MIXED TUMOURS OF THE MOUTH AND RESPIRATORY TRACT, WITH REPORT OF A CASE ARISING FROM THE ANTERIOR NARES.

By F. HOLT DIGGLE, F.R.C.S. (Eng.), Manchester.

INTRODUCTION.

MIXED tumours, *i.e.*, tumours presenting elements of ectodermal and mesodermal origin frequently arise in the salivary glands, but their origin in mucous membranes is a rarity.

New¹ in an analysis of 68 cases of mixed tumours occurring in the Mayo Clinic between the years 1912-18 gives the following sites of origin—Larynx 1, pharynx 4, palate 3, upper lip 3, sublingual region 1, cheek 1, submaxillary region 5, parotid 50; and Wood,² in 59 cases examined, records their occurrence as follows—Parotid 26, submaxillary 13, palate and pharynx 14, lip 4, neck 2, cheek 1. Verholf³ reports 5 cases occurring in the lachrymal gland, whilst Da Costa⁴ quoted the following cases—Tonsil 1, nasopharynx 2, superior maxilla 1, carotid body 2. Dembrowski⁵ records a case in which the tumour arose from the nares.

It will thus be seen that the salivary glands (parotid and submaxillary) are responsible for about 70 per cent. of the cases met with in the human subject.

CASE REPORT.—E. E., male, aged 62, was first seen in consultation on 25th November 1920, complaining of a swelling in the left nostril.

History.—He was perfectly well until eight years ago, when he fell and caught the tip of his nose on a bar of iron. His nose bled immediately after, but he suffered no further inconvenience until twelve months later, when he noticed that he could not breathe down the left side of his nose. Four years ago he noticed increasing nasal obstruction on the left side, and latterly some swelling of the face. He has had no epistaxis since the accident.

Examination.—The left nostril is completely occluded by a mass attached to the outer wall, of firm consistence, with an intact mucosa, and presenting an appearance not unlike an unripe strawberry. The swelling extends into and obliterates the left naso-labial fold. There is no pain, no enlargement of the lymphatic glands in the neck, and no involvement of the posterior nares. Transillumination shows that the left antrum is not involved.

Tumours of Mouth and Respiratory Tract

Operation.—20th December 1920. Thinking it was possibly a fibrosarcoma, I decided to remove a portion for microscopy. After dividing its outer attachment with turbinectomy scissors, it was discovered that the mass was free and could easily be shelled out of its capsule and expressed from the nose by pressure on the outside. There was very little bleeding, and after enucleation it was seen that the raw area, from which the tumour had arisen, was a small patch about half an inch in diameter just in front of the anterior attachment

SECTION OF TUMOUR SEEN UNDER LOW POWER.

- A. Islets of cartilage merging into the general connective tissue stroma.
- B. Cystic spaces containing mucin.
- C. Myxomatous connective tissue.
- D. Mass of spheroidal cells surrounding a cystic space.

of the left inferior turbinal. The rest of the nasal passage was normal; the remains of the capsule were easily pulled away.

On sectioning the tumour a quantity of brownish mucoid fluid escaped, and it cut with a firm, fibrous sensation. The cut surface presented a greyish colour interspersed with loculi containing a brownish mucoid fluid, and here and there small islands of a whiter colour and firmer consistence.

I am indebted to Dr Dible, Senior Lecturer, Pathological

F. Holt Diggle

Department, Manchester University, for the following histological description :—

“The tumour consists mainly of branching masses of large epithelial cells in a loose myxomatous matrix, having the general aspect of a so-called cylindroma. Closer observation reveals irregular islets of cartilaginous transformation in the matrix, and at one place a well-formed epithelial pearl is to be seen. The tumour corresponds closely to the common mixed tumour of the parotid region.

