Mucosal Malignant Melanoma

INTRODUCTION

- Malignant melanoma arising from the mucosal surfaces of the head and neck are very rare
- 91 percent of all malignant melanomas were cutaneous.
- For mucosal melanomas, the head and neck was by far the most common site with 55.4 percent of cases. Most common site for mucosal melanomas was in the nasal cavities and sinuses accounting for 69 percent, 22 percent occurred in the oral cavity and 9 percent in the pharynx, larynx and upper oesophagus.

MUCOSAL MELANOMAS TYPE AND SITE

- Poorer prognosis than cutaneous melanomas
- The prognostic factors for both cutaneous and mucosal melanomas are similar but, at the time of diagnosis, mucosal melanomas have already reached dangerous limits in terms of depth of invasion and tumour thickness.
- More refractory to treatment then cutaneous melanomas
- Mucosal melanoma is a very aggressive tumour that is derived from the malignant transformation of melanocytes in the basal layer of the mucosa.
- Majority arise in the nasal cavity; by contrast metastatic melanoma in these sites is very rare.
- Most sinonasal melanomas occur on the middle and inferior turbinates and the anterior nasal septum.
- Junctional changes seen in cutaneous melanoma are rarely seen in mucosal melanoma, no doubt because of the advanced stage of this disease at the time of histological examination.

PRESENTATION

- In the case of sinonasal melanoma, examination may show a sessile mass, a polyp or even a large obstructing tumour.
- Although usually pigmented, amelanotic lesions occur. The next commonest site after the sinonasal tract is the oral cavity. Eighty percent are located in the maxilla, usually the palatine mucosa.
- Very occasionally, malignant mucosal melanomas form over pre-existing longstanding melanosis.
- Once the malignant tumour becomes clinically evident it is locally invasive and tends to metastasize to the cervical lymph nodes fairly late, but distant metastases are frequent.
- All mucosal melanosis must be taken seriously because malignant melanoma cannot be excluded on clinical examination.
- In mucosal malignant melanoma, melanocytes in the basal layer tend to show bizarre atypical forms.
- Of interest is that primary acquired melanosis of the conjunctiva appears to be biologically different from other mucosal melanosis as it frequently progresses to malignant melanoma.
- Mucosal melanomas tend to occur in an older age group than their cutaneous counterpart (from the fifth to eighth decade) and men are more commonly affected than women. Mucosal melanoma of the larynx, pharynx and oesophagus is very rare.
HOST AND TUMOUR FACTORS

- Mean age was 73 years. Men > Women
- In the case of the sinonasal cavities, nearly all the lesions were on the nasal septum (usually anteriorly) or on the middle or inferior turbinate.
- Of oral cavity tumours, most developed on the palate and half this number on the gingiva.
- Approximately one-quarter of patients had amelanotic melanomas.
- Patients aged over 60 years had a significantly poorer tumour-specific survival than younger patients. Those with amelanotic lesions also did particularly badly.

DIAGNOSIS

- Whilst amelanotic malignant mucosal melanomas occur frequently and thus almost any lesion is suspect, pigmented lesions, particularly of the nasal cavities or the oral mucosa, are particularly suspicious. Due to anatomical constraints, an incisional biopsy is usually regarded as the first step in diagnosis. Whilst histological patterns do exists, immunohistochemistry has become a very important part of the histological diagnosis.
- Staining for the S100 protein.
- Identification of Melanoma Cytoplasmic Antigen (using HMB45, a monoclonal antibody) and S100 protein (using a Polyclonal Antibody) appears to identify nearly all melanomas regardless of site.

AETIOLOGY AND BIOLOGY OF MUCOSAL MELANOMA

- Also HLA DR, PCNA, Cytokeratin, Von Willebrand factor along with S100 and HMB45
- HMB45 produced the clearest and most specific staining.
- Conjunctival melanomas have a relatively good prognosis compared to other mucosal melanomas.
- Given that UV light exposure is such an important aetiological factor in cutaneous melanoma, but obviously not in mucosal melanoma
- Genetic basis (but no clear cut syndrome defined yet)
- There was a selective loss of, and abnormalities in, HLA class 1 expression and these abnormalities were greater in metastatic as opposed to primary lesions. Increased expression of high molecular weight melanoma-associated antigen of 110-kDa, the P97 antigen, (CEA) carcino-embryonic antigen, (NGF) neuronal growth factor-R and GD2 ganglioside were found to be associated with a particularly poor prognosis.

CLINICAL FINDINGS AND STAGING

- Clarkes' classification of cutaneous melanomas does not apply for mucosal melanoma because of the absence of histological landmarks analogous to the papillary and reticular dermis.
- The UICC and AJCC have yet to classify this disease, But the thickness of the melanoma is an important prognostic indicator as it is in the cutaneous tumour.
- MRI ➔ Hyperintesity on T1 weighted images although not universally so, and the addition of gadolinium enhancement probably improves sensitivity
- Because by the time most head and neck mucosal melanomas present they are invading bone, a computed tomography (CT) scan is also required.
**TREATMENT**

- Best Radical Excision + postop Radiotherapy (if distant mets not occurred)
- Mucosal melanomas initially spread radially, thus involving large areas of mucosa with margins which may be difficult to delineate. To be effective, surgical resection margins should be generous with inevitable aesthetic and functional deficit.
- **Chemotherapy** has usually been given as a last resort to terminally ill patients. regimes containing dimethyl triazeno imidazole carboxamide (**DTIC**) may be more effective than others.
- Malignant melanoma was one of the first cancers where immunotherapy was introduced. Initially, these attempts were crude using **BCG vaccination or DMCB treatment**.
- **Interferon + Cimetidine** which inhibits T suppressor cells and activates natural killer (**NK**) cells and the results were encouraging.
- More recent work on this subject validated **three vaccination strategies** for melanoma in mice. The three vaccines essentially comprised (1) Naked DNA, (2) peptide pulsed dendritic cells and (3) a mixture of peptide and the Escherichia coli toxin LTR72.
- Peptide pulsed dendritic cell based vaccine was the most promising and should be considered for a trial in human subjects.
- In the recent literature, mention should be made of boron neutron capture therapy.

**RECURRENT AND METASTASIS**

- Mucosal melanoma has a lower incidence of regional lymph node metastasis than cutaneous melanoma.
- The incidence of such metastasis for oral cavity melanoma is higher, local recurrence rates however seem to be higher for sinonasal disease than for oral cavity.
- The primary site recurrence rate following complete therapeutic ablation of disease varies from 55 to 82 percent.
- Of patients with complete local control, 76 percent died of distant metastases. Distant mets reported in less than a year.
- 5 yr survival 44% and 10 yr 33%
- Those with melanotic melanoma fared better at three years than those with amelanotic melanoma
- Women fared better than men
- Nasal cavity tumours fared better than tumours of the paranasal sinuses and the oral cavity.
- Patients with regional neck node metastasis should undergo full radical neck dissection, if necessarily staged and bilateral, followed by irradiation.
- Selective neck dissection appears to be inadequate in this disease.
- Certainly nearly all untreated patients are dead within four years.