in outpatient settings and is particularly feasible for application in children.

The technique is based on the following procedure: sampling, processing (including fixation and staining), observation by microscope.

Sampling consists of collection of cells from the superficial layer of the nasal mucosa, which may be performed by using a swab or by scraping with a small plastic curette, such as the Rhino-Probe (10). Swab sampling is performed by rotating and applying a moderate pressure to collect a high number of cells in correspondence to the mean portion of the inferior turbinate, which is known to have the right ratio (approximately 1:4) between ciliated cells and goblet cells.

Generally in small children swab sampling is preferred to scraping because it is quicker and less troublesome, though achieving abundant and good quality material, while scraping may be performed in children older than 6 years, who offer better collaboration. Sampling must always be performed under careful vision in anterior rhinoscopy by means of a nasal speculum and good illumination. As hinted before the technique is almost painless and does not require local anesthesia.

After sampling, the material is laid on a microscope slide, fixed in 95° alcohol for 4 s and stained by the May–Grunwald–Giemsa method, which is the most commonly used because of its ability to stain all the cell components present in nasal mucosa, including inflammatory cells, such as neutrophils, eosinophils, lymphocytes, and mast cells, as well as bacteria and mould spores. Observation is performed by a common optical microscope, provided it is able of a 1000× magnification. To analyze the cytogram the reading is performed by fields all around the slide (at least 10 fields) with the aim to detect the cells important for diagnosis and to evaluate their rate.

Nasal pathologies affect first ciliated cells, which are the most differentiated, with a rearrangement of the respiratory mucosa epithelium, which favors goblet cells (*metaplasia mucipara*), as showed in Fig. 2. This has important pathophysiologic and clinical consequences, in fact the decrease of the ciliated component and the proportional increase of goblet cells elicits an abundant mucus production and its consequent endonasal stagnation (11–13). The reduced mucociliar transport is a risk factor for inflammation, because of the facilitation of bacterial infections and of vicious circles leading to repeated inflammatory events. Considering that the usual turn-over of ciliated cells is about 3 weeks, recurrent inflammations prevent the recover of the normal relationship among the different cell types in the respiratory epithelium.

The nasal cytogram from a child suffering from non-allergic acute or chronic rhinosinusitis shows a higher rate of inflammatory cells (neutrophils, lymphocytes, and macrophages) than in normal subjects and a reverse of the ratio between ciliated and goblet cells with a prevalence of the latter. The cytologic feature of infectious inflammation, showed in Fig. 3, is the presence of abundant bacteria, which may be found in extracellular tissue and also inside neutrophils as a result of phagocytosis (14).

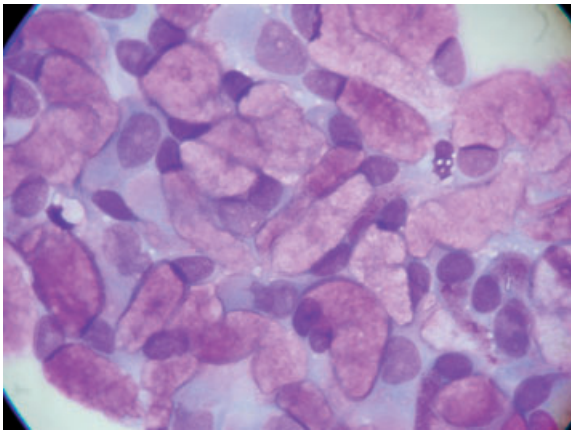

Fig. 2. Cytologic picture of *Metaplasia mucipara*.

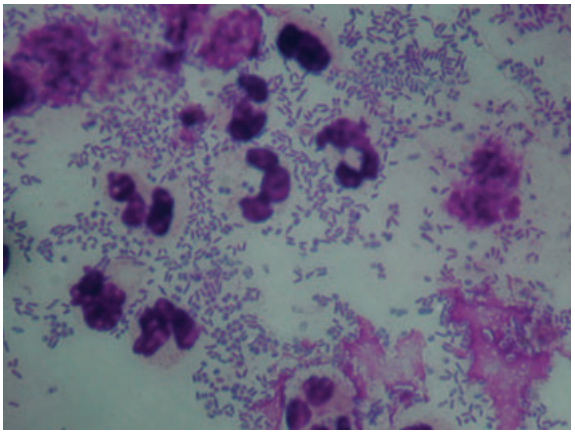

Fig. 3. Bacterial rhinosinusitis characterized by the presence of abundant neutrophils and bacteria, partly intracellular.

A remarkable finding we observed in a randomized study on a population of about 800 children aged up to 12 years is the condition of asymptomatic carrier of high nasal bacterial charge, which prevailed in the age range of 3–4 years. These subjects have a higher risk not only of rhinosinusal pathology but also of infections both loco-regional (as otitis or pharyngo-tonsillitis) and anatomically distant (as laryngo-tracheo-bronchitis, broncho-pneumonitis) as well as of rhino-bronchial syndrome. In such cases it is important to follow the disease during medical treatment by periodic cytologic controls, as only a significant reduction of inflammatory cells or the disappearance of bacteria in cytologic samples can confirm the resolution of the pathology.

Conflicts of interest

The authors have declared no conflicts of interest.

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