Rhinology, 25, 57-62, 1987

Abnormalities of cilia and chronic sinusitis

C. Fontolliet and G. Terrier, Lausanne, Switzerland

SUMMARY

An ultrastructural study was performed on 34 biopsy samples of the sinusal mucosa in 28 patients who were investigated for chronic sinusitis. Twelve specimens with normoplastic sinusitis and eighteen with hyperplastic sinusitis were studied. Four normal specimens served as controls. The incidence of ultrastructural ciliary abnormalities was 2%. Morphological changes of dynein arms have not been observed in the present study. Compound cilia were found in approximately 2/3 of the studied cases. Microtubular abnormalities occurred in roughly 50%.

The observed abnormalities, also seen in the control group, were independent on the sinusitis type and could not been correlated with mucociliary transport. Their significance is discussed.

INTRODUCTION

Ciliary defects have been observed in various diseases of the respiratory tract (Afzelius, 1983; Chao, 1982; Wissemann, 1981). It has been suggested that the presence of abnormal cilia could have pathogenetic significance and be responsible for a decrease of mucociliary function (Afzelius, 1983; Greenstone, 1983; Sleigh, 1983).

We recently observed the case of a 55 year old woman who presented repeated infections of the upper and lower respiratory tract accompanied by violent headaches since infancy. The intensity of symptoms decreased during adult life. Actually, our patient presented with a chronic rhinitis and a bronchitis associated with postnasal drip. Laboratory data were normal except for an elevated serum level of IgA of 458 mg/dl (normal: maximum 296 mg/dl). A sweat test was negative. Pulmonary function tests revealed a mixed obstructive and restrictive syndrome. The presence of a situs inversus was demonstrated by chest X-rays. The patient also presented with primary sterility. The diagnosis of Kartagener's Syndrome was made. In order to demonstrate ciliary abnormalities to confirm this diagnosis, biopsies of nasal, sinusal and bronchial mucosa were performed.

Paper presented at the 11th Congress of the European Rhinologic Society and 5th IAIAN, Athens (Greece), June 1986.

Nasal mucosa was obtained from the region posterior to the right middle concha. Sinusal mucosa was taken endoscopically from the right maxillary sinus and bronchial mucosa bronchoscopically from the right stem bronchus.
Ultrastructural study of the cilia showed completely or partially defective dynein arms (Figure 1). These abnormalities were observed in all biopsy specimens but only in a limited number of cilia. Therefore a series of patients with chronic sinusitis was studied to ascertain the frequency and the specificity of ciliary defects and to assess their significance.

MATERIAL AND METHODS

Thirty four biopsy specimens of the maxillary sinusal mucosa were examined. They had been taken from 28 patients, 17 male and 11 female, aged 10 to 79 years, who were investigated for chronic sinusitis. For each specimen, an endoscopic diagnosis was established according to the following classification:
Type O: normal mucosa.
Type I: normoplastic non secretory mucosa.
Type II: normoplastic secretory mucosa.
Type III: hyperplastic non secretory mucosa.
Type IV: hyperplastic secretory mucosa.
Twelve specimens with normoplastic sinusitis and eighteen with hyperplastic sinusitis were studied. Four normal specimens served as controls.
All specimens were processed for electron microscopy in the usual way (Fox, 1980 and 1981). They were observed with a Philips 300 microscope without a goniometer stage.
About 500 transversal sections of cilia were studied in each sample at a magnification of 18,000 ×. The ciliary defects were assessed in a semi-quantitative way. The outer and inner dynein arms on the peripheral microtubules were not counted. Representative microphotographs were taken.
Mucociliary transport with a dyed indicator was tested in 12 patients to evaluate the clearance of the maxillary sinus (Terrier, 1985). In this method, 0.5 ml of dye were deposited on the posterior sinus wall during sinusoscopy with the patient lying horizontally. The dye was introduced through the canulae used for puncture, and its migration toward the ostium was optically observed. The dye we used was a suspension of insoluble microionized indigo blue in a plasma substitute (Physiogel SRK).
In clinically normal sinuses, we observed that the first dye particles reached the ostium after less than 15′ after deposition. We therefore used this limit of 15′ to decide whether the mucociliary transport was rapid, normal or slowed down. This transport was occasionally aberrant, the dye particles moving in a wrong direction or just showing stagnation on the mucosa and forming unoriented reticulated traces.

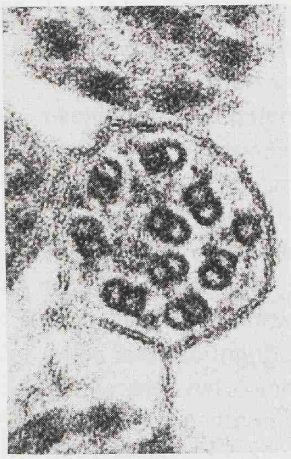

Figure 1.
Cross-sectioned cilia from a 55 year old woman with Kartagener's syndrome. Deletion of inner and outer dynein arms and abnormal arrangement of microtubules.
Magnification × 200000.

