

Malignant melanoma of the nasal cavity : a difficult case to diagnosis and determine primary or metastasis

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A 65-year-old man was presented with a unilateral nasal mass and repeated epistaxis. The histopathologic features of the nasal mass, which very mimics olfactory neuroblastoma and epithelioid schwannoma, are described. The various immunohistochemical and electron microscopic studies play important roles for confirmation of the diagnose as Malignant melanoma of the nasal cavity. We†also†discuss†the difficulty to determine whether it is primary or malignant melanoma. The final diagnosis in this case is primary nasal melanoma.

Key word: *Malignant melanoma.*

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ยากในการวินิจฉัยและกำหนดว่าเป็นชนิดปฐมภูมิ หรือแพร่กระจายมาจากที่อื่น.
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ผู้ป่วยชายไทย อายุ 65 ปี มีก้อนในโพรงจมูกข้างซ้าย และมีเลือดกำเดาออกหลายครั้ง ผล
การตรวจทางจุลพยาธิ พบมีลักษณะซึ่งใกล้เคียงกันมากระหว่างไฝมะเร็ง (*malignant melanoma*)
กับ *olfactory neuroblastoma* และ *epithelioid schwannoma* มีการนำอิมมูโนฮิสโตเคมีหลายๆ
ชนิด และจุลทรรศน์อิเล็กตรอน มาช่วยสนับสนุนในการวินิจฉัยว่าเป็นไฝมะเร็งของโพรงจมูก นอก
จากนี้จะได้อภิปรายถึงข้อสรุปที่คิดว่าเป็นปฐมภูมิ (*Primary*) มากกว่าเป็นชนิดที่แพร่กระจายมา
จากที่อื่น (*Metastasis*)

Primary malignant melanoma of the nasal cavity and paranasal sinuses is an uncommon tumor, accounting for only 0.5 - 2 % of all malignant melanomas.⁽¹⁾ Metastatic mucosal melanoma is extremely rare. Only 0.6 to 9.3 % of patients with cutaneous malignant melanoma will have metastases to the mucosa of the upper aerodigestive tract. These arose from a variety of cutaneous sites including the trunk and extremities and, in most instance, do not arise until 2 to 7 years after the initial cutaneous lesion. Most patients with metastases to the head and neck mucosa had disseminated disease. These two groups were compared for differences in clinical symptoms, histopathologic findings, treatment and survival rates.⁽²⁾

Case report

A 65-year-old man was presented to Chulalongkorn Hospital in January, 1996 with a unilateral nasal mass and repeated epistaxis. Examination of the left nasal cavity revealed a blue mass at nasal septum about 1 cm in diameter with active bleeding. The right nasal cavity and other systems were within normal limits. The supportive treatment consisted of anterior nasal packing in order to stop the bleeding. Later the excisional biopsy was performed.

Upon pathological examination, the specimen was found to consists of two pieces of light brown tissue measuring 0.5 x 0.5 x 0.4 cm and 0.4 x 0.3 x 0.2 cm. These were fixed in 10 % formalin and then embedded in paraffin. Sections were stained with hematoxylin and eosin (H & E), Fontana masson with and without bleach, and Prussian - blue. Sections of the paraffin - embeded tissue were also processed by

the peroxidase - antiperoxidase (PAP) indirect immunohistochemical method using unlabeled antibodies to neurofilament (NF), glial fibrillary acidic protein (GFAP), cytokeratin, vimentin, S-100 protein and HMB-45.

Microscopically, the sections of the nasal mass showed focal ulceration of surface stratified squamus epithelium. There was no junctional activity. The subepithelial layer displayed the nests of tumor cells infiltrating diffusely in the loosening myxomatous stroma and also frequently situated surrounding the proliferating blood vessels. They were medium to large tumor cells showed moderate displayed pleomorphism. The nuclear features showed a distinct nuclear border, with 1 to 2 conspicuous round and large nucleoli. Abundant golden brown pigment was seen in the plentiful clear to acidophilic cytoplasm. Few mitotic figures were present. There were scattered foci of hemorrhage and necrosis (Fig.1). The Fontana masson stain disclosed considerable pigment in the cytoplasm of the tumor cells which disappeared after bleaching. Hemosiderin, was scanty demonstrated by Prussian blue stain. The immunohistochemical study strongly and diffusely was positive for S-100 protein, vimentin and HMB-45 (Fig 2). Neuro-filaments were positive in few tumor cells but proved negativc for GFAP and cytokeratin.

Tissue for electron microscopy (JEOL-1210) was washed and refixed in gluteraldehyde and then embedded in epoxy resin. Ultrastructurally, there were ellipsoidal stage-II melanosomes in the cytoplasm of the neoplastic cells. Clusters of large epithelioid cells with prominent compact nucleoli were present (Fig.3).

