Smoker's melanosis or early melanoma- misdiagnosis trap?

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Abstract

Objective: First used by Hedin in 1977, "smokers' melanosis" is currently recognized as a clinical diagnosis without recourse to biopsy. Current research findings however suggest the disturbing possibility of mistaking a "silent" oral malignant melanoma for a benign smokers' melanosis. The objective of the current review is to stimulate an evidence-based rethink.

Method: This manuscript is based on a Pubmed search phrase "smokers' melanosis".

Result: A total of 24 studies resulted of which 16 were analyzed and 8 non-oral melanomas were excluded.

Reports ranged from claims of a "protective" role of melanosis to cases of melanoma from pre-existing melanosis. Alcohol synergistic potentiation of intra-oral melanosis and a categorization of smokers' melanoma as a differential for intra-oral smokers' melanosis were also found.

Conclusion: Since many cases of confirmed intra-oral malignant melanomas were preceded with a history of pre-existing "innocent" oral pigmented lesions, adopting a principle of universal biopsy is strongly suggested. This would change this age-long paradigm but would definitely save a few lives.

Keywords: Smokers' melanosis, early malignant melanoma, misdiagnosis

Introduction

The term "smokers' melanosis" was first used by Hedin in 1977[1]. It is a descriptive rather than definitive diagnosis based purely on clinical grounds. However, smokers' melanosis shares features with melanoma necessitating this call for updating diagnostic criteria for this entity.

"Patients with oral malignant melanoma often recall having an existing oral pigmentation months to years before diagnosis, and the condition may even have previously elicited comments from physicians or dentists" [2].

Unfortunately, current practice not only neglects biopsies for smokers' melanosis, it also actively discourages it despite submissions that "reports of previously existing pigmented lesions are common"[2] and "because oral malignant melanomas are often clinically silent, they can be confused with a number of asymptomatic, benign, pigmented lesions"[3]. Since smokers' melanosis comes under the group of so-called benign pigmented lesions, is it not time to have a rethink? A rethink appears inevitable in the light of growing evidence that intra-oral melanotic lesions may always be smokers' melanosis even when the patient is a smoker.

The current belief is that "generally, no laboratory studies are necessary to confirm the diagnosis of smoker's melanosis; clinical impression is usually sufficient, in combination with a history of smoking"[4] neglects the warning that "due to the onset in adulthood and the progressive darkening, malignant melanoma must be ruled out"[5]. It is worrying that two decades later, this advice has been widely neglected. Is it not time we adopted their recommendation as standard practice in both epidemiological research and clinical practice? It appeals to reason to adopt this recommendation in order not to misdiagnose those cases that could easily be missed simply because they are rare or are being observed in smokers.

It is noteworthy that certain dental authorities and groups are getting sensitized to the silent controversy generated by these different schools of thought. In response, the National Academy of Dentistry recommends that "Biopsy should be performed if there is surface elevation or increased pigment intensity or if the pigmentation is in an unexpected site"[6].

What informed the guidance on surface elevation as an indication for biopsy? Is it possible even remotely to have early malignant melanoma without elevation? Is it also possible that smokers' melanosis which obviously does not present with surface elevation could undergo malignant transformation?

It is clear that there are no clear-cut guidelines in the investigation, diagnosis, management and follow-up of intra-oral smokers' melanosis. It is also clear that diagnostic guidelines for this entity are not precise.

The flames of complacency over the years have been fuelled by the academic generalization of melanoma being rare and the likelihood of arising as a sequel to smoker's melanosis even rarer. The question however is "how much evidence is there to back this seemingly popular position?" Are the proponents of universal biopsy for all cases of benign intra-oral pigmented lesions simply prophets of doom? On the contrary, accepting the status-quo without compelling evidence will amount to negligence, especially when the result of continuing the current practice is often fatal.

Although there is no concrete evidence to support an association between smoking and an increased risk of melanoma, several studies suggest that when compared with non-smokers; (i) smokers are more likely to have metastasis on initial presentation of intra-oral malignant melanoma, (ii) smokers have lower disease-free survival rates after diagnosis, (iii) smokers are more likely to have visceral metastases, and (iv) smokers are more likely to die from melanoma than non-smokers.

Materials and method

A total of 24 studies resulted of which 16 were analyzed and 8 non-oral melanomas were excluded.

This manuscript is based on qualifying studies were scrutinized to determine their diagnostic criteria for intra-oral smokers' melanosis. The basis for diagnosis and the institution or absence of follow-up was recorded for each study. Biopsy was the only investigation of interest to the current search.

Results

The results of the PubMed search phrase" smokers' melanosis" yielded 24 studies. 7 studies were excluded because they were reports of melanosis and the anatomical sites of occurrence were not intra-oral.

