

## Fronto-ethmoidal mucocoeles: a histopathological analysis

VALERIE J. LUND, M.S., F.R.C.S.,\* CHRISTOPHER M. MILROY†

### Abstract

From a series of 118 fronto-ethmoidal mucocoeles, 40 specimens have been submitted to detailed histological analysis. The frequency of each epithelial and sub-epithelial component is considered and reveals features which support a dynamic theory of bone resorption and formation rather than that of pressure erosion in the pathogenesis of mucocoeles.

### Introduction

A mucocoele is an epithelial lined mucus-containing sac completely filling a paranasal sinus cavity and capable of expansion (Canalis *et al.*, 1978). It is a relatively uncommon condition but most frequently occurs in the fronto-ethmoidal region (Zizmour and Noyek, 1968; Wolfowitz and Solomon, 1972; Bordley and Bosley, 1973; Canalis *et al.*, 1978; Natvig and Larsen, 1978; Hu and Lin, 1982; De Wilde *et al.*, 1984). Mucocoeles are characterized by slow enlargement over many years (Lund, 1987) unless infection supervenes to produce a pyocoele.

A number of theories have been advanced to explain the formation of mucocoeles, including cystic degeneration of a seromucinous gland and pressure erosion (Palubinskas and Davies, 1959; Batsakis, 1980). However, as recent work on bone resorbing factors suggested a more dynamic process at the mucocoele/bone interface (Lund *et al.*, 1988), a detailed histological study has been per-

formed to consider the morphological differences between the mucocoele and normal sinus mucosa.

### Method and materials

From a series of 118 fronto-ethmoidal mucocoeles treated between 1962–1991, 40 tissue specimens of mucocoele lining (which had been personally removed by one of the authors) were submitted to detailed histological examination. The following elements were considered:

Epithelium:	squamous columnar cuboidal
Mucus-secreting elements:	goblet cells seromucinous glands
Cellular infiltrate:	neutrophils lymphocytes plasma cells eosinophils
Lymphoid aggregates	
Sub-epithelial:	fibrosis vascularity woven bone lamellar bone osteoblasts osteoclasts
Osseous elements:	

TABLE I  
TABLE SHOWING PERCENTAGE FREQUENCY OF EACH HISTOLOGICAL FEATURE ON SEMIQUANTITATIVE ANALYSIS

Histological features	% frequency			
	0	1	2	3
Squamous	51	30	19	0
Columnar	16	21	42	21
Cuboidal	95	5	0	0
Goblet cells	33	35	30	2
Seromucinous glands	58	35	5	2
Neutrophils	32	40	14	14
Lymphocytes	35	35	30	0
Plasma cells	9	35	28	28
Eosinophils	30	56	7	7
Lymphoid aggregates	86	14	0	0
Fibroblasts	21	30	28	21
Vascularity	16	49	26	9
Woven bone	65	21	7	7
Lamellar bone	26	53	12	9
Osteoblasts	55	26	7	12
Osteoclasts	72	21	7	0
Haemorrhage	77	12	9	2

n = 40.

TABLE II  
TABLE SHOWING RESULTS OF MICROBIOLOGICAL CULTURE

Microbiology	No. of cases	Length of history
Sterile	16	3 weeks–8 years
<i>Staphylococcus aureus</i>	4	1 week–6 months
<i>Staphylococcus albus</i>	6	3 weeks–7 months
<i>Streptococcus haemolytic</i>	4	1–14 months
<i>Streptococcus non-haemolytic</i>	2	3–6 months
<i>Haemophilus influenzae</i>	2	3 months
<i>Escherichia coli</i>	1	3 months

n = 33.

Multiple organisms grown in one case.

\*Senior Lecturer, Institute of Laryngology and Otology, London WC1X 8DA.

†Lecturer in Forensic Pathology, University of Sheffield.

All correspondence to V. J. Lund.

Accepted for publication: 25 July 1991.

