Histol Histopath (1987) 2: **299-306**

Histology and Histopathology

Primary malignant melanoma of the nasal cavity: report of two cases and review of the literature

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Summary. Primary malignant melanomas of the nasal cavity are rare, as only 400 cases have been reported to date. The present paper describes two cases recently seen in Caucasian women. The authors point out the difficult clinical diagnosis, as the symptoms are rather aspecific. From the histopathological point of view, diagnosis is easy in the melanotic cases while can show interpretating problems in the amelanotic ones, when melanoma is almost indistinguishable from other malignant neoplasms. A correlation between histological grading and prognosis was not detected, as both cases showed local recurrences within one year after surgery although they were, respectively, of epithelioid and indifferentiated type. While surgery appears to be the choice treatment of the primary lesion, the treatment of cervical metastasis is still disputable. On the whole, most authors think that the role played by radio- and mainly chemo-therapy is still limited and that cervical adenopathies should be treated by a simple lympho-adenectomy rather than by a neck dissection.

Key words: Mucosal melanoma — Histopathological features — Differential diagnosis

Introduction

Primary malignant melanoma of the nasal cavity is infrequent. Nevertheless, it poses a number of anatomo-clinical problems as regards the aspecific symptomatology and morphological features, often superimposable on those observed in anaplastic carcinomas and sarcomas.

The hystogenesis also poses problems, as it is not always easy to define whether this tumor is a primary or secondary lesion. Prognosis, finally, is worse than for cutaneous localizations. The aim of the present paper is to discuss these points on the basis of two cases observed recently and data reported in the literature.

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Materials and methods

Case 1: L.L. a 70-year-old Caucasian female with a 3-year history of recurrent right epistaxis, nasal obstruction and blood stained nasal discharge. She had been treated in another hospital, two moths before, for a nasal septum haematoma, with no relief. The physical examination revealed a darkish fleshy polyp, ulcered in its peripheral portions, covered by bloody secretion, filling the right nasal fossa up to the choanal region. Radiology, including CT scan, revealed an opaque right fossa and maxillary antrum, destruction of the medial bony maxillary wall, involvement of the pterigo-maxillary fossa and ethmoidal labyrinth but no orbital involvement (Fig. 1a, b) (stage IA according to Conley and Hamaker, 1977). The E.S.R. was altered. The tumor, which seemed to originate from the maxillary and nasal fossa floor, was removed via lateral rhinotomy. The upper and middle turbinals were irregularly covered by darkish mucosa. After three months, cyclophosphamide treatment (1.4 gr intravenously every 3 weeks) was begun, as cervical adenopathies, dysphonia and dysphagia had occurred. One year after surgery, although the adenopathies were reduced, the clinical picture was almost unchanged and a recurrence in the maxillary antrum was detected (Fig. 2 a, b).

Case 2: R.R. a 59-year-old Caucasian female with a two-month history of recurrent left epistaxis but no nasal obstruction. This symptomatology had been referred to the anticoagulant treatment administered for a previous cardiosurgical operation. Physical examination revealed left esophthalmus and the presence, in the left nasal fossa, of a blackish friable tumor, bleeding on contact. Radiology, including CT scan, revealed an opaque left nasal fossa, maxillary antrum and ethmoidal labyrinth, with bone destruction only towards the orbit (Fig. 3). (Stage I according to Conley and Hamaker, 1977). E.S.R. was altered and a slight hypocromic anaemic state was detected. The tumor was biopsied and removed via lateral

rhinotomy. Orbit involvement was not confirmed. A local recurrence was detected after eight months, without cervical adenopathies.

Results

Case 1: The tumor was composed of polygonal cells with bulky vacuolated nuclei and prominent nucleoli (Fig. 4). In the cytoplasm several granules of pigment, positive with Masson-Fontana stain, were present. Cellular cohesion was scanty and some fibrovascular septa dividing the tumor mass into rough masses of malignant cells were present. Multinucleated giant tumor cells were abundant (Fig. 5), while mitotic figures were rare. The tumor had involved and destroyed much of the mucosa. Nevertheless, in some areas the tumor surface was preserved and covered by a squamous metaplastic epithelium, with aspects suggesting a