“The epithelial elements are for the most part spheroidal, with an abundant cytoplasm and a pale oval or round lightly-staining nucleus. They seem to pass by insensible degrees into the branching connective tissue cells, which are distributed through the myxomatous portions of the section and which appear responsible for the production of this area of the tissue. It is noteworthy that certain authors, *e.g.*, C. Kaufmann, regard these growths as being essentially of connective-tissue origin, a position which appears untenable in the case of some parotid tumours in which squamous epithelium predominates. Krompecher, on the other hand, believes that many of them are basal-celled carcinomata in which the cartilaginous portions are formed by metaplasia of the epithelium. In the present tumour there seems to be a definite transition from the epithelium-like cells to those of the connective tissue. It is hard to say why metaplasia should be invoked on the part of one tissue at the expense of another: granted that the two tissues are present together as new formations, it seems more reasonable to derive them both from multipotential cells by a process of development.

“The tumour is definitely encapsulated, and in such cases, where removal is total, recurrence is not a usual sequel.”

After History.—The patient was last seen on 2nd February 1922, and there was no sign of recurrence local or remote.

GENERAL CHARACTERISTICS OF MIXED TUMOURS.

These tumours are of slow growth, very frequently encapsuled, and unless modified by sarcomatous or carcinomatous changes, never cause glandular involvement or internal metastases. It is generally believed that the female sex predominates; but Martin,⁶ after a careful scrutiny of published cases, arrived at the conclusion that there is no predilection for either sex. Sturgis⁷ states that the usual opinion that mixed tumours occur more frequently in young people is non-proven; for in a series of collected cases 50 per cent. occurred after 40 years of age, and 35 per cent. after 50 years; and of the cases occurring after 40 years of age, four were stated to have begun at 43, 51,

Tumours of Mouth and Respiratory Tract

52, and 59 years of age respectively. Wood, however, records a case as early as 7 months, and Wagener, a sublingual tumour in an infant of 12 weeks.

The patients generally seek advice because of increase in size of a tumour which has been in existence for several years. In New's cases, already quoted, 33 had been in existence for more than five years, and 22 for more than ten years, 5 cases for more than thirty years.

Etiology.—The etiology of these tumours has given rise to much controversy and research. The difficulty has been to account for the multiplicity of tissues incorporated in the tumour, and from an attempt to derive them from a common source whether this be epiblast or mesoblast.

Histologically, the tumour is of very complex structure, presenting epithelial elements, arranged either in columns (cylindroma), alveoli or diffused masses, bound together by mesoblastic elements of hyaline, cartilaginous, mucoid or connective tissue structure. Two or more of the mesoblastic elements may be found in the same tumour.

Originally these tumours were regarded as carcinomata, and the cartilaginous element was looked upon by Virchow as derived from the connective tissue by metaplasia, whilst Cohnheim accounted for it as an inclusion from the branchial arches.

Later, Kaufmann⁸ considered the cells as derived from connective tissue cells and classified the tumours as sarcomata.

Wartmann,⁹ in 1879, later supported by Volkmann,¹⁰ labelled them endotheliomata, and maintained that the cells were formed from the endothelium of the lymphatics and blood-vessels. The French School (Collet¹¹ and Pittance¹²), however, opposed the endothelial, and strongly supported the epithelial origin of the cells. In 1899 the French School were supported by Hinsberg¹³ and Ribbert, the former, by a series of embryological studies, showing that the cells might originate from masses of salivary gland epithelium isolated during evolution.

Krompecher¹⁴ regarded them as basal-celled carcinomata, and found that the epithelial cells, by a process of fibrillation, form the connective tissue stroma resembling mucoid or embryonic connective tissue, and that by further metaplasia cartilage is formed.

Ehrich, again, referring to salivary-gland tumours, has shown that they are derived from the proliferation of duct epithelium, *i.e.*, they are adeno-carcinomata.

F. Holt Diggle

Whilst accepting the epithelial origin of these tumours the difficulty has been to explain the presence of cartilage; but Fraser,¹⁵ by a series of experiments, including ligation of the ducts and the injection of irritants into the ducts, was able to artificially produce tumours resembling, histologically, the common parotid tumour. Further, by suitable staining, he demonstrated the formation of cartilage from the epithelium.

It is thus seen that the origin of these tumours is still *sub judice*, but their present status may be quoted from Ewing.¹⁶

- “(1) The endothelial origin has been disproved.
- “(2) No single source of the mixed tumours meets all the requirements. Some are distinctly adenomatous, and probably arise from the acini and ducts of the gland in which they are well incorporated, while others are encapsuled or extra-glandular, these probably arising from misplaced and occasionally embryonal portions of the gland tissue; branchial remnants may possibly be connected with this group.
- “(3) The derivation of mucous tissue and cartilage from epithelium has been proved.”

