MALIGNANT MELANOMAS OF THE UPPER RESPIRATORY TRACT

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SYNOPSIS

Malignant melanomas of the upper respiratory tract are rare tumours. There were 5 cases of primary melanomas of the upper respiratory tract in our series. They were collected from the Singapore Institute of Pathology over a 21 year period (1950-1970). Of these cases, three arose from the nasal cavity, one from the maxillary sinus and one from the nasopharynx.

The ratio of malignant melanomas of the nasal cavity and sinus to skin melanomas was appreciably higher in Singapore than in Western countries, this however is probably due to the low incidence of skin melanomas in Singapore. Approximately two percent of all cancers of the nasal cavity and sinuses were malignant melanomas. The age—standardised incidence of malignant melanoma of the nasal cavity and sinuses in Singapore was 0.10 per 100,000 per year for males and 0.03 per 100,000 per year for females. There was only one case of nasopharyngeal melanoma in this series; one other well documented and acceptable case was found in the literature.

Malignant melanomas may arise in any organ or tissue in which melanocytes are found. Consequently, while an overwhelming majority of these neoplasms are found in the skin, they are also found in the eye (choroid plexus and ciliary body), mucous membranes of the head and neck, vagina, vulva, penis, anorectal region, oesophagus, gall bladder, adrenals and leptomeninges (Attie and Khafif, 1964; Evans, 1966). The upper respiratory tract, comprising the nasal cavity, paranasal sinuses, nasopharynx and larynx, is rarely the site of this malignancy. This report is based on the histopathological records of the Singapore Institute of Pathology over a 21 year period (1950-1970). Apart from the rarity of melanomas of the upper respiratory tract, it was of interest to investigate their frequency in Singapore in view of the high frequency of cancers of the upper respiratory tract and the relatively low frequency of melanomas in this country.

METHOD

The main types of cancers of the upper respiratory tract were ascertained by analysis of the biopsy and necropsy records of the Singapore Institute of Pathology between 1950-1970. Subsequently, the histological sections of all cases reported as melanomas, sarcomas and tumours of doubtful histogenesis were reviewed. The sections were from paraffin blocks of formalin fixed tissues and were stained with haematoxylin and eosin, Fontana's method for melanin and Perl's method for iron pigment. The diagnosis of malignant melanoma was based on the cytological features, infiltrative nature of the neoplasms and the presence of intracellular melanin pigment.

Comprehensive cancer registration in Singapore began in 1968 but the Singapore Institute of Pathology has maintained, since 1947, a register of all histologically diagnosed cancer cases (biopsy and necropsy) in the Singapore population. The relative frequency of melanomas of the nasal cavity and paranasal sinuses was calculated as a percentage of all cancers arising from the region and as a ratio to skin melanomas. Minimum incidence levels, adjusted to world population (Doll *et al*, 1970), were calculated for the 1967-1970 period by referring the histologically diagnosed cases to the 1970 census population.

RESULTS

There were five cases of melanoma of the upper respiratory tract in our series. There were two additional cases in which melanomas of the nasal cavity were found in patients with melanomas of the lacrimal sac and big toe respectively. These cases were not included in our series as the possibility of their being secondary tumours cannot be excluded.

The relative frequency of malignant melanomas of the upper respiratory tract compared to other cancers in this region is shown in Table I. 2% of all primary cancers of the nasal cavity and sinuses were malignant melanomas. There was only one case of melanoma of the nasopharynx compared to 2,241 cases of nasopharyngeal cancers.

The age, sex, race and clinical features of the cases are shown in Table II. Of the five cases in our series, there were 3 males and 2 females. They were from the middle and older age groups, the youngest being 46 years and the oldest 73 years with a mean age of 60 years. Three cases arose from the nasal

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TABLE I

MALIGNANT TUMOURS OF THE UPPER RESPIRATORY TRACT IN SINGAPORE

Site	1950 - 1970					
	All Cancers			Malignant Melanoma		
	M	F	Total	M	F	Total
Nasal cavity and sinuses	141	61	202	3	1	4 (2%)
Nasopharynx	1619	622	2241	—	1	1
Larynx	422	38	460	—	—	—