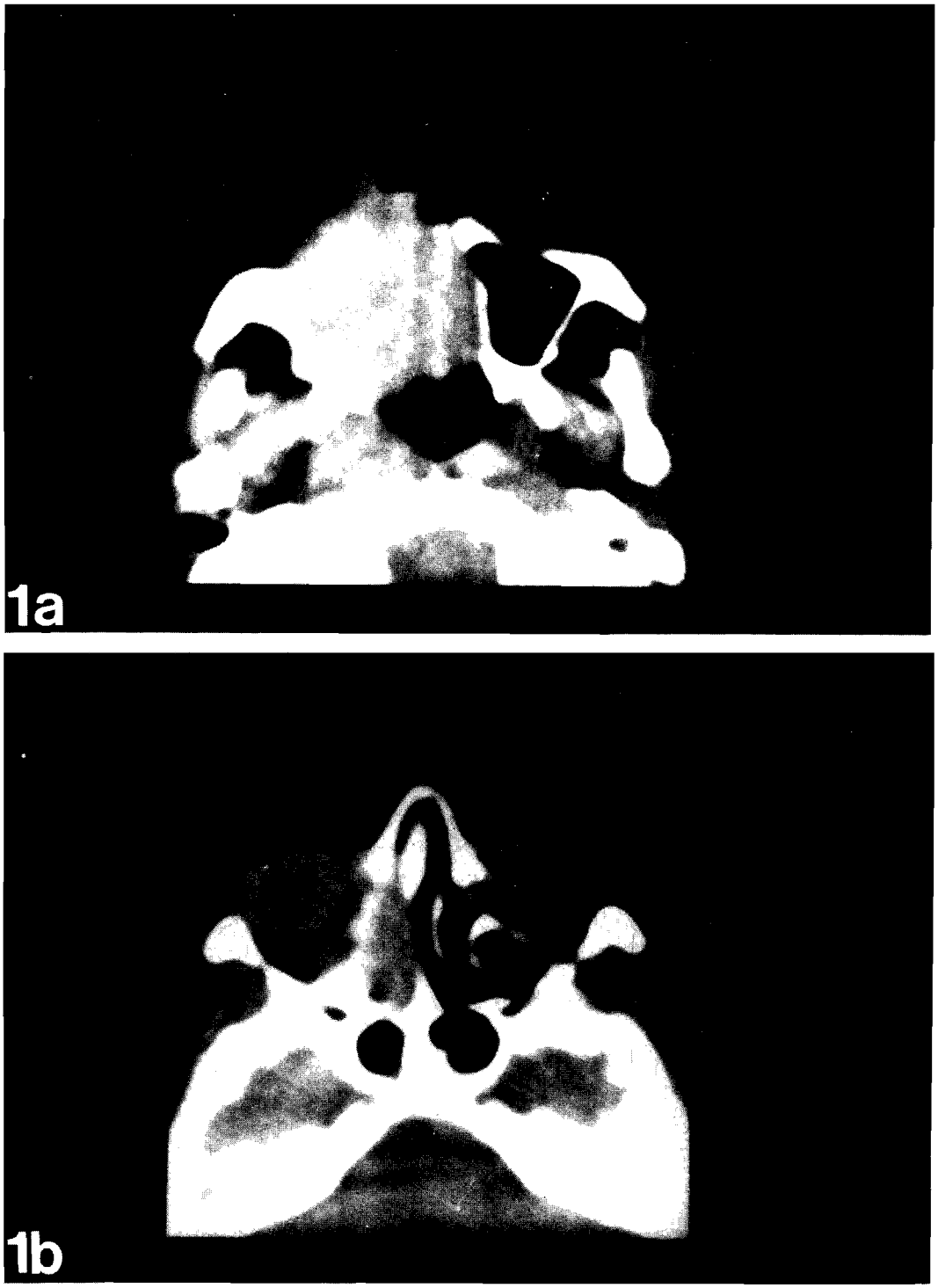

Fig. 1. L.L: Preoperative CT scan showing involvement of the right maxillary antrum, ethmoidal labyrinth and nasal fossae, with destruction of the right intersinusonasal wall (a). The infero-medial wall of the right orbit seems involved but no endo-orbital neoplastic tissue can be detected (b).

junctional activity (Fig. 6). The wall of the blood vessels was often infiltrated by neoplastic cells (Fig. 7). Inflammatory cells were rare. Respiratory epithelium adjacent to tumor showed chronic rhinitis with infiltration of the lamina propria by mononuclear cells; glandular and epithelial hyperplasia.