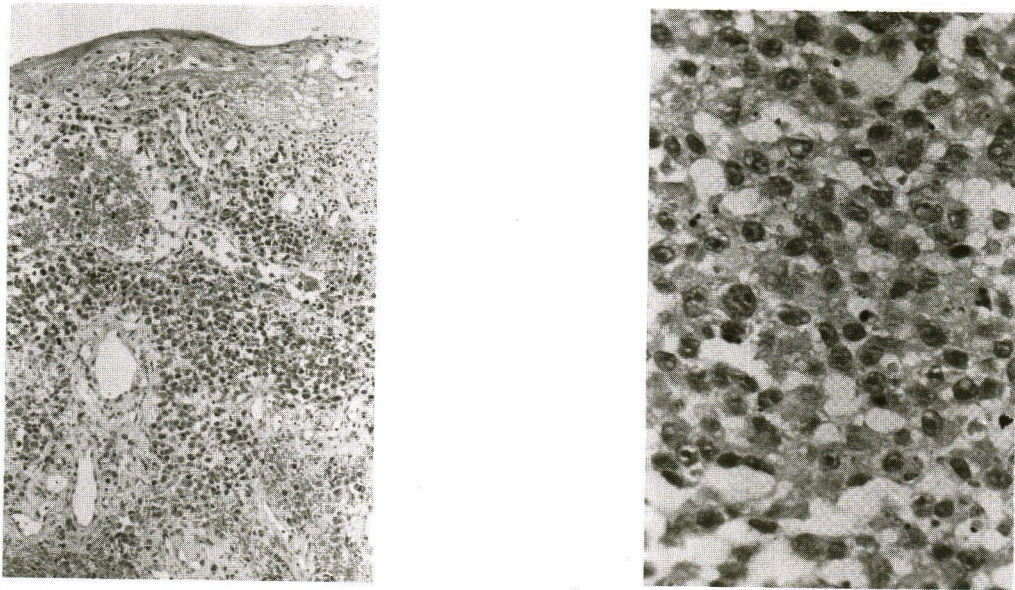
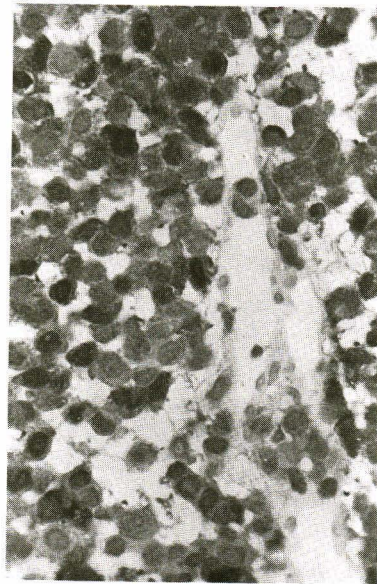
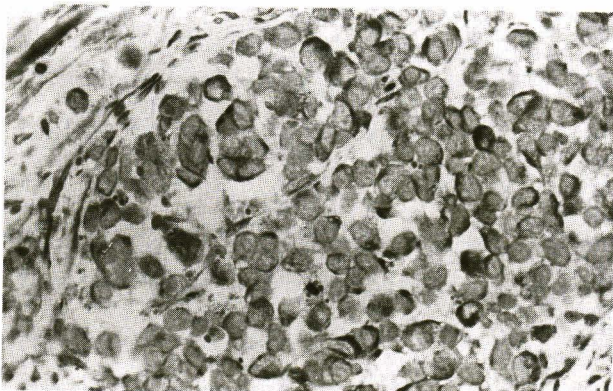


Figure 1. A. Photomicrograph showing intact lining epithelium without junctional activity. Tumor grows around blood vessels.(H & E x 100)
B. Tumor cells with pleomorphism, vesicular and distinct nucleoli. (H & E x 400)

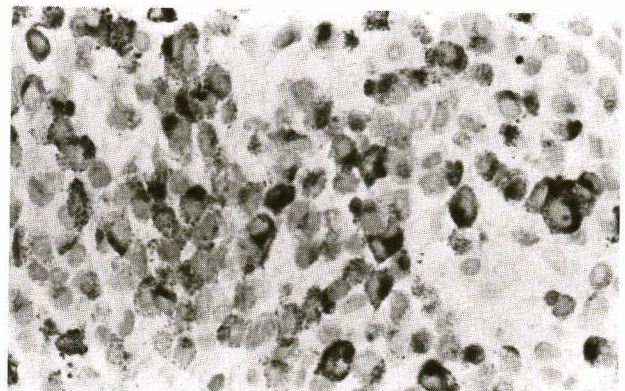
Figure 2. Tumor cells reactive to



(A) S-100 protein,



(B) vimentin,

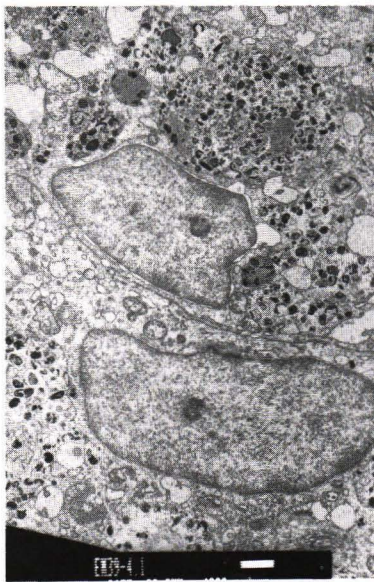


(C) HMB-45 (H & E x 400)

The final pathological diagnosis was malignant melanoma. The patient was thoroughly examined by chest roentgenograms, an abdominal sonogram, a computerized tomography scan and a

bone scan. The results were unremarkable. He was intended for further immunotherapy after the wide-excision but following the operation he was lost to follow-up.

