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# Amelanotic oral malignant melanoma in a 16 year-old girl

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## Summary

Rarely occurring mucosal melanomas constitute a distinct biologic and prognostic disease. Only sporadic cases of paediatric mucosal melanomas have been reported. A case of a primary amelanotic oral melanoma in an adolescent girl is presented. Pathomorphology of mucosal/oral melanomas are also presented and their epidemiology and prognoses are discussed.
**Key words:** oral mucosal melanoma, young age, pathomorphology, epidemiology, prognosis.

# Czerniak złośliwy błony śluzowej jamy ustnej u 16-letniej pacjentki

## Streszczenie

Rzadko występujące czerniaki złośliwe błon śluzowych stanowią odrębną biologicznie i prognostycznie formę czerniaka. Czerniaki śluzówkowe w pediatrycznej grupie wiekowej opisywane są jedynie sporadycznie. Praca opisuje przypadek amelanotycznego czerniaka złośliwego jamy ustnej u dorastającej dziewczyny. Przedstawiono również cechy morfologiczne czerniaków śluzówkowych oraz omówiono ich epidemiologię i rokowanie.
**Słowa kluczowe:** czerniak złośliwy, młody wiek, patomorfologia, epidemiologia, prognoza.

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## Introduction

Mucosal melanomas occurring in vagina, vulva, penis, oral mucosa, oesophagus, anus, gallbladder, nasal cavity, and conjunctiva constitute a distinct entity, which differs both biologically and prognostically from their cutaneous counterparts. They comprise about 2% of all melanoma cases [1].

Oral melanomas are rare; they make up only 0.05% of all intraoral malignant tumours. However, the occurrence of mucosal melanomas is significantly variable in various parts of the world, and interestingly, oral melanomas make up 12% of all melanoma cases in Japan. Paediatric cases of oral melanoma are extremely rare [2]. Hidden tumour localisation and amelanotic lesions make the diagnosis very difficult [3,4].

We report a case of primary amelanotic melanoma in oral mucosa of an adolescent girl. Comprehensive data concerning the pathomorphology of mucosal melanomas are surveyed, and their epidemiology and prognosis in the young are discussed.

### *Case report*

A 16 year-old girl visited her general practitioner with a slowly growing painless nodule in the right submanidibular region, which had been observed by the patient for two months. Different malignant tumours, not closely specified, were noticed in her father's family, both in adults and children. Melanoma or dysplastic nevi were observed neither in the patient, nor in her relatives.

The patient was referred for consultations to a dentist and laryngologist. An oval, well demarcated, slightly elevated, non-pigmented and non-ulcerated lesion on the dental line-

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level in the right cheek mucosa was discovered. Clinically, the lesion was not suspected as malignant.

Fine needle biopsy was performed twice, although diagnosis could not be established. Thereafter, an incision biopsy of the oral tumour and excision biopsy of the cervical lymph node were made.

Histologically, the tumour consisted of monotonous proliferation of fusiform cells with little to moderate atypia. No necrosis was found. The number of mitoses was low, 1-2/10 HPF. The subepithelial connective tissue and even a fragment of skeletal muscle were infiltrated by the tumour. The tumour infiltrate reached the epithelium without invading it. Focal reactive pseudoepiheliomatous hyperplasia was noticed in the squamous epithelium above the lesion *(Figure 1 and 2)*. The tumour cells were negative for epithelial markers (AE1/AE3, MNF), vascular markers (CD34, factor-VIII) and melan-A. Strong positivity was observed for S-100, HMB-45 and vimentin *(Figure 3, 4 and 5)*. Melanin

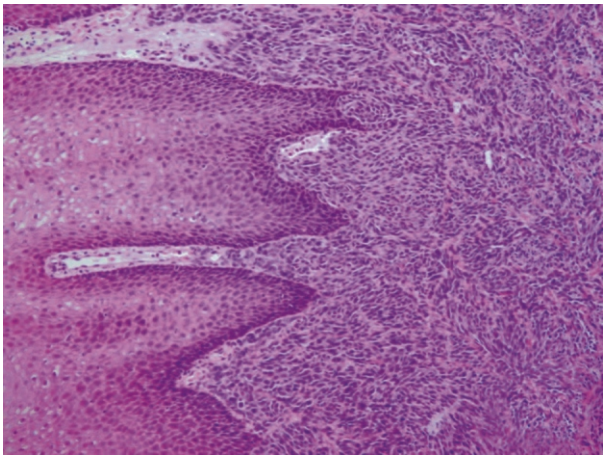

**Figure 1.** Oral mucosa with infiltration of malignant melanoma and reactive pseudoepitheliomatous proliferation of the overlying squamous epithelium (H-E; 100x).