Clinical Types:—Pharynx.—Mixed tumours present a uniform swelling with intact mucous membrane, situated in the lateral wall or to one side of the middle line. If small, they are frequently mobile under the mucous membrane. As they increase in size the surface mucous membrane ulcerates from pressure atrophy. Owing to the slow growth of the tumour the patients at first complain of little discomfort, but later dysphagia and dyspnoea supervene.

Larynx.—New records the only case occurring in the larynx. It presented as a subglottic infiltration without ulceration. The patient had suffered from increasing dyspnoea for eight years.

Lips.—The upper lip is most frequently affected. Wood records the only case of a mixed tumour arising in the lower lip. The tumour starts to one side of the middle line, is firm and elastic in consistence with occasional fluctuating areas; frequently mobile it causes little or no discomfort.

Palate.—Mixed tumours occur more frequently in the hard than the soft palate. Sturgis collected fourteen cases of soft palate tumours. The bulk of the tumour causes interference with phonation, deglutition, and respiration. Their usual site is

Tumours of Mouth and Respiratory Tract

on either side of the middle line—the only median tumour collected by Sturgis was reported by Van Gabourd,¹⁷ and grew from the superior surface of the palate near the nasal fossa. Gabourd described it as a fibrolipoma. In the fourteen cases of soft-palate tumour there is no mention of recurrence, glandular involvement or metastases, but their site demands early removal.

Prognosis.—This depends upon the age and rate of growth of the tumour, its encapsulation, and its complete removal at operation. Although, as already stated, these tumours are characterised by slow growth, extending over years, yet in a few cases sudden and rapid increase in size results from sarcomatous or carcinomatous changes with glandular involvement and internal metastases.

Encapsulated tumours, owing to their better chance of complete removal at operation, offer the best prognosis. Incomplete removal leads to extensive local recurrence, and repeated unsuccessful operative attempts at total ablation are very liable to set up sarcomatous or carcinomatous changes. Wood, in his series, found that 45 per cent. of the parotid cases recurred locally, and of these, 20 per cent. showed evidence of internal metastases.

Treatment.—This rarely presents any difficulties, except on account of the size of the tumour and its inaccessibility. The tumour usually shells out quite readily when once the capsule has been incised. Some large pharyngeal tumours may necessitate approach from the side of the neck by a lateral pharyngotomy.

BIBLIOGRAPHY.—¹ G. B. New, *Mayo Clinic Reports*, 1912-1918. ² Wood, *Annals of Surgery*, 1904. ³ Verholf, *S. Med. Res.*, 13. ⁴ J. C. Da Costa, *Modern Surgery*, Ed. 8, Philadelphia, 1919. ⁵ Dembrowski, *Deutsche Zeitschrift. für Chirurgie*, 32, 1891. ⁶ Martin, *International Clinic*, 4, 1918. ⁷ Sturgis, *Surg. Gynæ. Obst.*, 18, 456-459, 1914. ⁸ Kaufmann, *Langenbeck's Archiv. f. Chirurgie*, 26. ⁹ Wartmann, *Diss.*, Strasburg, 1879. ¹⁰ Volkmann, *Deutsche Zeitschrift. f. Chirurgie*, p. 41. ¹¹ Collet, *Centralblatt f. Allg., Pathologie*, 1896, and *Thesis*, Paris, 1894. ¹² Pittance, *Thesis*, Paris, 1900. ¹³ Hinsberg, *Deutsche Zeitschrift. f. Chirurgie*, 51. ¹⁴ Krompecher, *Zeigler's Beiträge, z. Path. Anat.*, 28, 37, 44. ¹⁵ Fraser, *Surg. Gynæ. Obst.*, p. 19, No. 27, 1918. ¹⁶ Ewing, *Neoplastic Diseases*. ¹⁷ Gabourd, *Gaz. des Hôpitaux*, lxi., 650, Paris, 1888.