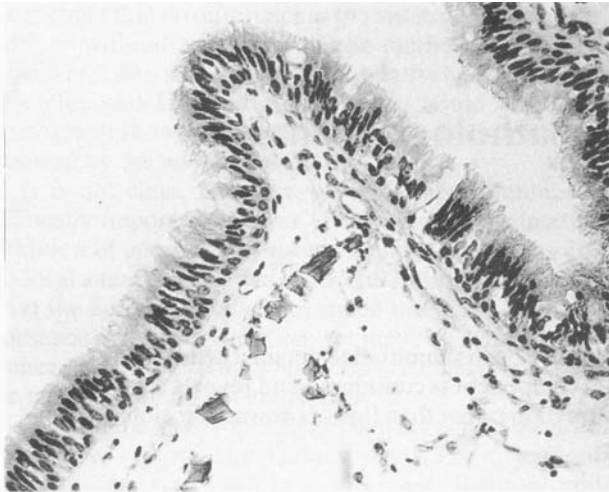


FIG. 1

Photomicrograph showing fronto-ethmoidal mucocoele lined by respiratory epithelium. Haematoxylin and eosin  $\times 200$ .

#### Haemorrhage.

The features were scored using a semiquantitative system on a scale of 0–3. The frequency with which each element occurred overall was considered and correlated with the length of history, presence of clinically acute infection and positive microbiology. These results could be compared with tissue taken at autopsy or from ostensibly normal mucosa in the fronto-ethmoidal region at craniofacial resection (taken from the contralateral side from the disease in non-irradiated non-smokers).

#### Results

The relative percentage frequency for each element by a gradation of 0–3 is shown in Table I. The duration of symptoms ranged from 1–120 months (mean 11 months). Twenty-six per cent of patients exhibited clinical features of acute infection and positive microbiology was found in 52 per cent of submitted specimens (Table II). Only 7/13 patients with clinically acute exacerbations had positive microbiology, possibly as a consequence of antibiotic therapy. Of these, staphylococci were the commonest infecting organisms.

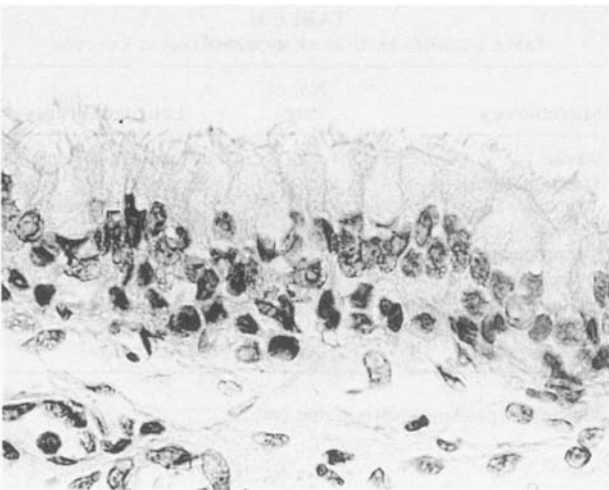


FIG. 2

Photomicrograph showing mucocoele lining with prominent goblet cells. Haematoxylin and eosin  $\times 400$ .

Pseudostratified columnar epithelium predominated (Fig. 1) but was sometimes associated with areas of squamous (15/40) or in one case with both squamous and cuboidal epithelium. The presence of squamous epithelium did not correlate with length of history. Goblet cells were present in 67 per cent of cases and showed evidence of hyperplasia in half of these cases (Fig. 2). The number of seromucinous glands was not increased compared with normal sinus epithelium.

The cellular infiltrate of neutrophils, lymphocytes and plasma cells was consistent with chronic inflammation. As expected neutrophils were significantly increased when there was clinical evidence of acute infection (unpaired t-test,  $P < 0.001$ ) (Fig. 3).

Fibrosis was found in 79 per cent of cases, with significantly increased numbers (grades 2 and 3) in 49 per cent though this was not related to duration of symptoms (Fig. 4). Eighty-four per cent showed vascularity in the submucosa, grades 2 and 3 in 35 per cent. Woven bone (35 per cent) and lamellar bone (74 per cent) were found in the mucocoele specimens and other evidence of new bone formation and bone resorption in the shape of osteoblasts and osteoclasts was found in 44 per cent and 28 per cent respectively. Significant haemorrhage was present in 23 per cent of specimens.