Case 2: The tumor was predominantly ulcered, necrotic and haemorrhagic, with very scanty cellular cohesion. Neoplastic cells varied greatly in size and shape (Fig. 8). Nucleoli were always present but true mitosis were rare. Nests of spindle cells were focally present. Intracytoplasmatic pigment was abundant and easily identifiable by the Masson-Fontana stain for melanin. On the whole, the pattern was anaplastic. The tumor surface contained some small areas of metaplastic squamous epithelium without ulceration, with aspects suggesting junctional changes (Fig. 9). Infiltration of the blood vessels was frequent but there was no inflammation

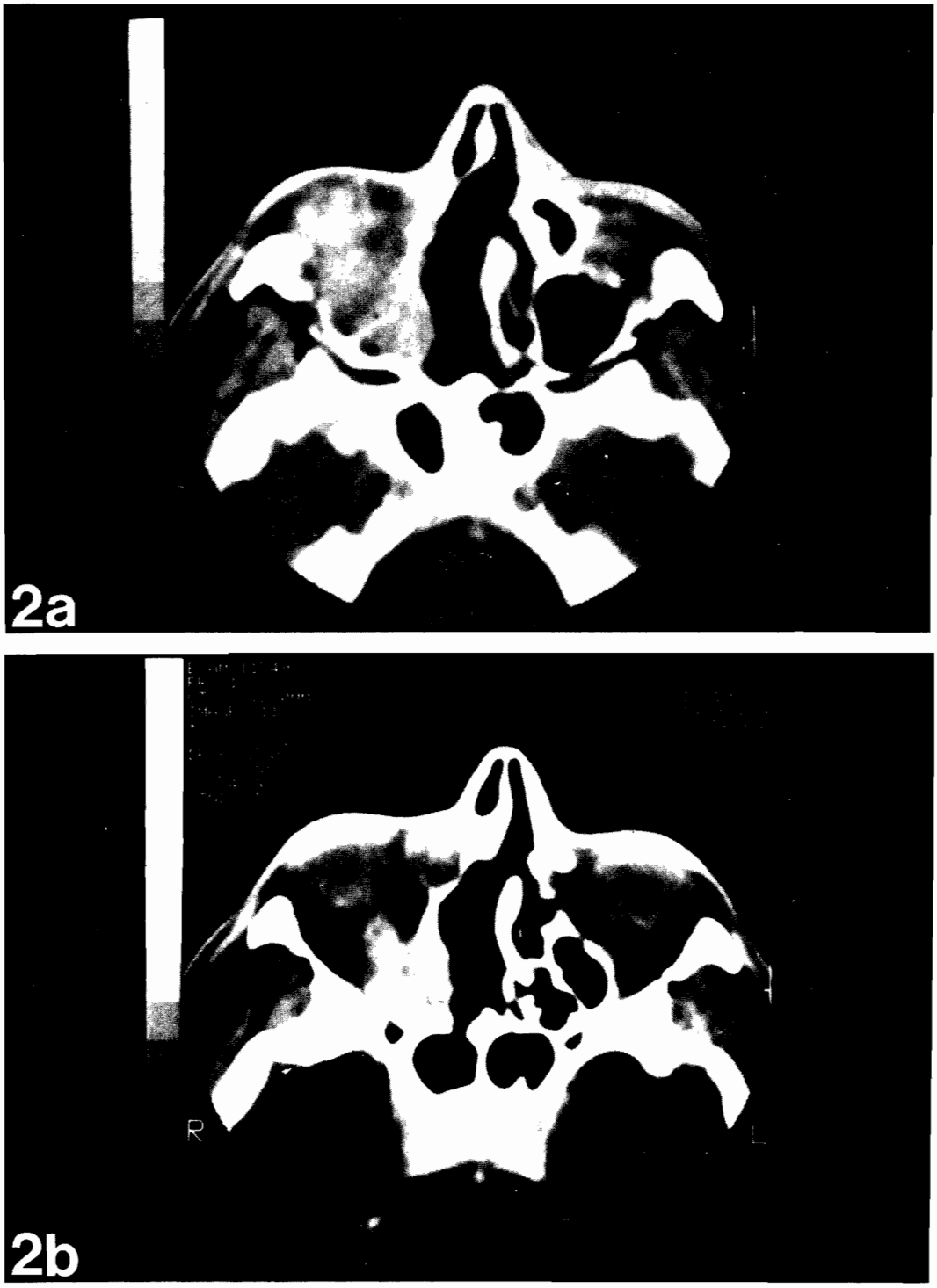

Fig. 2. L.L.: Follow-up CT scan showing the presence of neoplastic tissue in the right maxillary antrum (a), with involvement of the right orbit floor (b).