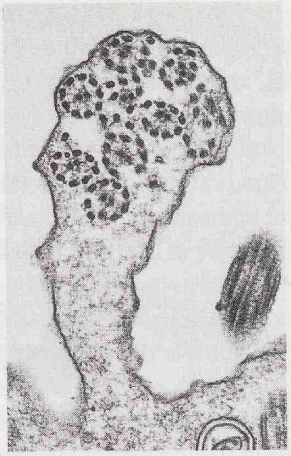

Figure 2.
Longitudinal section of compound cilia.
Magnification × 26000.

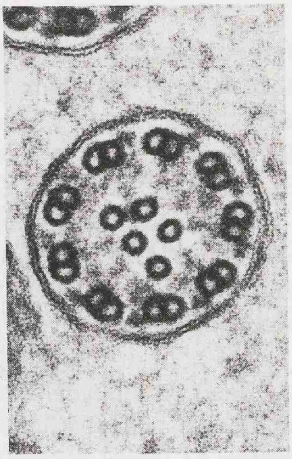

Figure 3.
Transverse section of a cilia showing supernumerary central microtubules.
Magnification × 200000.

RESULTS

The incidence of ultrastructural ciliary abnormalities was 2%. No morphological changes of dynein arms could be demonstrated. Compound cilia, i.e. cilia with more than one set of 9 + 2 microtubular structures within the axoneme, were observed. They showed considerable variation in the arrangement and number of the microtubules (Figure 2). The following microtubular abnormalities were noted: 1. supernumerary pairs of central microtubules; 2. supernumerary simple microtubules; 3. eccentric location of central pairs; 4. deletion of microtubules (Figure 3).

Compound cilia were found in 17 specimens, abnormal microtubular structures in 13. In 12 specimens the ciliary pattern was normal. Compound cilia associated with microtubular abnormalities were present in 8 specimens. Ciliary abnormalities were observed in all types of chronic sinusitis as well in normal mucosa. Of 18 specimens with hyperplastic mucosa 13 had ciliary defects. Five of the 12 specimens with normoplastic mucosa had abnormal cilia (Figure 4).

A mucociliary transport test with colored indicator was performed in 12 patients. Four patients without sinusitis endoscopically were considered normal and

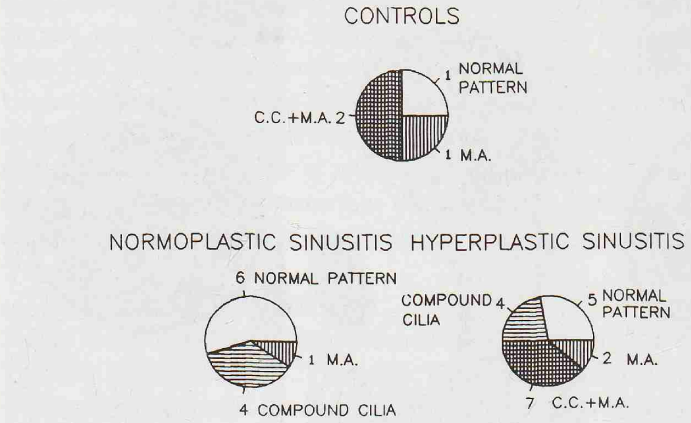

Figure 4. Ciliary abnormalities and chronic sinusitis. C.C.: Compound cilia. M.A.: Microtubular abnormalities.

served as controls. Normoplastic sinusitis was present in four, hyperplastic sinusitis in four other patients. The velocity of transport was independent on the type of sinusitis. Transport was slow in two controls. Ciliary abnormalities were found in patients with normal, fast or slow transport. Abnormal microtubular structures were more often observed than compound cilia in patients presenting a normal mucociliary transport. Compound cilia were observed in all six patients with fast transport. They were associated with abnormal microtubular structure in three of these patients. Of the two patients with slow transport one had a normal ciliary pattern, the other had microtubular defects (Figure 5).

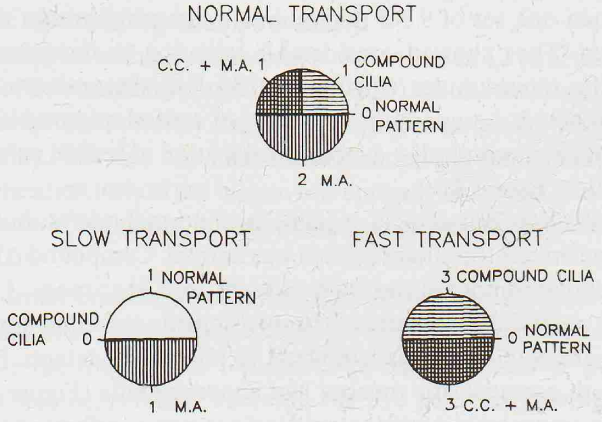

Figure 5. Ciliary abnormalities and mucociliary transport. C.C.: Compound cilia. M.A.: Microtubular abnormalities.

