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CASE REPORT

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Melanin pigmented oncocytic metaplasia of the nasopharynx

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Abstract A 64-year-old man presented with a history of discomfort of the throat of a few weeks' duration. Nasoscopic examination revealed multiple small, brown pigmentations at the left suprapharynx, the base of the left nasal cavity and the pharyngeal openings of the auditory tube on both sides. Microscopically, the lesion showed a glandular pattern of oncocytic epithelium with abundant pigmented granules and melanophages in the surrounding stroma. Immunohistochemically, the dendritic cells in the basal layer were positive for S-100 protein. Electron microscopic study revealed numerous fully melanized melanosomes and hypertrophied mitochondria in the oncocytic cells. Oncocytic cells do not produce melanin for themselves, melanin granules apparently being transferred from the adjacent dendritic cells to the oncocytic cells.

Key words Melanin · Oncocytic metaplasia · Nasopharynx · Electron microscopy

Introduction

Oncocytic metaplasia and hyperplasia of the seromucinous glands (minor salivary glands) is a rare tumour-like lesion in the upper respiratory tract [7]. Most such lesions are asymptomatic and are discovered incidentally during endoscopic examination for another disease, and it is rare for them to show melanin pigmentation. They are then usually referred to as melanotic oncocytic metaplasia of the nasopharynx or as a pigmented variant of benign oncocytic lesion of the pharynx [3, 8]. This paper describes a case of melanin-pigmented oncocytic metaplasia.

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Clinical history

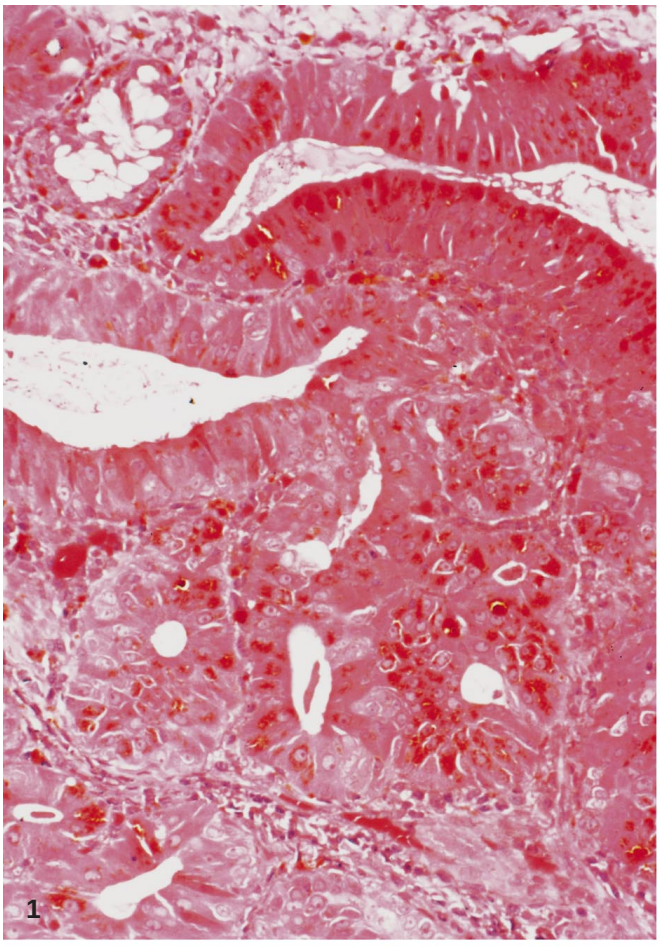
A 64-year-old Japanese man presented with a history of discomfort of the throat that had gone on for several weeks. He was otherwise in good health and had been taking no medicine regularly for the past few years. Nasoscopic examination revealed multiple small, flat elevations with brown discoloration, measuring up to a few millimetres in diameter. Pigmented lesions were found bilaterally around the pharyngeal openings of the eustachian tubes, the left suprapharynx and the base of the left nasal cavity. A malignant tumour was suspected on macroscopic examination. The lesions were biopsied twice: one biopsy was prepared for routine microscopic examination, and the other for electron microscopy.

