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Ciliocytophthoria: Cytomorphologic Modifications in Viral Infections of the Nasal Mucosa

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Abstract

The term ciliocytophthoria (CCP) (Greek etymology) describes a degenerative phenomenon of the ciliated cells secondary to respiratory viral infections and characterized by specific morphological changes.

In the winter 2014-2015, we examined 12 patients, aged between 12 and 32 years (mean age 21, F/M: 4/8) who attended the clinic of Rhinology of the University Hospital Center of Bari (Italy) with a viral infection of the upper airways.

All subjects underwent nasal cytology for microscopic examination and preparations were stained using the technique of May-Grünwald Giemsa.

Our study describes CCP precisely in all its developmental stages by means of microscopic examination of the nasal mucosa (nasal cytology).

Keywords: Virosis; Ciliocytophthoria; Nasal cytology; Rhinitis

Introduction

"Ciliocytophthoria" (CCP) is a term that describes a degenerative process of the ciliated cells secondary to viral infections and characterized by specific morphological changes.

Already in the1800s, the naturalist Joseph Leidy (1823-1891) described "Asmathosis ciliaris" in samples of the respiratory epithelium of asthmatic patients and determined that those features were no more than respiratory cells [1].

Later on, in 1930, Hilding noticed aberrant nasal cells, apical and anucleated remains of the epithelial cells similar to parasitic cells. In 1956 George N Papanicolau coined the term "Ciliocytophthoria" (CCP) to refer to the degenerative process observed in the ciliated cells of the bronchial epithelium, secondary to clinical virosis and bronchial carcinoma [2,3].

Since then, many other publications have been written on CCP, although in some of them the Authors used terms as "pseudoprotoza" and "pseudomicrobe" rather than CCP: this testifies the confusion between the degenerative process of the ciliated cells and the presence of flagellated protozoa frequently found in the respiratory tract [4-7].

Several in vitro studies using electron microscopy clearly highlighted the characteristics of CCP and correctly included it among the degenerative phenomenon typically present in respiratory infections [8], with the bronchial mucosa being the target of the cytopathological changes in cases of respiratory infections (with major involvement of the ciliated cells) [9].

CCP has been reproduced experimentally by exposing porcine respiratory epithelium to a wide variety of pathogens and has also been associated to respiratory affections in horses [10,11]. In humans, CCP can be seen in acute tonsillitis and viral infections [12,13], as well as in respiratory tract specimens, gynecologic samples and peritoneal washings [3,14-16].

The majority of the articles present in the current literature describe CCP as characterized by "cellular fragments", with no nuclei, with a regular rhythmic movement of the cilia at one edge and a well distinguishable "terminal bar", hence the difficulty of distinction with parasitic flagellates.

In our paper we studied and illustrated the distinct and characteristic phases of CCP by means of the optical microscopy of the nasal mucosa (nasal cytology).

Materials and Methods

During the winter season 2014-2015, 12 patients, aged between 12 and 32 years (mean age: 21 years; M/F: 8/4-66, 7%), attended the outpatient Center of Rhinology of the University Hospital of Bari (Italy). All patients were affected by viral infections of the upper airways. Serological data confirmed the clinical virosis in all cases (Influenza virus type A). From a clinical point of view, all patients referred nasal congestion, sneezes, watery rhinorrhea, cough, fever, headache and chills, all signs of an on-going viral infection. Anterior rhinoscopy generally showed hyperemia of the inferior turbinates and presence of clear, abundant, nasal mucous while, at the oropharyngoscopy, hyperemia of the tonsillar pillars and of the oropharyngeal posterior wall were noticed [17,18].

All patients underwent nasal cytology for microscopic examination. The procedure was performed by scraping the middle part of the inferior turbinate with a Rhino-Probe® (Arlington Scientific). The sample was smeared on a slide, air-dried, and stained with the May-Grünwald Giemsa preparation. The type and cell number were examined using microscopy (Nikon® E600). Cell types were identified, and intracellular components were studied at 1000 X in oil immersion. The mean number per 50 fields was calculated and reported [19-21].

Results

All patients had abnormal rhinocytograms, with cytopathic alterations attributable to viral infections. In addition to numerous neutrophils and lymphocytes, we observed some columnar cells, part of the ciliated cells, with various degrees of CPP.

In Figure 1, we describe the most common morphologic alterations we observed, assignable to CCP.

In Figure 1a, the typical normal ciliated cell is visible, with its well-conformed ciliary apparatus, with a homogeneous cytoplasm, a finely represented chromatin in the nucleus, an easily recognizable nucleolus and the characteristic hyperchromatic supranuclear stria (HSS). In the case of clinical virosis, at least three distinct phases of CCP are distinguishable.

The first phase (Figure 1b) is characterized by an initial rarefaction of the ciliary apparatus, with the disappearance of the HSS, initial vacuolization of the cytoplasm and an internal reorganization of the chromatin (heterochromatin) that forms little clumps.

The second phase (Figure 1c) is characterized by a further rarefaction of the ciliary apparatus, which leads to its disappearance and to the confluence of the intracytoplasmic vacuoles; in the nucleus, chromatin tends to coalescence and to compact, with a peripheral halo where the nucleolus is clearly visible.

