Nasal polyps: a comparative study of morphologic and etiopathogenetic aspects

G. Paludetti, M. Maurizi, A. Tassoni, M. Tosti and G. Altissimi, Perugia, Italy

SUMMARY

16 nasal polyps belonging to 10 male subjects aged between 40 and 70, have been removed during the same number of ethmoidectomies; the polyps have been sectioned and specimens of mucosa corresponding to the pedicle and to the different parts of the body have been collected. During the operation parts of the mucosa of the inferior turbinates were removed. All the specimens have been prepared and observed at the scanning electron microscope. The epithelium of the inferior turbinates, of the small polyps and of the apical part of all polyps were almost normal. Marked alterations of the epithelial layer have been observed in bigger polyps. Surface characteristics of nasal polyps seem to be influenced by their relationship with neighbouring structures and by their position in the nasal cavity, but mostly by their size. On the basis of these findings the authors discuss the most recent etiopathogenetic theories of nasal polyps and of the inferior turbinates of three confirmed allergic subjects and discuss their possible clinical implications.

INTRODUCTION

Nasal polyps are round, translucent, pale and smooth structures which originate from the maxillary and ethmoid sinuses and project in the nasal cavities. They are formed by a body, extremely variable in shape and dimensions, connected by a pedicle to the structures from which they originate.

They usually are a feature of an allergic rhinitis (Andersen, 1943; Shermann, 1968) but they can result from other pathologies (Caplin et al, 1971; Delaney, 1976) such as mucoviscidosis (Lanoff et al., 1973) and inflammatory diseases. As few scanning electron microscopy studies of nasal polyps have been reported in the literature (Mygind, 1974; 1978) and as many uncertainties are still present regarding their etiology it is our aim, in the present investigation to verify the possible correlations between surface morphology and etiological theories and to observe if some structural characteristics can be of some value in differential diagnosis.

MATERIALS AND METHODS

10 male subjects aged between 40 and 70,5 of which had a confirmed diagnosis of allergy, underwent transmaxillary and transmasal ethmoidectomy. During the operation, performed under general anesthesia, small specimens of the mucosa of the inferior turbinates were collected and a total of 16 polyps were cautiously removed and selected for observation.

After having accurately washed the specimens in physiological saline, they were immediately fixed in a 2.5% glutharaldeid solution buffered with 0.1 M sodium cachodylate (Ph 7.4). After approximately 12 hours every polyp was sectioned in fragments corresponding to the pedicle and to the lateral, the anterior, the posterior and the inferior walls (Figure 1). The obtained specimens were again separately fixed. After other 12 hours the specimens were stored in a sodium cachodilate buffer 0.1 M (Ph 7.4).

Figure 1. The specimens of the mucosa of nasal polyps were collected from the pedicle (ped.) and from the anterior (ant.), posterior (post.), lateral (lat.) and inferior (inf.) parts of the body.

Post, Ped. Ant. at. at. Inf.



Figure 2. Mucosa of the anterior third of an inferior turbinate belonging to a subject with nasal polyps covered by squamous epithelium $(2500 \times)$.



Figure 3A, B. Anterior third of the inferior turbinate of a subject with nasal polyps covered by transitional epithelium. Near to regions with scarsely represented cilia $(A, 1250 \times)$ regions where they are far more numerous can be observed, $(B, 3000 \times)$.

After an average interval of 36 hours the specimens were progressively dehydrated through a series of aceton solutions between 10 and 100% and in Freon 113. Specimens were then dried by means of the "critical point method" in liquid CO_2 , positioned on stubs using Copper Print and finally coated with 10 nm of gold by means of the Sputtering Polaron Equipment LTD SEM Coating Unit E5100. Observation was performed with a scanning electron microscope Philips SEM 501/B at a voltage of 30 KW and photographed with a Polaroid Polopan Land-Film type 52 with a Stockman camera. Calibration bar of every photograph is 10 μ .

RESULTS

Concerning the mucosa of the inferior turbinate in all subjects we have observed characteristics almost similar to those of normal individuals: the anterior regions are covered by squamous and transitional epithelium (Figures 2, 3A, B), while in the intermediate and posterior regions a complete carpet of almost normally looking cilia can be observed (Figure 4).