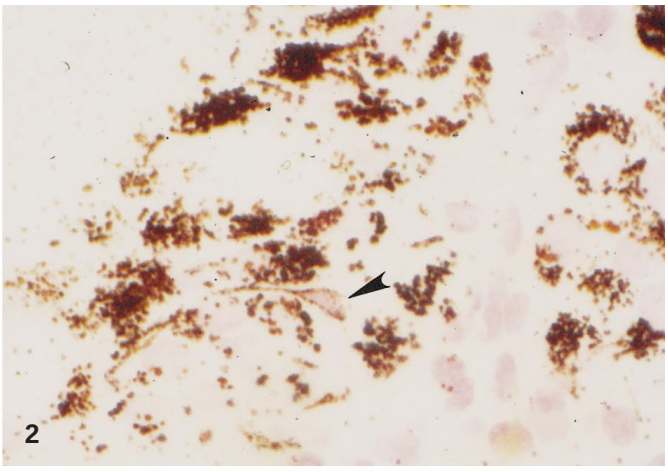
Pathological findings

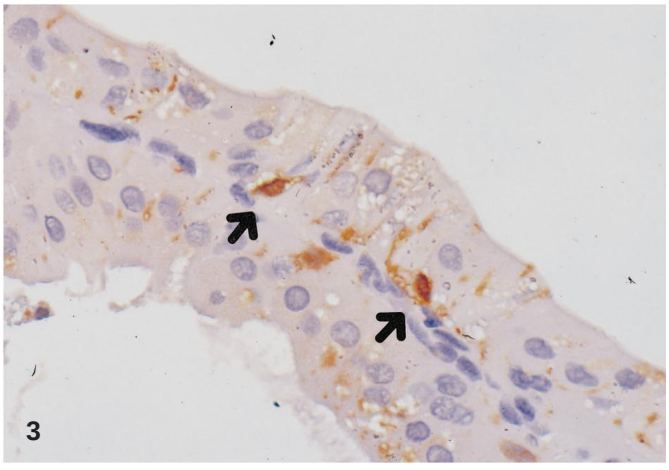
For histological study, the tissue was fixed in 10% neutral buffered formalin, embedded in paraffin and stained with haematoxylin and eosin.

The surface of the lesion was covered with normal respiratory epithelium. Oncocytic cells with abundant eosinophilic cytoplasm were arranged in a tubular and microcystic pattern. The nuclei were small and pyknotic. Numerous brown granules were found in the cytoplasm of oncocytic cells (Fig. 1), and there were many melanophages in the stroma surrounding the oncocytes. The brown granules were also scattered in the respiratory epithelium of the surface. The granules were positive for Fontana-Masson staining, and negative for Berlin blue staining. They were bleached after potassium permanganate and oxalic acid treatment. Fontana-Masson staining revealed a few dendritic cells in the basal layer row of oncocytes (Fig. 2).

For immunostaining, paraffin-embedded thin sections were prepared after bleaching, and the streptavidin-biotin peroxidase complex method was applied using a SAB-PO kit (Nichirei, Tokyo, Japan). Antibodies against S-100 protein (Dako, Glostrup, Denmark; dilution, 1:500) were used. A few dendritic cells in the basal layer of oncocytes were positive for S-100 protein (Fig. 3). Small pieces of biopsied specimen were fixed in 2.5% glutaraldehyde, post-fixed in 1% osmium tetroxide solu-