DISCUSSION AND CONCLUSIONS

One of the main problems in the assessment of ultrastructural ciliary abnormalities lies in the focal nature of the changes (Fox, 1980 and 1983). We have tried to overcome this problem by examining large numbers of cilia, at least 500 in each specimen. We have established an overall incidence of ciliary defects of 2%, which is in according with the findings of others (Carson, 1985). Morphological changes of dynein arms have not been observed in the present study. It should be stressed that dynein arms are difficult to visualize (Fox, 1983). Their identification is probably influenced by the fixative used, the quality of the section and the orientation of the cilia. Possible artefactual changes have to be taken into account when interpreting the results of such a study.

In our material compound cilia were observed with a sightly incidence than microtubular abnormalities. Compound cilia and microtubular defects were found in all types of chronic sinusitis as well in the control group. An increased incidence of ciliary abnormalities was found in hyperplastic sinusitis. The mucociliary transport was not modified by the presence or absence of ciliary abnormalities. Our results, however, are based on too few observations to allow definitive conclusions. Other factors than ciliary structure, particularly mucus dependent factors, may influence the mucociliary transport as well (Sleigh, 1983).

The results of the present investigation tend to rule out the pathological significance of compound cilia and microtubular abnormal configuration unassociated with loss of dynein arms. These changes are probably acquired and do not have any known functional importance.

RÉSUMÉ

Notre étude porte sur l'ultrastructure de 34 prélévements de muqueuse sinusale faits chez 28 patients investigués pour une sinusite chronique. 12 prélévements ont été effectués chez des patients présentant une sinusite normoplasique, 18, chez des patients avec une sinusite hyperplasique. 2% des cils examinés montraient des anomalies structurales. Nous n'avons pas observé, dans cette étude, d'altération des bras de dynéine. Environ deux tiers des cas étudiés comportaient des cils composés, 50%, des anomalies touchant les microtubules. Ces modifications, également retrouvées dans le groupe de contrôle, étaient indépendantes du type de sinusite chronique, et sans corrélation avec les épreuves fonctionnelles. Leur signification est discutée.

REFERENCES

1. Afzelius BA, Camner P, Mossberg B. Acquired ciliary defects compared to those seen in the immotile-cilia syndrome. Eur J Respir Dis 1983; 64, Suppl 127: 5–10.
2. Afzelius BA. Ultrastructural basis for ciliary motility. Eur J Respir Dis 1983; 64, Suppl 128: 280–286.

3. Carson JL, Collier AM, Hu SS. Acquired ciliary defects in nasal epithelium of children with acute viral upper respiratory infections. New Engl J Med 1985; 312: 463–468.
4. Chao J, Turner JAP, Sturgess JM. Genetic heterogeneity of dynein-deficiency in cilia from patients with respiratory disease. Am Rev Resp Dis 1982; 126: 302–305.
5. Fox B, Bull TB, Arden GB. Variations in the ultrastructure of human nasal cilia including abnormalities found in retinitis pigmentosa. J Clin Pathol 1980; 33: 327–333.
6. Fox B, Bull TB, Makey AR, Rawbone R. The significance of ultrastructural abnormalities of human cilia. Chest 1981; Suppl 80: 796–799.
7. Fox B, Bull TB, Oliver TN. The distribution and assessment of electron-microscopic abnormalities of human cilia. Eur J Respir Dis 1983; 64, Suppl 127: 11–18.
8. Greenstone M, Stanley P, MacWilliam L, Dewar A, Cox T, Mackay IS, Cole PJ. Mucociliary function and ciliary ultrastructure in patients presenting with rhinitis to Brompton Hospital Nose Clinic. Eur J Respir Dis 1983; 64, Suppl 128: 457–459.
9. Sleigh MA. Kartagener's syndrome, ciliary defects and ciliary function. Eur J Respir Dis 1983; 64, Suppl 127: 157–161.
10. Sleigh MA. Ciliary function in transport of mucus. Eur J Respir Dis 1983; 64, Suppl 128: 287–292.
11. Terrier G. L'évaluation de la clearance du sinus maxillaire par l'épreuve du transport muco-ciliaire coloré. Rev Med Suisse Romande 1985; 105: 239–245.
12. Wisseman CL, Simel DL, Spock A, Shelburne JD. The prevalence of abnormal cilia in normal pediatric lungs. Arch Pathol Lab Med 1981; 105: 552–555.

C. Fontolliet, M.D.
Institute of Pathology
CHUV
CH-1000 Lausanne
Switzerland