Concerning nasal polyps, their pedicle in all cases resulted to be extensively covered by almost normally looking cilia, both regarding density and morphology (Figures 5A, B).



Figure 4. A complete carpet of cilia can be observed in the intermediate part of the inferior turbinate of a subject with nasal polyps $(1875 \times)$.



Figure 5A, B. The mucosa of the pedicle of nasal polyps is covered by cilia almost normal in density and shape $(A, 2500 \times ; B, 5000 \times)$.



Figure 6. Cilia sticking together ("wet spaghetti") observed on the surface of a small nasal polyp ($1 \text{ cm} \times 1 \text{ cm}$) ($3000 \times$).



Figure 7. Distal part of a small nasal polyp (1.3 cm \times 1 cm); the cilia are scarsely represented while several cells covered by microvilli can be observed (3000 \times).



Figure 8A, B. Big nasal polyp (3.5 cm \times 2.5 cm). In its distal part the cilia are totally absent, cylindric cells appear hypertrophied and a marked distension of intercellular spaces is visible (A = 1250 \times); rare ducts of mucous glands can be observed (B = 1250 \times).

Small polyps (max. $1-1.5 \times 1-1.5$ cm) showed the presence of cilia even on their distal parts but several ciliary patterns such as cilia sticking together ("wet spaghetti", Figure 6), regions with poorly represented cilia (Figure 7), but never a total absence of ciliated cells could be observed.

In bigger polyps instead, while findings concerning the pedicle are almost similar, we have observed, especially in the distal parts of the polyps a progressive cellular distension with large intercellular spaces with a typical "cobble stones" epithelium (Figure 8A), a total absence of cilia and rare glandular ducts (Figure 8B). In the anterior part of the polyps a marked hypertrophy of cylindric cells (Figure 9) and localized areas of squamous metaplasia, especially in the parts extensively exposed to the air flow, have been detected (Figure 10). On the lateral and medial walls often a completely altered epithelium with loss of specific structures can be noted (Figure 11). In mucosal specimens of the inferior turbinate and on polyps of three of the allergic patients some peculiar structures which, in our knowledge, have never been reported in the literature, have been observed (Figure 12, A.B.C.D.). They present variable size and shape. In some cases they resemble to "flowers" in some others to "sea urchins" or to "straw bundles". It is important to notice that they can be observed exclusively on the mucosal surface and not on the sectioned one.



Figure 9. Anterior part of a nasal polyp of conspicuous dimensions $(3.5 \text{ cm} \times 2.5 \text{ cm})$. The cylindric cells appear markedly hypertrophied $(1500 \times)$.



Figure 10. Anterior part of a nasal polyp of conspicuous dimensions (4 cm \times 3 cm). A squamous metaplasia can be detected when the epithelium is directly in contact with the airflow (640 \times).



Figure 11. Lateral part of a polyp tightly adherent to another one: none of the specific characteristics of the epithelium is visible $(1250 \times)$.



Figure 12A, B, C, D. Findings observed on the mucosal layer of nasal polyps $(A = 1250 \times ; B = 5000 \times)$ and on the posterior third of a degenerated turbinate of a confirmed allergic subject (C and D = 2500 \times). Several peculiar structures of different dimensions and shape ("flowers", "sea urchins", "straw bundles") have been detected.



DISCUSSION

Although nasal polyps are not unfrequent, their etiology and pathogenesis are still matter of discussion. In the past their formation has been referred to an adenomatosis (Billroth, 1855) or to a fibromatosis (Hopmann, 1885), to a mixomatous degeneration (Mackenzie, 1884) or to an inflammatory hyperplasia (Zuckerkandl, 1882) of the mucosa or to a necrosis of the ethmoidal septa with consequent mixomatous reaction (Woakes, 1885). According to Hajek (1896) the formation of polyps starts with a submucosal oedema and with an increase of glandular contents which detach the mucosal layer pressing it caudally, while Yonge (1907) referred the pathogenesis of polyps to a cystic degeneration of glandular ducts causing an obstruction of blood vessels of the nasal mucosa and following oedema. Eggston and Wolff (1947) hypothesize that polyps' formation is strictly related with periphlebitic and perilymphangitic phenomena due to infection. Krajina (1963) believed that inflammatory localized infiltrations of the nasal mucosa during chronic infections and allergic episodes and that a localized increase of nasal glands both causing bulging of the mucosa, were of great importance in the pathogenesis of nasal polyps.