Fig. 3. R.R.: Preoperative CT scan showing a large mass involving the right maxillary antrum, ethmoidal labyrinth and nasal fossae.

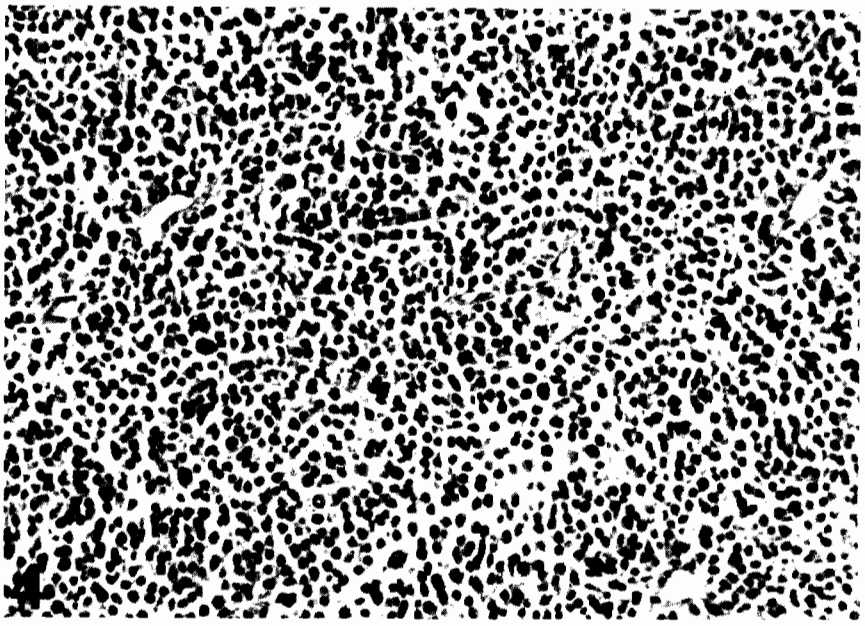

Fig. 4. Case n. 1 (L.L.) Nasal melanoma composed of small polygonal cells with a medullary pattern. H. and E. ×200

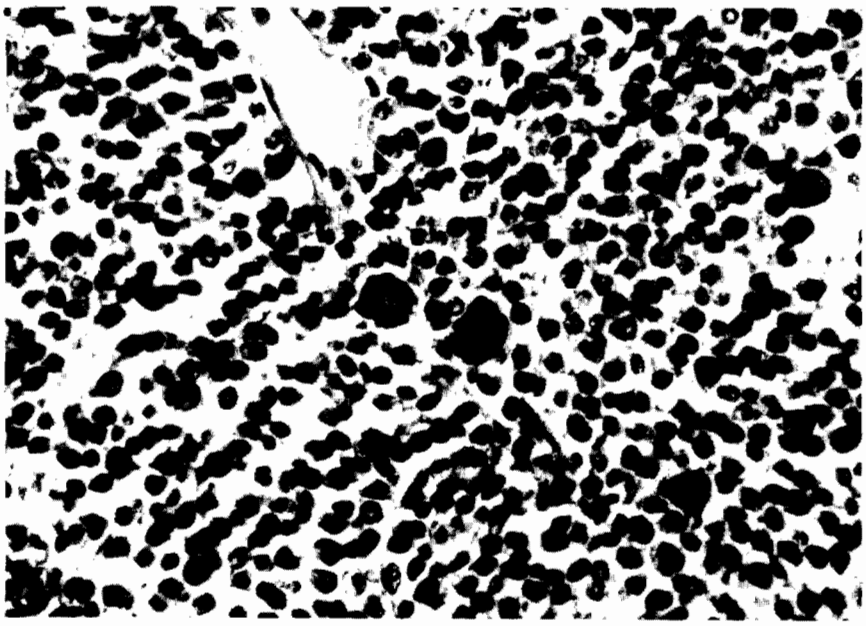

Fig. 5. Case n. 1 (L.L.). Several multinucleated giant cells are present among polygonal tumor cells. H. and E. x400

Table 1. Primary malignant melanomata of nasal cavities. Review of the main clinical series.

