

Rising incidence of head and neck mucosal melanoma in Australia

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Abstract

Objective: To establish Australian population-based incidence trends for mucosal melanoma of the head and neck.

Methods: Cases between 1985 and 2009 were identified in the Australian Cancer Database. Age-standardised incidence trends were established, including subgroup stratification by sex and site.

Results: A continuously progressive increase in incidence was evident in the 353 cases identified over the 25-year study period. This was particularly evident in sinonasal mucosal melanoma in men, despite the overall incidence remaining higher in women.

Conclusion: There is such paucity in published global incidence trends of head and neck mucosal melanoma. Comparisons of incidence patterns between countries can provide insight into aetiological factors of this rare disease.

Key words: Malignant Melanoma; Nasal Mucosa; Incidence; Australia

Introduction

Mucosal melanomas are rare and aggressive malignant tumours that arise from melanocytes of mucosal surfaces. These melanomas occur in the respiratory, gastrointestinal and urogenital tracts. The nose and sinuses are the most commonly affected regions within the respiratory tract, and, alongside the oral cavity, comprise almost all cases of head and neck mucosal melanoma. These mucosal sites are frequently in unexposed areas, resulting in late presentation and very poor outcomes.

There is little doubt that cutaneous malignant melanoma rates continue to increase principally because of increasing levels of ultraviolet exposure.¹ The trends in rates of mucosal melanoma are far more complex, with much controversy in the recent literature. Some reports have described increases in the rates of malignant mucosal melanoma,^{2–5} but other studies have found no change,^{6–8} whilst another reports a decrease in rates.⁹ To date, there have been no studies analysing this trend in the Australian population, which has some of the highest rates of cutaneous malignant melanoma in the world.

Mucosal melanomas comprise approximately 1.4 per cent of all melanomas, with a mucosal melanoma rate in the USA of approximately 2.2 per million per year. Higher rates are reported in females as compared to

males (2.8 vs 1.5 per million per year) because of higher rates of genital tract melanoma in the former group.⁸

The majority of mucosal melanomas occur in the head and neck (55.4 per cent), followed by the anorectal (23.8 per cent), female genital (18 per cent) and urinary tract sites (2.8 per cent).¹⁰

Sinonasal melanomas have a reported incidence of 0.41–0.5 per million per year.^{11,12} McLaughlin *et al.* separated this into 0.3 per million per annum for nasal and 0.2 per million per annum for sinus mucosal melanoma.⁸ The most common sites of origin within the sinonasal tract are the septum, inferior turbinate, and maxillary and ethmoid sinuses.^{2,13,14}

Mean age at presentation with head and neck mucosal melanoma within the sinonasal cavity is 63.4 years.¹⁵ The larynx, tracheobronchial tree and lungs are only very rarely affected.

Mucosal melanomas tend to occur in older individuals when compared to cutaneous melanomas and have a very poor prognosis. The rates of mucosal melanoma amongst whites is 2 times higher than that amongst blacks, whereas cutaneous melanomas are up to 13.8 times higher.¹⁶

We sought to establish Australian population-based incidence trends for mucosal melanoma of the head and neck.

Materials and methods

We analysed trends in the incidence of head and neck melanomas in Australia between 1985 and 2009.

The 2011 Australian Cancer Database was used for data collection. This national database of cancer incidence is compiled by the National Cancer Statistics Clearing House with information received from the cancer registry in each state and territory. Mandatory reporting of all cancers is legislated throughout Australia; this involves the collection of basic demographic data and clinical details about the cancer for each patient. Exemption from full ethical review was granted by the Royal Brisbane and Women's Human Research Ethics Committee.

We identified patients from 1985 to 2009 with diagnosis codes for all histological variants of melanoma (8720–8799) using topography codes and grouped according to region, as detailed in Table I. Age at diagnosis, year of diagnosis and sex were collected for each patient.

The calendar period was divided into five-year segments. Incidence was analysed by year of diagnosis and sex to describe the average annual incidence per five-year period per million persons. The age distribution in Australia for each segment was used as a standard. Changes in the annual age-standardised incidence rates over the calendar period were explored by calculating the total percentage change. Subgroup analysis involved stratification by sex and site.

Results

We identified 353 cases of head and neck mucosal melanoma in the Australian Cancer Database between 1985 and 2009. This included 288 cases of sinonasal melanoma and 65 cases of non-sinonasal disease. Table II demonstrates the distribution of cases by sex, age at diagnosis and location of disease.

In all, 54.7 per cent of cases occurred in females. The majority of cases occurred in later life, with 64 per cent of patients aged over 65 years. The most common site of origin was the nasal cavity (60.3 per cent), followed by the paranasal sinuses (17.8 per cent) and the oral cavity (15.0 per cent).

The incidence of head and neck mucosal melanoma in Australia has steadily increased over the 25-year period. The age-standardised incidence rate increased from 0.59 to 0.80 cases per million for men and 0.74 to 0.92 cases per million for women. This represents a total percentage change of 35.8 per cent and 24.5

TABLE II
CHARACTERISTICS OF HEAD AND NECK MUCOSAL MELANOMA PATIENTS

Characteristic	Patients (n (%))*
Sex	
– Male	160 (45.3)
– Female	193 (54.7)
Age (years)	
– 0–24	2 (0.6)
– 25–34	6 (1.7)
– 35–44	13 (3.7)
– 45–54	47 (13.3)
– 55–64	59 (16.7)
– 65–74	82 (23.2)
– 75–84	106 (30.0)
– 85+	38 (10.8)
Site	
– Nasal cavity	213 (60.3)
– Paranasal sinuses	63 (17.8)
– Nasopharynx	12 (3.4)
– Total sinonasal	288 (81.6)
– Oral cavity	53 (15.0)
– Oropharynx	12 (3.4)
– Total non-sinonasal	65 (18.4)

*Total n = 353

per cent respectively. Total percentage changes in age-standardised incidence rates for subgroups are displayed in Table III. The rate of increase was most pronounced in men with sinonasal melanomas, as illustrated in Figure 1.