Figure 3. Electron micrograph.



(A) Large epithelioid melanoma cells with prominent compact nucleoli and clusters of stage II melanosome. x 6000



(B) Ellipsoidal stage II melanosome with a striated core in the cytoplasm of a neoplastic melanocyte. x 45000

Discussion

According to his clinical features, we first diagnosed olfactory neuroblastoma (esthesioneuroblastoma). This occurs in both children and adults, with an average age of onset of about 50 years.^(3,4) While males and females are equally affected. But in the reported cases of nasal melanoma reveals equally in elderly males and females, though the older literature indicates a male predominance, with a median age of about 70 years.^(5,6) The predominant symptoms of olfactory neuroblastoma are nasal stuffiness,

epistaxis and typified by a unilateral mass which is similar to this case. In the malignant melanoma, the presenting symptom predilection is mass rather than bleeding. Two thirds of these melanoma are on the lateral nasal wall or septum.⁽⁷⁾

Histologically, pigmentation of the tumor is an important diagnostic criterion. This is addition to the growth pattern and architecture of the tumor cells which are helpful to differentiate malignant melanoma from olfactory neuroblastoma or epithelioid schwannoma. The feature of nests of tumor cells in

the loosening stroma and surrounding the blood vessels mimics neuroblastoma. In this type, melanin pigment may be found in the cytoplasm of the tumor cells. but the tumor size and background are different. The olfactory neuroblastoma discloses uniform small cells with round nuclei, scanty cytoplasm, indistinct nuclear membranes, and a prominent fibrillary or reticular background. Rosettes of the Homer Wright type may be found.⁽³⁾ Both malignant melanoma and olfactory neuroblastoma are very similar when are composed of medium size cells but the backgrounds are very different. The epithelioid schwannoma, the tumor cells arrange in sheets or cords of large polygonal cells with deeply eosinophilic cytoplasm. The immunohistochemistry is useful for identifying melanocytic differentiation.⁽⁹⁾ The neoplastic melanocytes are positive†for S-100 protein, vimentin and HMB-45, but they are usually negative for keratin, NF and GFAP.⁽³⁾ The olfactory neuroblastoma yields a positive reaction for keratin, NF and GFAP but the epithelioid schwannoma is reactive to S-100 protein and vimentin but negative for keratin and HMB-45.⁽⁹⁾ The electron microscopic studies, which is helpful the definite diagnosis in the current case, display clusters of epithelioid cells with large, centrally located, round compact nucleoli and stage-II melanosome.^(10,11) There is no evidence of neuroblast cell bodies, neuritic processes or neurosecretory granules which are found in cases of olfactory neuroblastoma.⁽¹²⁾

The histopathologic diagnosis of malignant melanoma is confirmed. We also discuss whether it

is primary or metastasis. Billings KR, et al, demonstrates the histopathologic distinctions between primary or metastasis mucosal melanoma. Junctional activity in the overlying or adjacent mucosa distinguishes primary mucosal melanoma from metastatic disease, in which the overlying mucosa is usually intact.⁽²⁾ In this case, the overlying mucosa was intact and possessed no junctional activity, thus on histologic criteria, it should have been a case of metastatic mucosal melanoma. Nevertheless, the complete physical examination and other investigations asserted no primary site, It was recommended that regression of primary lesion may be occur, but the complete regression is not common.⁽¹³⁾

From the aforementioned discussion, we conclude that metastatic mucosal melanoma is very rare and associated with no evidence of primary site. We prefer to diagnose of “primary malignant melanoma of the nasal cavity”. Guzzo M. et al. reported a series of 48 cases of malignant mucosal melanoma diagnosed from 1975 to 1990. There were 34 males and 14 females, and their ages ranged from 21 to 79 years (mean 58). The sites of origin of the tumor were the nasal cavity in 26 cases, the oral cavity in 15, the larynx in two, lip mucosa in two, the pharynx in two and the upper esophagus in one cases. From this series, the predilection of site of origin was the nasal cavity. The neoplasm was limited to the primary site in 60.4% of the patients.⁽¹⁴⁾ In more recent literature the tumor demonstrates a high rate of local recurrence and disseminated metastases. Five-year survival rates range from 0 % to 33 %.^(15,16)

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