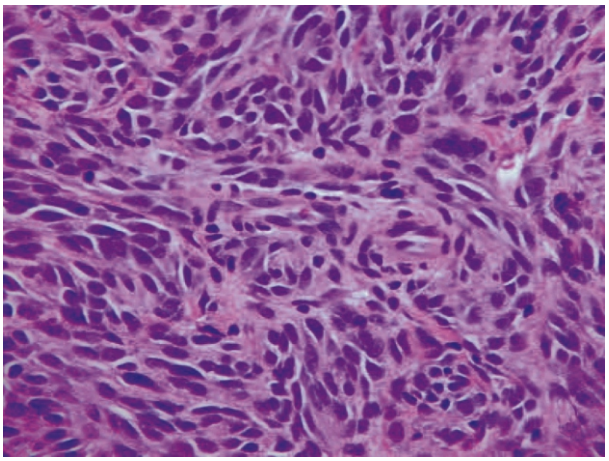

**Figure 2.** Melanoma infiltrate consists of monomorphic spindle cells with mild to moderate atypia (H-E; 400x).

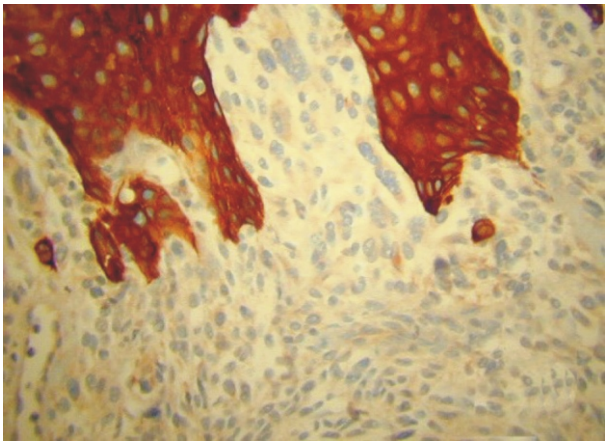

**Figure 3.** Immunostaining for cytokeratin - positive staining in the overlying epithelium, while negative reaction in tumour cells (MNF monoclonal antibody - DAKO, ABC-DAB; 200x).

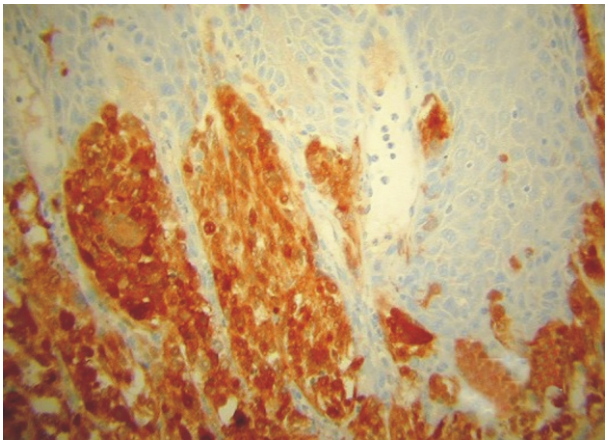

**Figure 4.** Immunostaining for S-100 protein - negative staining in the overlying epithelium, while positive reaction in tumour cells (S-100 polyclonal antibody - DAKO, ABC-DAB; 200x).

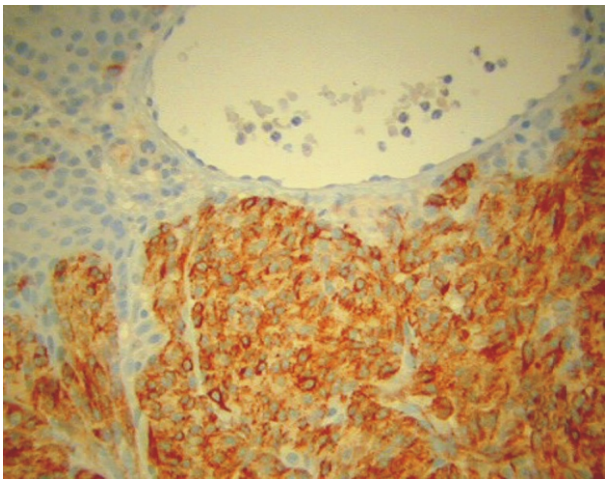

**Figure 5.** Immunostaining for HMB-45 - strongly positive reaction in tumour cells (HMB-45 monoclonal antibody - DAKO; ABC-DAB; 200x).

pigment was not demonstrated. Diffuse metastasis with same feature was found in the cervical lymph node *(Figure 6)*.

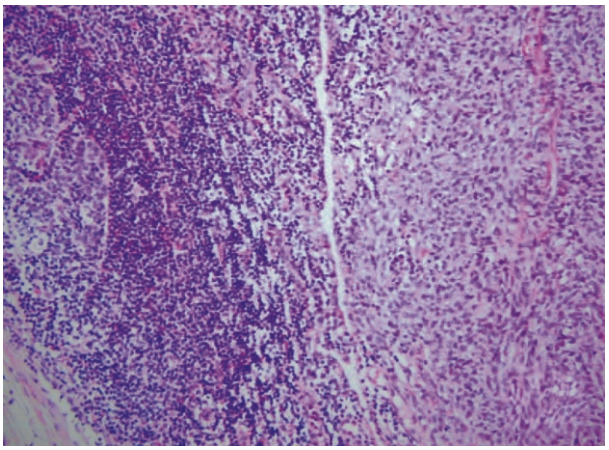

**Figure 6.** Metastasis of malignant melanoma in the cervical lymph node (H-E; 100x).

The patient was referred to a large number of additional clinical investigations, but no other tumour was found elsewhere. Wide, radical excision of the oral lesion and rightsided cervical lymph node dissection sec. Crile were performed.