Cauna (1972) claimed that the increase of vascular permeability and the consequent oedema were due to the absence of nervous structures on the vessels of the polyps. According to the most recent etiopathogenetic theory (Tos and Mogensen, 1977) the reduced air flow through the upper part of an allergic and chronically infected nose is the main etiological factor of nasal polyps. Infiltration and oedema of the nasal mucosa result in the rupture of the epithelium followed by the appearance of granulation tissue which gradually becomes lined with pseudostratified columnar epithelium.

During the growth of the polyp the formation of a vascular stalk and of mucous glands occurs, the latter becoming long and stretched owing to the growth of the polyp.

The results of the present scanning electron microscopy study seem to confirm this last theory. In fact surface morphology of the inferior turbinates of patients with nasal polyps in which the oedema is reduced and does not cause the rupture of the epithelium is very similar to the normal mucosa (Mygind, 1975; Mygind and Winter, 1979) even if in most areas cilia are less represented.

In bigger nasal polyps the epithelium is formed by hypertrophic cylindric cells with a marked intercellular distension and is characterized by a total loss of cilia. These findings could be due to the rupture of the original epithelium and by the following formation of a new and different one lining the granulation tissue.

Another hypothesis to explain the differences of the epithelial characteristics could be that the epithelium in small polyps is younger and that instead in the bigger ones it is older, if we accept that the difference in size of the polyps is age related.

Nasal polyps

A quite different surface morphology can be observed as compressive forces act on the epithelium; in these cases epithelial cells become flat and loose all their specific features.

According to the statements of Tos and Mogensen (1977) we agree with the observation of rare outcomes of glandular ducts that seem to confirm that mucus glands are scarsely represented in nasal polyps.

If Wihl and Mygind (1977) state in the conclusive part of their discussion that none of the surface characteristics are able to clearly differentiate mucous membranes of allergic subjects from those with other pathologies, the peculiar features we have observed on the polyp's surface and on the mucosa of the inferior turbinates in the three proved allergic subjects are, in our opinion, quite interesting. We do not believe that they are artifacts due to the preparation of the specimens as they have been observed only on the mucosal surface and not on the sectioned ones. The absence of reports in the literature concerning similar structures leads us just to hypothesize some etiological theories. They could be:

a. cilia with completely altered characteristics and without any flexibility;

- b. crystaloid structures of unknown nature but maybe typical of allergic mucous membranes;
- c. allergens.

These findings need obviously further experimental evidence but they could be of some interest in differential diagnosis if they result to be specific of some nasal pathology.

RÉSUMÉ

16 polypes naso-sinusaux de 10 sujets masculins, agés de 40 à 70 ans, ont été extirpés pendant des interventions d'ethmoidectomie. On a sectionné les polypes et on a recueilli des fragments de muqueuse du pédicule et de differentes parties du corp. Pendant l'intervention on a prélevé aussi des fragments de muqueuse des cornets inferieurs. Toutes les observations ont été faites à l'aide d'un microscope à balayage. L'epithelium des cornets inferieurs, des polypes les plus petits et de la portion apicale des polypes était presque normal. Par contre, des évidentes alterations ont été notées en observant l'epithelium des polypes plus grands.

Les charactéristiques de la surface des polypes semblent influencées par le rapport avec les structures les plus proximes, par leur localisation dans la cavité nasale, mais surtout par leurs dimensions.

Sur la base de leurs observations les auteurs discutent les plus récentes théories étiopathogénetiques des polypes naso-sinusaux. Enfin ils décrivent des particulières structures observées sur la muqueuse des polypes et des cornets inferieurs de trois sujets atopiques et discutent les possibles implications cliniques.