#### Discussion

It has been suggested that one possible mechanism for mucocoele formation is cystic degeneration of a seromucinous gland, thus constituting a retention cyst (Batsakis, 1980). There is no clinical or histological evidence from this or previous studies to support this contention. Indeed retention cysts are commonest in the maxilla where mucocoeles are least often found (Paparella, 1963). In none of the 118 cases has a cyst been found almost filling a

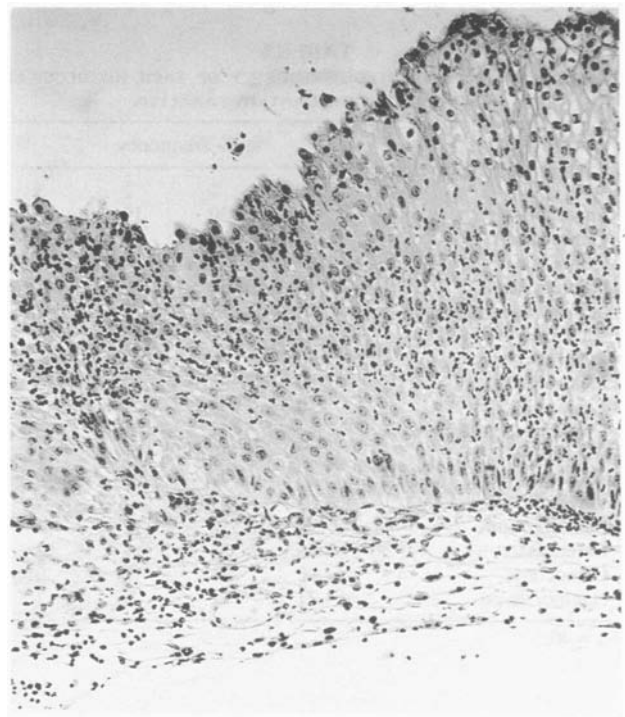


FIG. 3

Photomicrograph showing actively inflamed mucocoele lined by squamous epithelium. Haematoxylin and eosin  $\times 100$ .

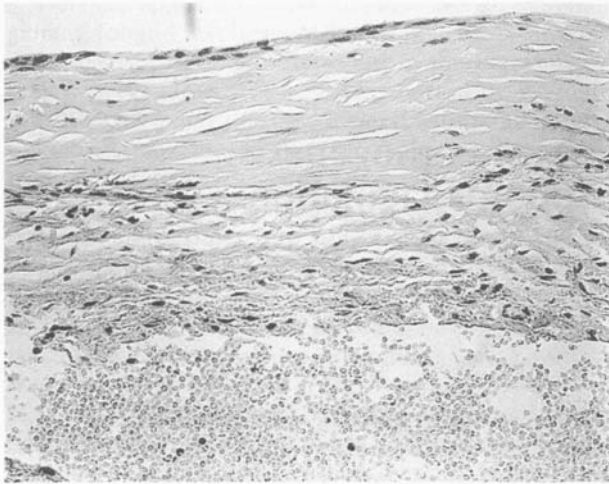


FIG. 4

Photomicrograph showing mucocoele lined by a single layer of cuboidal epithelium. There is prominent sub-epithelial fibrosis. Haematoxylin and eosin  $\times 200$ .

sinus cavity or a double epithelial lining seen histologically. As stated by Canalis *et al.* (1978), the sinus mucoperiosteum always appears to constitute the mucocoele lining.

In the few published accounts of the histological aspects of fronto-ethmoidal mucocoeles (Schuknecht and Lindsay, 1949; Zizmour and Noyek, 1968; Canalis *et al.*, 1978; Natvig and Larsen, 1978; Batsakis, 1980), the lining epithelium is described as pseudostratified columnar which becomes progressively compressed into low columnar or cuboidal epithelium with occasional goblet cells. This transformation is said to increase with the length of the history and to support the theory of pressure erosion. By contrast in our cases, which constitutes one of the largest published series, cuboidal epithelium was rare and the goblet cell population was increased rather than diminished, compared with the normal sinus distribution (Tos and Mogensen, 1978).

However, squamous metaplasia, fibrosis and a chronic inflammatory infiltrate were commonly encountered irrespective of length of history with additional histological and clinical evidence of acute infection. Those with clinically acute infection had all received oral and/or parenteral broad spectrum antibiotics which may explain the absence of positive microbiology in over half these cases. Conversely positive microbiology was found in a significant number (9/17) of 'sterile' mucocoeles.