TABLE II

CLINICAL DATA

Patient	Sex	Age	Race	Location of Primary	Presenting Symptoms	Course
LSH 10.3.56	M	46	Chinese	Left nasal vestibule	Swelling left nose and epistaxis	No follow up
TKS 31.7.67	M	51	Chinese	Left inferior turbinate of nasal fossa	3 months history of nasal obstruction and epistaxis	Defaulted treatment
KKC 4.2.69	M	70	Chinese	Posterior end of right inferior and middle turbinates	Few months history of nasal obstruction and epistaxis	3 months after biopsy tumour infiltrated into naso-orohypopharynx. Cervical lymph nodes enlargement and metastatic nodules on chest wall were noted 2 months later.
KTH 9.6.70	F	58	Chinese	Left maxillary sinus	Enlargement of left cervical lymph nodes and ulcerating mass in the upper alveolar margin	Surgical excision of tumour and block dissection of neck done. 5 months later, tumour spread to nasopharynx and hard palate. Radiotherapy given. Patient still alive.
LCK 11.6.70	F	73	Chinese	Nasopharynx	3 months history of nasal obstruction and epistaxis	Given 1 course radiotherapy. Defaulted further treatment.

NB Dates shown beside patient's initials denote date of biopsy.

cavity, one from the maxillary sinus and one from the nasopharynx; there were no cases from the larynx. Of the 3 cases from the nasal cavity, one originated from the nasal vestibule and two from the turbinates.

Clinically, melanomas of the nasal cavity presented with nasal obstruction and epistaxis. Enlarged cervical lymph nodes and an ulcerating mass of the upper alveolar margin were the presenting symptoms of the melanoma from the maxillary sinus. The tumour from the nasopharynx presented with epistaxis and nasal obstruction. The follow-up of these cases were regrettably inadequate as most of the patients defaulted treatment early.

Pathology

Macroscopically, these neoplasms were mostly friable, pigmented tumour masses. Three were haemorrhagic and one was secondarily infected. The degree of pigmentation varied, the majority were dark and black while one case was a pinkish tumour.

The microscopic appearance of the neoplasms in our cases was not unlike melanomas of the skin. They were mostly arranged in sheets of cells and as interlacing bundles; an alveolar pattern was seen in one case. The tumour was highly cellular with little supporting tissue. In three cases, the tumour cells were spindle-shaped and presented a sarcomatous appearance (Fig. 1). In one case, the cells were rounded and discrete (Fig. 2). Epitheloid cells formed the majority of cells seen in the remaining case (Fig. 3). Cellular pleomorphism, variation in nuclear size and shape, increased nuclear cytoplasmic ratio, plentiful mitotic figures and varying amounts of intracellular melanin pigment were noted in all cases.

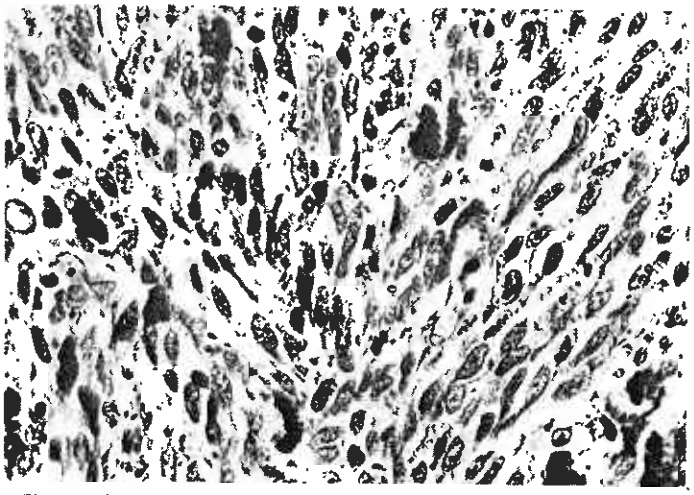

Fig. 1. Spindle-shaped tumour cells containing intracytoplasmic melanin pigment. Mag × 500.