ACKNOWLEDGEMENT

The authors thank sincerely Prof. Mirko Tos, Director of the ENT Dept. of the Gentofte Hospital, Copenhagen, Denmark for useful suggestions.

REFERENCES

- 1. Andersen, H. C., 1943: Studies on the clinical aspects, etiology and pathogenesis of nasal polyps and hyperplastic sinusitis with special reference to eosinophilia. Acta otolaryng. (Stockh.) Suppl. 50.
- 2. Billroth, T., 1855: Über den Bau des Schleimpolipen. Georg Reimer, Berlin.
- 3. Caplin, I., Haynes, J. T. and Spahn, J., 1971: Are nasal polyps an allergic phenomenon? Ann. Allergy 29, 631.
- 4. Cauna, N., Hinderer, K. H., Manzetti, G. W. and Swanson E. W., 1972: Fine structure of nasal polyps. Ann. Otol. (St. Louis), 81, 41.
- 5. Delaney, J. C., 1976: Aspirin idiosyncrasy in patients admitted for nasal polypectomy. Clin. Otolaryng. 1, 27.
- 6. Eggston, A. A. and Wolff, D., 1947: Histopathology of the Ear, Nose and Throat. Williams and Wilkins, Baltimore.
- 7. Hajek, M., 1896: Über die Pathologischen Veränderungen der Sibbein-Knochen in Gelfoge der Entzündlichen Schleimhauthypertrophie und der Nasenpolypen. Arch. Laryng. Rhinol. 4, 277.
- 8. Hopmann, A., 1885: Über Nasenpolypen. Mschr. Ohrenheilk., 19, 161.
- 9. Krajina, Z., 1963: A contribution to the aethiopathogenesis of the nasal polyps. Pract. Oto-Rhino-Laryng. 25, 241.
- 10. Lanoff, G., Daddono, A. and Johnson, E., 1973: Nasal polyps in children: a ten year study. Ann. Allergy, 31, 551
- 11. Mackenzie, N., 1884: Die Krankheiten des Halses und der Nase. A. Hirschwald, Berlin.
- 12. Mygind, N., Bretlau, P. and Sørensen, H., 1974: Scanning electron microscopic studies of nasal polyps. Acta otolaryng. 78, 436.
- 13. Mygind, N., 1975: Scanning electron microscopy of the human nasal mucosa. Rhinol. 13, 57.
- 14. Mygind, N., 1978: Nasal allergy: Blackwell scientific Publications. Oxford.
- Mygind, N., Sørensen, H. and Pedersen, B. C., 1978: The nasal mucosa during longterm treatment with Blecomethasone Dipropionate aerosol: a light and scanning electronic microscopic study of nasal polyps. Acta otolaryng. 85, 437.
- 16. Mygind, N., and Winther, B., 1979: Light- and scanning electron-microscopy of the nasal mucosa. Acta Oto-Rhino-Laryngol. Belg. 33, 591.
- 17. Sherman, W. B., 1968: Hypersensitivity. Saunders, Philadelphia.
- 18. Tos, M. and Mogensen, C., 1977: Pathogenesis of nasal polyps. Rhinol. 15, 87.
- 19. Tos, M. and Mogensen, C., 1977: Mucous glands in nasal polyps. Arch. Otolaryng. 103, 407.
- 20. Wihl, J. A. and Mygind, N., 1977: Studies on the allergen-challenged human nasal mucosa. Acta otolaryng. 84, 281.
- 21. Woakes, E., 1885: Über Nekrotisierende Ethmoiditis und ihre Beziehung zur Entwicklung von Nasenpolypen. Brit. Med. Journ. 4, 701.
- 22. Yonge, E. S., 1907: Observations on the determining cause of the formation of nasal polyps. Brit. Med. Journ. 12, 964.
- 23. Zuckerkandl, E., 1882: Normale und pathologische Anatomie der Nasenhöhle und ihrer pneumatischen Anhange. Vol. II. Braumuller, Wien.

Dr. Gaetano Paludetti Istituto di Clinica Otorinolaringoiatrica Università di Perugia 06100 Perugia Italy