YEAR	AUTHORS	N. OF CASES
1960	Ravid and Esteves	118
1965	Pantazopoulos	10
1968	Mesara and Burton	12
1969	Holdcraft and Gallagher	77
1973	Freedman et al.	29
1976	Harrison	40
1979	Pearman	6
1982	Lund	36
1984	Berthelsen et al.	20
Total		348

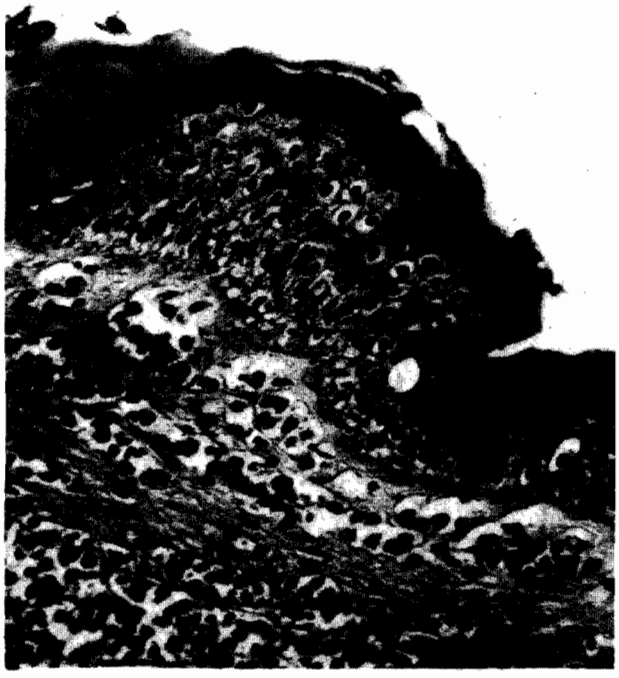

Fig. 6. Case n. 1 (L.L.). Aspects suggesting junctional changes in squamous metaplastic epithelium. H. and E. ×200