The third and final phase (Figure 1d) is characterized by the "decapitation" of the apical portion of the ciliated cell, secondary to the latero-lateral confluence of the cytoplasmic vacuoles from which only the caudal portion of the cell, represented by the nucleus and its nucleolus, surrounded by a thin cytoplasm remnants, are visible.

Discussion

It is well known that acute inflammations of the upper airways are caused mainly by viruses, even though after the viral infection a bacterial overlapped infection follows, partly favored by the cytopathic effect of the virus itself on the mucosa. Ciliated cells are the most differentiated of the cells of the nasal mucosa and therefore they are more prone to attack from infectious agents. The most frequently responsible viruses for respiratory inflammation are the Rhinovirus, Myxovirus (Influenza virus), Paramyxovirus (Parainfluenza virus), Coronavirus, Adenovirus and Respiratory Syncytial Virus (RSV). In 30-35% of cases, the infectious viral agents are not identifiable.

CCP represents a morphologic cellular aspect of great diagnostic importance. Although studied since the early 19th century, clear description of the cytomorphologic phases of this phenomenon are not depicted in the currently available literature. Nowadays, it is thanks to nasal cytology, a branch of Rhinology, that the different phases of CCP have been detected and described.

Classically, CCP was described as a condensation of the nuclear chromatin together with the formation of a "perinuclear" halo. The presence of material of inclusion and the depletion of the ciliary apparatus completes the cytological features of CCP [22,23]. We agree with all the previous reports, except for the presence of the perinuclear halo.

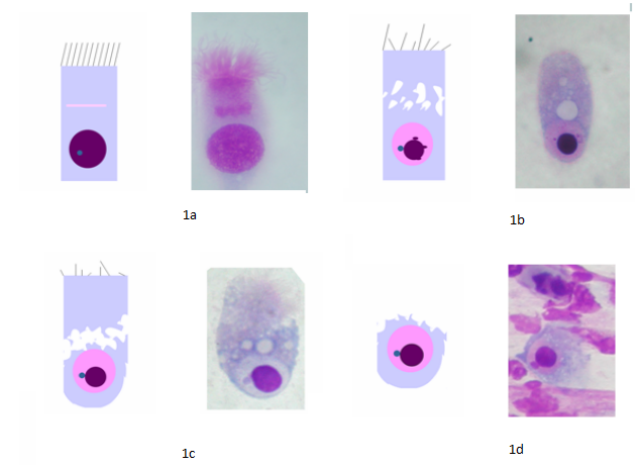

Figure 1: (a-d): Ciliocytophthoria. We describe the most common morphologic alterations we have observed, assignable to CCP. **1a:** Ciliated cell with well-conformed ciliary apparatus, homogenous cytoplasm, and the typical Hypercromatic Supranuclear Stria (HSS). **1b:** Ciliated cell with rarefaction of the ciliary apparatus, HSS disappearance, cytoplasmic vacuolization, condensation of the nuclear chromatin with intranuclear halo. **1c:** Ciliated cell with coalescence of multiple intracytoplasmic vacuoles. Condensation of the nuclear chromatin with visualization of the nucleolus in the intranuclear halo. **1d:** Ciliated cell. "Decapitation" of the apical portion of the ciliated cell, due to the latero-lateral confluence of the cytoplasmic vacuoles. Secondarily to this, it is possible to observe only the caudal portion of the cell, with the nuleus and the nucleolus, all surrounded by a thin cytoplasmic remnant.

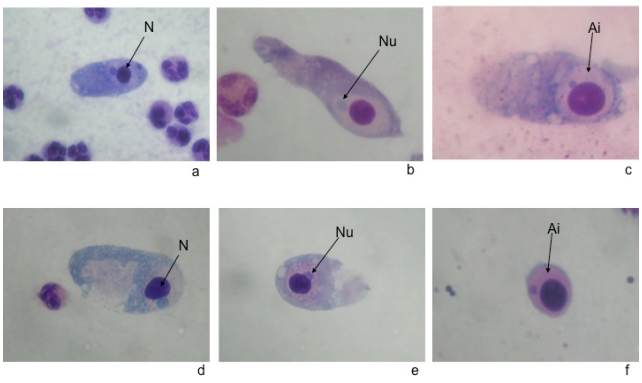

Figure 2: (a-f); Ciliocytophthoria. It is clearly visible in all the cells (a-e) the hyperchromatic nucleus (N), the "intranuclear" halo (Ai) and the nucleolus (Nu). d) "naked" nucleus with no cytoplasm. It is noticeable the condensation of the chromatin, the intranuclear halo and the nucleolus.

Our experience demonstrated that the halo which surrounds the nuclear chromatin is just that portion of the nucleus where the chromatin is absent. The condensation of the hyperchromatic nuclear content would be responsible for formation of the rarefied "intranuclear halo" in which the nucleolus is visible (Figure 2a-2f).

Further studies of electron microscopy focused on CCP are needed to confirm our preliminary impressions.

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