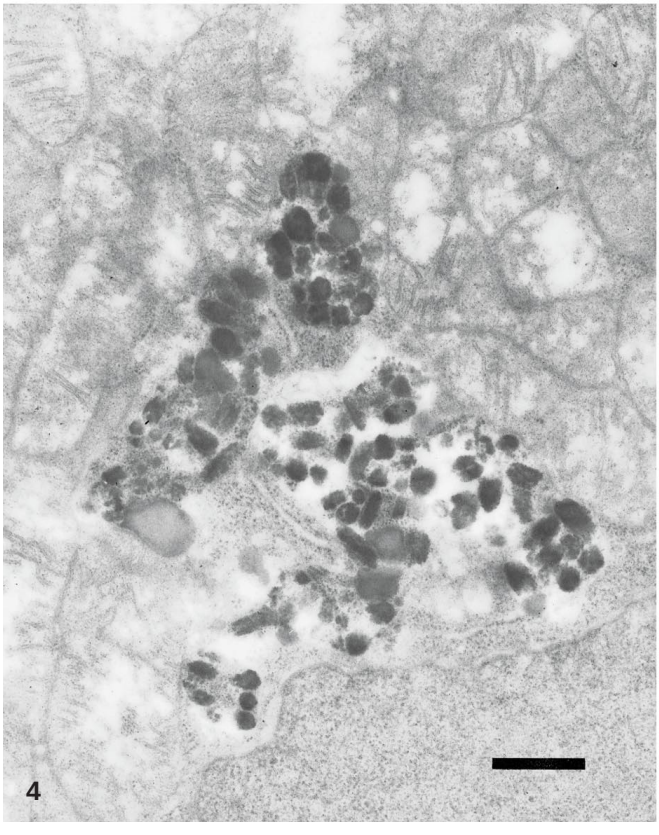


Fig. 1 Oncocytic ducts arranged in a glandular and cribriform pattern with a large amount of pigmented granules. Haematoxylin-eosin, ×220

Fig. 2 Fontana-Masson staining, showing black granules in oncocytes and a nucleus of dendritic cell (*arrowhead*) in the basal layer row of oncocytes. ×850

Fig. 3 Dendritic cells in the basal layer, showing immunoreactivity for S-100 protein (*arrows*). ×530

Fig. 4 Electron micrograph showing numerous hypertrophic mitochondria with denser melanosomes. ×23,000, *bar* 500 nm

tion, and then embedded in Epon 812. After staining with uranyl acetate and lead citrate, ultrathin sections were observed with a JEOL JEM-200CX electron microscope (JEOL, Tokyo, Japan). Oncocytic cells contained numerous hypertrophied mitochondria with generally clear matrices and numerous denser melanosomes (Fig. 4). However, oncocytic cells did not contain premature melanosomes (premelanosomes), which have the characteristic transverse striations and zigzag pattern.

Discussion

Oncocytic metaplasia and hyperplasia are characterized by the replacement of ducts and acini of seromucinous glands by cells with abundant brightly eosinophilic granular cytoplasm [2, 7]. Oncocytic metaplasia in salivary glands and the upper respiratory tract is common. The percentage of the population with focal oncocytic metaplasia increases with age, and oncocytes are present in the larynx in approximately 80% of people over the age of 50 [4, 5]. The feature peculiar to this case is the presence of melanin pigment in the oncocytes. These pigmented oncocytic lesions have been described as melanotic oncocytic metaplasia or a pigmented variant of benign oncocytic lesion, and three cases have been reported in the literature [3, 8]. All cases, including ours, have been in men. The average age of the patients was 66 years, and all were in their sixties. Symptoms included otitis media and tinnitus, and in all reported cases the condition pursued a benign clinical course.

Dendritic melanocytes were found in the nasal cavity and the larynx [1, 9]. Melanocytes were distributed in the stroma of the propria mucosa beneath the columnar epithelium and the squamous epithelium, and in the pseudostratified columnar epithelium. Oncocytes are unlikely to produce melanin, and melanocytes can transfer melanin to adjacent keratinocytes in the epidermis [6]. In this case, electron microscopy identified no premature melanosomes in the oncocytes, so that we assume the melanin pigment in oncocytes had been transferred from the adjacent dendritic melanocytes in the basal layer of oncocytes. The presence of pigment-laden melanophages in the surrounding stroma is probably due to the inability of oncocytic cells to accept more melanin granules. This transfer of melanin seems to occur after the onset of oncocytic metaplasia; little melanin pigment was present in the normal respiratory epithelium. It is possible that oncocytic cells produce a migration factor and trophic substances that stimulate melanin production of the melanocytes.

It is possible that these lesions might be clinically misdiagnosed as malignant tumours, and especially as malignant melanoma, because of their pigmentation. However, they are usually quite small, and the growth potential seems to be limited. Simple excisional biopsy is usually a sufficient treatment, and extensive surgery should be avoided.

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