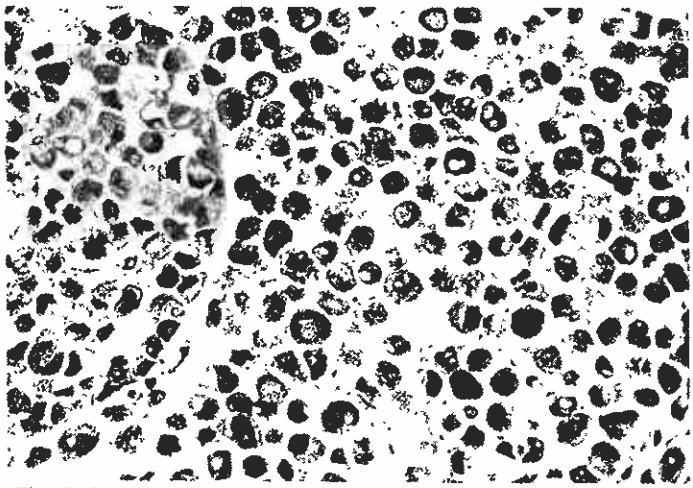

Fig. 2. Round Polygonal tumour cells containing intracytoplasmic melanin pigment. Mag × 500.

DISCUSSION

The upper respiratory tract melanomas are conveniently discussed according to their sites of origin.

(i) Malignant melanomas of the nasal cavity and paranasal sinuses.

(ii) Malignant melanomas of the nasopharynx.

(iii) Malignant melanomas of the larynx.

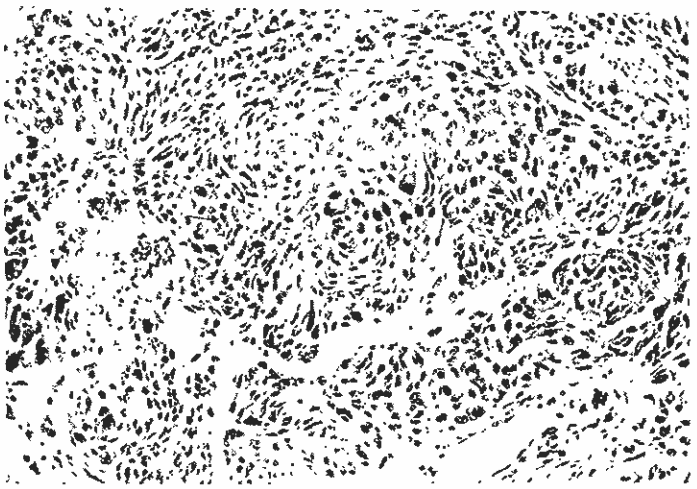

Fig. 3. Epitheloid shaped cells of malignant melanoma with scanty melanin pigment. Mag × 150.

Malignant melanomas of the nasal cavity and paranasal sinuses.

Malignant melanomas of the nasal cavity and paranasal sinuses are rare tumours. A total of 229 cases have been reported in the world literature up to 1969. In 1960, Ravid and Esteves reviewed 118 cases in the literature. Their review, however, included many cases which were poorly documented and lacking in histological details. Between 1960-1969, there were 77 well documented cases. These were reviewed by Holdcraft *et al* (1969). In their paper, they presented a series of 39 additional cases from the records of the Armed Forces Institute of Pathology. Hormia *et al*, in 1969 presented 5 cases from Finland which were not included in previous reviews; they were all histologically proven.

In this series, there were 4 cases of malignant melanoma of the nasal cavity and sinuses. During the same 21 year period, 94 cases of skin melanomas were diagnosed (Singapore Cancer Registry, Unpublished data). The ratio of melanomas of the nasal cavity and sinuses to skin melanoma is 1:24 in Singapore. This ratio could be used to compare the relative frequency of melanomas of nasal cavity and sinuses between different series. The ratios of other series are shown in Table III. The ratio in Singapore

TABLE III

RATIO OF MALIGNANT MELANOMA OF NASAL CAVITY AND SINUSES TO SKIN MELANOMA BETWEEN DIFFERENT SERIES

Author/Country	Malignant Melanoma		
	Nasal cavity + sinuses	Skin	Ratio
Pantazapoulos (Greece)	2	142	1 : 71
Hormia (Finland)	5	1047	1 : 209
Allen + Spitz (U.S.)	10	835	1 : 84
This series (Singapore)	4	94	1 : 24

when taken to compare with ratios from other series, all of which came from Western Countries, tend to show a higher frequency of this neoplasm relative to that of skin melanomas. However, the incidence of skin melanomas in Singapore, age adjusted to world population, is 0.7 per 100,000 per year for males and 0.1 per 100,000 per year for females (Singapore Cancer Registry, Unpublished data). The corresponding figures in Finland are 2.4 for males and 2.0 for females (Doll *et al*, 1970). In the light of this, it is not possible to conclude that the incidence of melanomas from the nasal cavity and sinuses is higher in Singapore than in other series.