Discussion

Our results show an increase in rates of head and neck mucosal melanoma, particularly in male sinonasal malignant melanoma, of 37.8 per cent over this 25-year period in Australia.

Marcus *et al.* reported that from 1987 to 2009 the total percentage change in the age-adjusted incidence rate for all patients with head and neck mucosal melanoma was 50 per cent, with an annual percentage change of 2.4 per cent ($p < 0.01$).⁵ Jangard *et al.* showed a similar increase in Sweden between 1960 and 2000.² In accordance with our findings, they demonstrated higher incidence amongst females, but with a more rapid increase amongst males.

Jangard *et al.* attributed the increase in incidence to a possible improvement in diagnostic methods such as immunohistochemical markers.² This is plausible given that 30 per cent of sinonasal melanomas in their series were amelanotic. However, this would fail to explain our common finding that rates were increasing

TABLE I
GROUPS BY TOPOGRAPHY CODES

Region	Topography codes
Oral cavity & pharynx	Mucosal lip (C00.3–C00.9), tongue (C01.9–C02.9), other oral cavity (C03.0–C06.9), tonsils (C09.0–C09.9), oropharynx (C10.0–C10.9), hypopharynx (C12.9–C13.9), other pharynx (C14.0–C14.8)
Sinonasal	Nasopharynx (C11.0–C11.9), nasal cavity (C30.0), paranasal sinuses (C31.0–C31.9)

Subgroup	Total % change
Site	
– Sinonasal	29.4
– Non-sinonasal	24.8
Sex	
– Male	35.8
– Female	24.5
Sex & site	
– Sinonasal male	37.8
– Sinonasal female	24.6

*For subgroups of head and neck mucosal melanoma patients between 1985 and 2009.

faster amongst males than females despite a lower overall incidence within that group.

There is limited published information about risk factors for mucosal melanoma, although exposure to formaldehyde has been suggested as a possible causative factor.¹⁷ The functions of melanocytic neuroectoderm-derived cells within the nose and sinuses are not clearly understood. It has been postulated that they are likely to be fulfilling immunological and antimicrobial functions as part of the innate immune system including cytokine production, antigen presentation and phagocytosis.¹⁸

Differing epidemiological trends in the various subsites of mucosal melanoma may point to differing pathological entities. Genetic analyses demonstrate that mucosal melanomas only rarely carry the BRAF mutations¹⁹ common in cutaneous malignancy, but that 15.6 to 39 per cent carry alterations in KIT genes.^{20,21}

Despite the increased rates of detection of these lesions, the prognosis for survival is poor. Surgery is the mainstay of treatment, with the role of radiotherapy being controversial. With increasing understanding of the genetic abnormalities present in mucosal

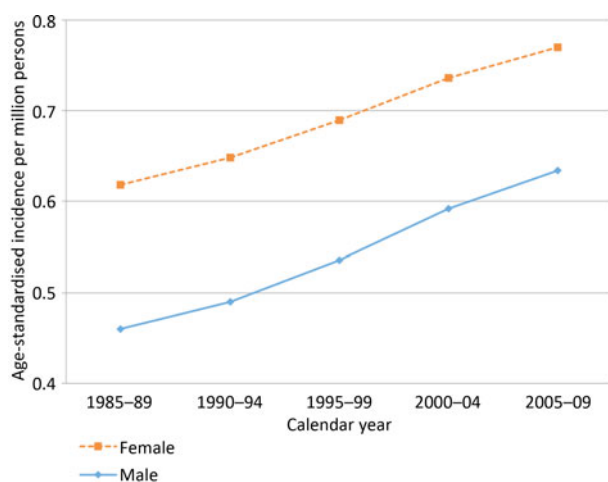


FIG. 1

Age-standardised incidence rates for sinonasal melanoma from 1985 to 2009 by sex.

melanomas, immunotherapeutic and chemotherapeutic treatments may prove useful in the future. However, given the rarity of head and neck mucosal melanoma, effective treatment paradigms will remain difficult to formulate.

- **The most common sites for head and neck mucosal melanoma are the nasal cavity and paranasal sinuses**
- **Little is known of the aetiological factors of head and neck mucosal melanoma in comparison to cutaneous melanoma**
- **Published data on worldwide incidence trends are limited in number and conflicting in nature**
- **This paper presents Australian population incidence trends of head and neck mucosal melanoma, which demonstrate a rise over a 25-year study period**
- **This increasing incidence is most pronounced in the male sinonasal subgroup**
- **Case-ascertainment bias does not explain the difference in rates of increase between subgroups**

The increasing incidence of head and neck mucosal melanoma that we have described in Australia is noteworthy. Somewhat limiting our analysis is the inability to account for case-ascertainment bias. Disease staging data, were it available, might have helped in this respect by determining if cases are being detected before progressing to a more advanced stage.

Conclusion

There are few studies describing incidence trends of head and neck mucosal melanoma globally, other than those referred to in this paper. It would be useful for comparisons to be made between the patterns described in Australia with those in other countries, to provide further insight into the true incidence trends of these rare melanomas. Undoubtedly, the next challenge ahead must be identifying aetiological factors to account for these observed trends.

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