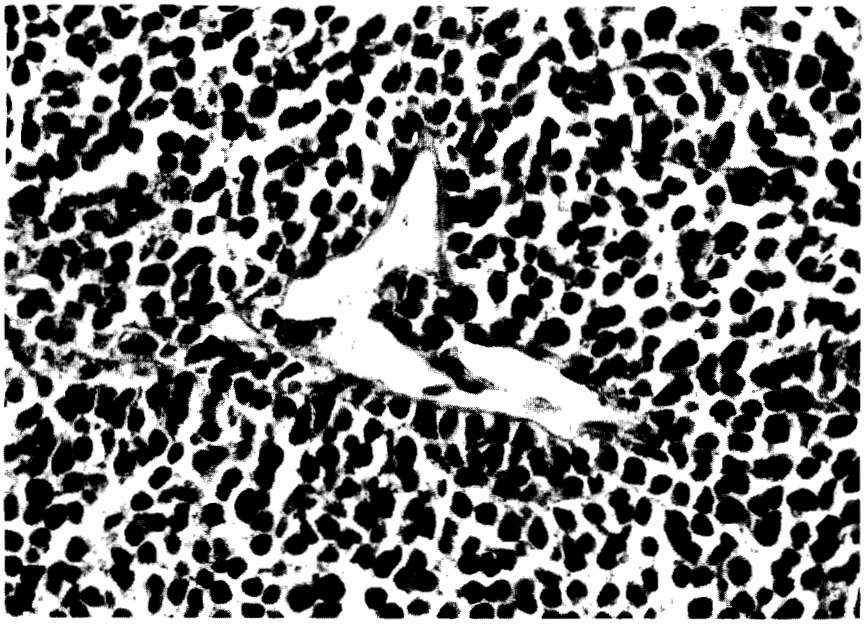

Fig. 7. Case n. 1. (L.L.).
Vascular infiltration.
H. and E. ×400

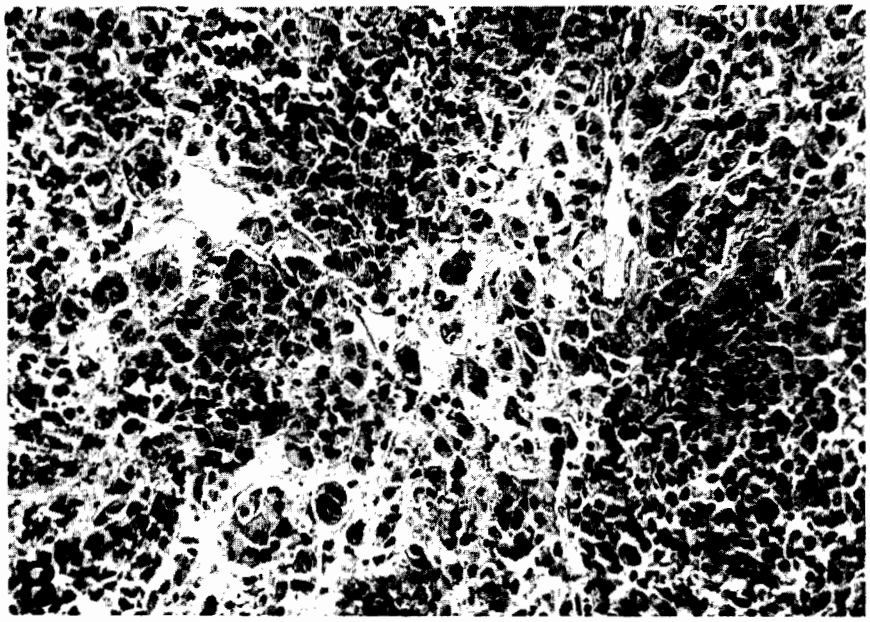

Fig. 8. Case n. 2. (R.R.).
Nasal melanoma composed of anaplastic cells.
H. and E. ×200

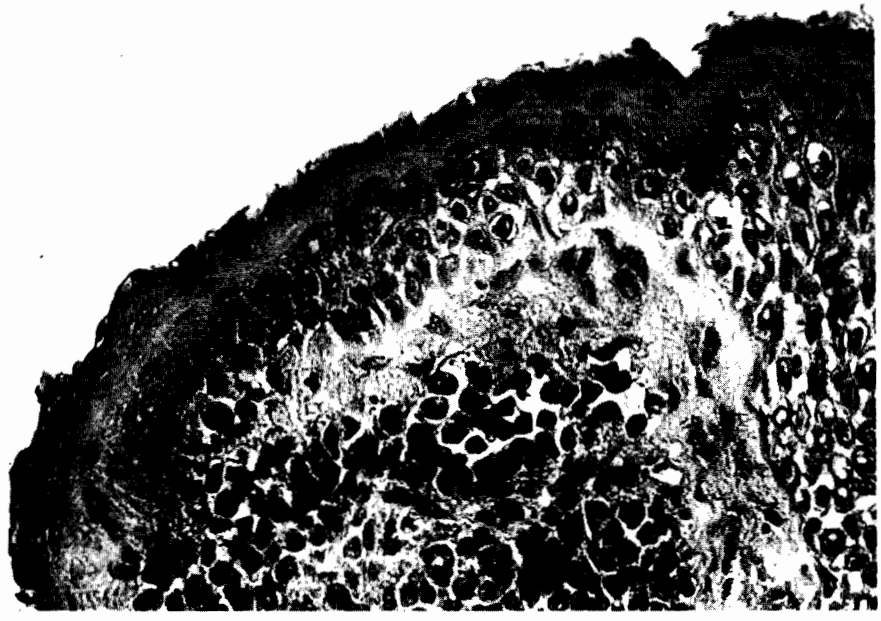

Fig. 9. Case n. 2. (R.R.).
Aspects suggesting junctional changes in squamous metaplastic epithelium. H. and E. ×400

present. In the mucosa adjacent to the tumor, squamous metaplasia and chronic rhinitis with glandular hyperplasia were observed. Some melanocytes were interspersed within the superficial stroma.

Discussion

Primary malignant melanoma originating within the nose and paranasal cavities is rare. Since 1869, when Lücke reported the first case, no more than 400 cases have been reported in literature. In Table 1. the main reviews and clinical series are reported, to which some isolated descriptions must be added (Maurizi, 1963; Cenci and Milanesi, 1964; Cove, 1979; Pastore et al., 1983; Siardet et al., 1985). However, most of the published cases have not been adequately documented with hystopathological studies confirming the true nature of the lesion (Ravid and Esteves, 1960).

The incidence varies according to race; in Caucasians it is about 1% of all melanomata, in dark-skinned races the incidence increases to 2.6% (Lewis and Martin, 1976); this increase is relative since the overall incidence of cutaneous melanomata in Negroes is lower (Crombie, 1979). Malignant melanoma represents 4% of all primary nasal neoplasms (Stewart, 1951) and 2% of all melanomata of the upper respiratory tract (Mesara and Burton, 1968).