The surgical material showed the same histology that was seen in the excision biopsy. The chromosome translocation t(12;22)(q13;q12), pathognomic for clear cell sarcoma, was not found. Only a small metastasis was detected in one of the additional cervical lymph nodes. The final diagnosis was: primary mucosal amelanotic malignant melanoma.

## Discussion

### *The epidemiology of mucosal/oral malignant melanomas of young age*

Oral melanomas are very rare in patients less than 18 years of age, however, interestingly, cases have been described even in less than 10-year old, and the youngest patient with oral malignant melanoma *in situ* being only 3 months old [2].

*In situ* malignant melanoma in the oral mucosa was described in a boy with dyspalstic nevus syndrome [5].

Surveying the literature, we have found only one report of amelanotic oral melanoma, with almost identical histology as in our case, in an oriental girl who was younger than 18 years old [1].

### *The pathomorphology of mucosal/oral malignant melanomas*

Seventy-five percent of primary oral melanomas involve the maxillary parts of the mouth, such as the palate and the upper gum. Twenty percent of oral melanomas represent metastases. [6].

Compared with skin melanomas, mucosal melanomas, as a rule, are diagnosed late and at a more advanced stage, i.e. the primary lesions in the case of mucosal melanomas are thicker and the regional lymph node metastases are more frequent. In 50% of cases, metastases are already present at the time of diagnosis, as observed in our case, too [1].

Grossly, the oral lesions may form a pigmented macula or an elevated polypoid, pigmented or amelanotic, ulcerated or non-ulcerated tumour. In more advanced lesions, destruction of the jaws may occur, which is followed sometimes by toothlessness [7].

Microscopically, the dominant form of oral melanoma is similar to cutaneous acral lentiginous melanoma and consists of quite a monomorphic population of spindled or dendritic melanocytes. The tumour cells often have a contact with epithelium, but pagetoid spreading is not typical. Other forms of oral melanomas are similar to nodular melanoma without preexistent radial phase. The tumour cells can be spindled, epithelioid, or mixed. If melanin pigment is present, the Masson-Fontana staining may confirm its nature. Immunohistochemistry is indispensable for the diagnosis, especially if the lesion is amelanotic or poorly pigmented. S-100 protein is positive in 97%, HMB-45 in 71% and melan -A in 74% of cases of mucosal melanomas. Detection of melanosomes by electron microscopy may be conclusive for the final diagnosis [8].

Diagnostically difficult cases with intraoral neurotropic and desmoplastic melanomas have also been reported [9]. Some cases with malignant melanoma show even pseudoepitheliomatous hyperplasia of the overlying epithelium. Vascular invasion is described more often in mucosal melanomas than in their skin counterparts. Only 2-10% of mucosal melanomas are amelanotic, while in the skin the occurrence of amelanotic melanoma is more frequent (30%) [4].

In the differential diagnosis for a flat-pigmented lesion, the following entities must be taken into account: mucosal naevi, melanoacanthoma, lentigo simplex and amalgam tattoo. In nodular lesions: spindle cell sarcoma, and among other things *clear cell sarcoma,* which shows the same immunohistological profile, squamous cancer of the spindle cell type and even cell rich benign tumours as cellular schwannoma and fibrous epulis should also be considered [4]. Based on histologic features and findings in immunohistochemistry, two entities were taken in account in the differential diagnosis of our case, i.e. malignant melanoma and clear cell sarcoma of the soft part. The unequivocal positive staining with S-100 antibody and the lack of t (12;22)(q13;q12) chromosome translocation, which occurs about 80% of clear sarcoma cases (10), strongly favour a malignant melanoma.

### *The prognosis of mucosal/oral malignant melanomas*

Prasad et al. examined statistically the significance of ten morphological parameters in the prognosis of mucosal

malignant melanoma of the head region. They noticed worsening in the prognosis only in the case of large cell tumours with polymorphism, necrosis and vascular invasion. Some parameters, which are of crucial importance in the prognosis of skin melanomas, are of no significance in their mucosal counterparts. Tumour thickness, the level of invasion, tumour diameter, ulceration, metastases to local lymph nodes do not have any effect on the outcome of mucosal melanomas [11]. In another analysis, the increased tumour thickness correlated well with shorter life expectancy [6].

Oral melanomas are considered to have a worse prognosis than their skin counterparts. The 5-year-survival is only 5% in mucosal melanomas [12]. Furthermore, the amelanotic tumours are usually even more aggressive than common pigmented melanomas [4]. According to a single case report, these data concernig adult patients are not necesserely applicable to paediatric patients. Mucosal melanoma in the young age, even in the case of a non-radically removed tumor, may have a surprisingly long course [13]. Although, the followup period in our case is very short, this conclusion concerning the relatively better prognosis may hopefully also be applicable to our patient.

Careful followup of all available cases may give clearer insight into the pathobiology and prognosis of mucosal melanomas, particularly in paediatric and aldolescent patients.

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