The incidence of malignant melanoma of the nasal cavity and sinuses in Singapore, adjusted to world population, was 0.10 per 100,000 per year for males and 0.03 per 100,000 per year for females for the period 1967-1970. Unfortunately, incidence levels of this neoplasm are not available from any other country to permit a direct comparison.

In our series there were 3 males and 1 female. Their ages ranged from 46-70 years with a mean age of 56 years. This was similar to the series by Holdcraft *et al* (1969) which consisted of 24 males and 15 females; their ages ranged from 17-84 years with a mean age of 61 years. Mason and Freedman (1955) recorded 11 cases of which 8 were males and 3 females, their ages ranged from 41-70 with a mean of 57 years.

All cases in our series were Chinese. However this should not be taken to reflect a racial predisposition as Chinese formed 74.4% of the population in Singapore (Singapore Yearbook 1969). Malignant melanomas of the nasal cavity and sinuses have been described in Caucasians, Negroes, Orientals and Indians (Holdcraft *et al*, 1969; Hormia *et al*, 1969; Kacker *et al*, 1965; Moore *et al*, 1955; Pantazapoulos, 1965; Ravid *et al*, 1960).

Malignant melanomas occur more commonly in the nasal cavity than in the sinuses. Catlin (1967) reported 9 cases from the paranasal sinuses (6 maxillary, 2 ethmoid and 1 frontal) as compared to 13 from the nasal cavity. There were 7 cases from the sinuses (4 maxillary, 2 ethmoid and 1 frontal) and 21 cases from the nasal cavity in the series by Holdcraft *et al*, 1969. Thus for the paranasal sinuses, the sites of origin of this neoplasm in order of frequency are: maxillary sinus, ethmoid sinus and frontal sinus.

In the nasal cavity malignant melanoma will present itself no differently from other tumours. Because of its anatomical location, nasal obstruction and epistaxis are the common presenting symptoms (Allen *et al*, 1953; Holdcraft *et al*, 1969; Hormia *et al*, 1969; Pantazapoulos, 1965). The tumour is highly malignant and disseminates widely. Holdcraft *et al* (1969) reported that of 31 cases the survival from time of biopsy averaged 30 months with a range of 6 days—8 days. 26 of the 31 cases died of metastatic disease; metastases were found in the lungs, brain, lymph nodes, adrenal, liver and skin.

Malignant melanomas of the nasopharynx

The nasopharynx is an exceptionally rare site of origin for malignant melanomas. It was only in 1967 that the presence of melanocytes in the nasopharynx was reported by Ali. In the literature, we found only one well documented and histologically proven case of nasopharyngeal melanoma (Pande, 1970). Two other cases were reported but they were poorly documented lacking photomicrographs and histological details (MacComb *et al*, 1967; Vaeth, 1960).

This neoplasm is located in a rather inaccessible region and it is conceivable that cases of nasopharyngeal melanomas were missed despite the rarity of this tumour. An examination of the nasopharynx would be indicated in cases of metastatic melanoma where no other primary focus is identified.

Melanoma of the nasopharynx is very rare in Singapore although the incidence of nasopharyngeal carcinomas is among the highest in the world. During the 21 year period, there was only one case of malignant melanoma as compared to 2,241 cases of nasopharyngeal carcinomas. The aetiological factor or factors that may be responsible for nasopharyngeal carcinoma are probably not operative in malignant melanoma.

Malignant melanoma of the larynx

There were no cases of primary laryngeal melanoma in this series. Reports of these rare neoplasms (Loughead, 1952; Moore *et al*, 1955; Vuori, 1969) indicate that there are no distinctive pathological features and that the symptomatology is not unlike other cancers of the larynx.

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