The surrounding bone showed osteoblastic activity with osteoid and sclerosis alternating with areas of active bone destruction. This supports the previously suggested dynamic theory of mucocoele pathogenesis. Radiologically the classical appearances are of an expanded frontal sinus showing loss of the scalloped margin and an overall loss of translucence of the affected side can be seen in the majority of plain sinus X-rays. In addition to osteolysis, a zone of sclerosis at the margin may be seen in some cases (Wigh, 1950) and macroscopic calcification on X-ray has been reported in 5 per cent (Zizmour and Noyek, 1968) reflecting the presence of new bone formation.

**Key word: Mucocoele**

Previous studies show that the lining of the mucocoele is capable of producing bone-resorbing factors, most notably PGE2 and collagenase (Lund *et al.*, 1988) in significantly higher amounts than those present in normal frontal sinus mucosa. Fibroblasts appear to be the major source of these factors in response to cytokines such as interleukin-1. On the basis of these results, a sequence of events in the pathogenesis of the fronto-ethmoidal mucocoele has been postulated. Following obstruction of the frontonasal recess by overt or covert causes and in the absence of alternative pathways, a superadded infection leads to chronic inflammation mediated by bacterial antigens. Continued stimulation of lymphocytes and monocytes leads to the production of cytokines which enhance prostaglandin and collagenase synthesis by fibroblasts in the lining mucosa. These factors in turn stimulate bone resorption and so accommodate mucocoele expansion.

The histological findings of the present study offer further support for this theory and serve to discount the concept of pressure erosion. They will provide the basis for further work on the cellular origin of such bone-resorbing factors.

#### References

- Batsakis, J. G. (1980) Tumours of the head and neck. Williams and Wilkins, Baltimore.
- Bordley, J. E., Bosley, W. R. (1973) Mucocoeles of the frontal sinus: causes and treatment. *Annals of Otolaryngology, Rhinology and Laryngology*, **82**: 696–702.
- Canalis, R. F., Zajchuk, J. T., Jenkins, H. A. (1978) Ethmoidal mucocoeles. *Archives of Otolaryngology Head and Neck Surgery*, **104**: 286–291.
- De Wilde, R., Fossion, E., Raas, P., Ostyn, F. (1984) Mucocoeles of the paranasal sinuses. *Acta Stomatologica Belgica*, **81**: 91–106.
- Hu, X. H., Lin, D. Z. (1982) Mucocoele des sinus. *Revue de Laryngologie, Otolologie et Rhinologie*, **103**: 199–201.
- Lund, V. J. (1987) Anatomical considerations in the aetiology of fronto-ethmoidal mucocoeles. *Rhinology*, **25**: 83–88.
- Lund, V. J., Harvey, W., Meghji, S., Harris, M. (1988) Prostaglandin synthesis in the pathogenesis of fronto-ethmoidal mucocoeles. *Acta Otolaryngologica*, **106**: 145–151.
- Natvig, K., Larsen, T. E. (1978) Mucocoele of the paranasal sinuses. *Journal of Laryngology and Otolaryngology*, **92**: 1075–1082.
- Palubinskas, A. J., Davies, H. (1959) Roentgen features of nasal accessory sinus mucocoeles. *Radiology*, **72**: 576–584.
- Paparella, M. M. (1963) Mucosal cyst of the maxillary sinus. *Archives of Otolaryngology*, **77**: 650–657.
- Schuknecht, H. F., Lindsay, J. R. (1949) Benign cysts of the paranasal sinuses. *Archives of Otolaryngology*, **49**: 609–630.
- Tos, M., Mogensen, C. (1979) Mucus production in the nasal sinuses. *Acta Otolaryngologica. Supplement 360*: 131–134.
- Wigh, R. (1950) Mucocoeles of the fronto-ethmoidal sinuses. *Radiology*, **54**: 579–590.
- Wolfowitz, B. L., Soloman, A. (1972) Mucocoeles of the frontal and ethmoid sinuses. *Journal of Laryngology and Otolaryngology*, **86**: 79–82.
- Zizmour, J., Noyek, A. M. (1968) Cysts and benign tumours of the paranasal sinuses. *Seminars in Roentgenology*, **3**: 172–185.

Address for correspondence:

Miss V. J. Lund, M.S., F.R.C.S.,  
Senior Lecturer in Rhinology,  
Royal National Throat, Nose and Ear Hospital,  
Gray's Inn Road,  
London WC1X 8DA.