Although the majority of cases have been reported in white males, it is not clear whether this predominance is significant. Both our patients were Caucasian females.

Our patients, in agreement with literature data, were in the sixth and seventh decades which corresponds to the peak incidence (Holdcraft and Gallagher, 1969) although cases have been reported in the second (Harrison, 1976) and ninth decades (Pearman, 1979).

Since the most important symptoms were nasal obstruction and nasal bleeding, the clinical picture is, according to literature (Ravid and Esteves, 1960; Maurizi, 1963; Holdcraft and Gallagher, 1969; Freedman et al., 1973; Harrison, 1976; Pearman, 1979; Pastore et al., 1983; Siardet et al., 1985), rather aspecific. This leads to a delayed diagnosis in many cases.

In our cases the exact site of origin was difficult to ascertain due to the extension of the tumor, which involved the maxillary antrum in both cases. In earlier stages the commonest sites of origin would be nasal septum and inferior and middle turbinals (Holdcroft and Gallagher, 1969; Cove, 1979; Pearman, 1979). This type of tumor seldom originates in the maxillary antrum (Maurizi, 1963).

The histopathological features of our cases permitted ready diagnosis. The Masson-Fontana stain for melanin and Perl's technique, ruling out iron pigments, confirmed the presence of melanin in the neoplastic cells. However 45% of mucosal melanomata cases are amelanotic (Allen and Spitz, 1953) and might be misdiagnosed as anaplastic carcinoma and sarcoma (Holdcroft and Gallagher, 1969; Mesara and Burton, 1968; Genton et al., 1981; Siardet et al., 1985), unless immunohistochemical and ultrastructural studies are performed (Carstens and Kuhns, 1981; van Duinen et al., 1984).

The ectodermal origin of nasal cavities and paranasal sinuses (Balinski, 1965) and the presence of melanocytes within the nasal mucous membranes (Zak and Lawson, 1974), clarified the histogenesis of primary melanoma, which was previously regarded as deriving from multipotential squamous cells due to respiratory epithelium metaplasia (Ravis and Esteves, 1960) or metastasis of a silent or recently excised cutaneous melanoma (Willis, 1948). Difficulties are nevertheless encountered in identifying melanoma as a primary or secondary lesion. In our patients the absence of cutaneous or ocular lesions and the presence of junctional changes in the epithelium overlying the tumor allowed the diagnosis of primary malignant melanoma of the nasal cavitiy (Allen and Spitz, 1953; DasGupta et al., 1969).

The natural history of nasal melanoma varies and is unpredictable (Harrison, 1976). The prognosis seems to be worse than for cutaneous melanoma on the basis of the behaviour in the other mucosal localizations (Allen and Spitz, 1953). Metastasis, according to Mesara and Burton (1968), are usually a later feature, occurring usually after a 3-year period, while local recurrences are earlier. Cervical node metastases usually make the prognosis worse (Wright and Heenan, 1974), the average survival time being 8 moths (Harrison, 1976). In our series, cervical adenopathies occurred only in the first case shortly after surgery, while in the second a local recurrence became evident without adenopathies.

Surgery is the treatment chosen for this melanoma (Freedman et al., 1973; Conley and Pack, 1974; Harrison, 1976; Pearman, 1979). The role played by radio and chemio-therapy is still controversial, probably because (Harrison, 1976) they depress the immunological defence mechanisms, favouring tumor recurrences and their spreading. However positive results with radiotherapy have recently been reported (Ghamrawi and Glennie, 1974) and chemiotherapy associated with surgery has been proposed to increase the survival rate (Pastore et al., 1983). As regards lymph node metastasis, Harrison (1976) and Pearman (1979) state that neck dissection is not justified, while a single lympho-adenectomy should be performed when a cervical node is involved.

The 5-year survival rate is about 30% (Freedman et al., 1973; Harrison, 1976). The bizarre clinical course is also due to the fact that metastases can arise later, even after 8 years, according to Harrison (1976).

Acknowledgements. This work was supported by Research Funds «40%» and «60%» granted to Institute of Pathological Anatomy and Histology (I Chair) - University of Peruqia-from the Italian Ministry of Education.

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Accepted February 20, 1987