The results also included observations of contradictions in literature by the author. While one study described the presence of smokers' melanosis was indeed protective, yet early lesions of smokers' melanosis have sometimes pre-existed the development of intra-oral malignant melanoma. There is a synergistic potentiation of intra-oral melanosis in smokers who also drink alcohol.

Discussion

One prominent finding of this report is the fact that all the patients who presented with melanin pigmentation of the gingiva were smokers. The choice of the phrase "smokers' melanosis" was therefore completely justified[1]. However, the most important findings relevant to the current quest are the basis for diagnosis lack of follow-up. It is clear from the pioneer report that diagnosis was based exclusively on clinical presentation and a history of smoking.

Only 6 (37.5%) of the 16 studies reported carrying out biopsy on intra-oral smokers melanosis **(Table1)** and only two[7,11] described the detailed histological characteristics of smokers' melanosis with one study by Hedin describing ultra-structural changes of the epithelium in smokers' melanosis[7].

Table 1: PubMed articles on "Introral Smoker's melanosis"

Study Reference	Sample Size	Biopsy& Histopathology performed
Sujatha D, Hebbar PB, Pai A. Prevalence and correlation of oral lesions among tobacco smokers, tobacco chewers, areca nut and alcohol users. Asian Pac J Cancer Prev. 2012; 13:1633-7.	1028	NO
Mehrotra R, Thomas S, Nair P, Pandya S, Singh M, Nigam NS, Shukla P. Prevalence of oral soft tissue lesions in Vidisha. BMC Res Notes. 2010 25; 3:23. doi: 10.1186/1756-0500-3-23.	3030	YES
Alvarez Gómez GJ, Alvarez Martínez E, Jiménez Gómez R, Mosquera Silva Y, GaviriaNúñez AM, GarcésAgudelo A et al. Reverse smokers' and changes in oral mucosa. Department of Sucre, Colombia. Med Oral Patol Oral Cir Bucal. 2008;13:E1-8.	46	YES
Nwhator SO, Winfunke -Savage K, Ayanbadejo P, Jeboda SO. Smokers' melanosis in a Nigerian population: a preliminary study. J Contemp Dent Pract. 2007 1;8:68-75.	253	NO
Marakoglu K, Gürsoy UK, Toker HC, Demirer S, Sezer RE, Marakoglu I. Smoking status and smoke -related gingival melanin pigmentation in army recruitments. Mil Med. 2007;172:110-3.	908	NO
Ali AA. Histopathologic changes in oral mucosa of Yemenis addicted to water-pipe and cigarette smoking in addition to takhzeen al -qat. Oral Surg Oral Med Oral Pathol Oral RadiolEndod. 2007;103:e55-9.	33	YES
Azzeh MM. Treatment of gingival hyperpigmentation by erbium -doped: yttrium, aluminium, and garnet laser for aesthetic purposes. J Periodontol. 2007;78:177-84.	6	NO
Saraswathi TR, Ranganathan K, Shanmugam S, Sowmya R, Narasimhan PD, Gunaseelan R. Prevalence of oral lesions in relation to habits: Cross -sectional study in South India. Indian J Dent Res. 2006;17:121-5.	2017	NO
Thavarajah R, Rao A, Raman U, Rajasekaran ST, Joshua E, R H, Kannan R. Oral lesions of 500 habitual psychoactive substanc e users in Chennai, India. Arch OralBiol. 2006;51:512-9.	500	NO
Sarswathi TR, Kumar SN, Kavitha KM. Oral melanin pigmentation in smoked and smokeless tobacco users in India. Clinico -pathological study. Indian J Dent Res. 2003;14:101-6.	49	YES
Unsal E, Paksoy C, Soykan E, Elhan AH, Sahin M. Oral melanin pigmentation related to smoking in a Turkish population. Community Dent Oral Epidemiol. 2001;29:272-7.	496	NO
Ramer M, Burakoff RP. Smoker's melanosis. Report of a case. N Y State Dent J. 1997;63:20-1.	1	NO
Hedin CA, Pindborg JJ, Axéll T. Disappearance of smoker's melanosis after reducing smoking. J Oral Pathol Med. 1993;22:228-30.	NOT ACCEESSIBLE	NO
Hedin Ca, Pindborg JJ, Daftary DK, Mehta FS. Melanin depigmentation of the palatal mucosa in reverse smokers: a preliminary study. J Oral Pathol Med. 1992;21:440-4.	129	YES
Hedin CA. Smoker's melanosis may explain the lower hearing loss and lower frequency of Parkinson's disease found among tobacco smokers -a new hypothesis. Med Hypotheses. 1991 Jul;35(3):247-9. PubMed PMID: 1943869.	Not available	Not available

One prominent finding that permeates through the studies is the dose-response relationship between smoking and melanosis as reported by Araki et al in 1983[8]. While this is welcoming for "true" cases of benign smokers' melanosis, the nagging question remains; "do these lesions stay benign?" and "how do we guarantee the continual benign status of such lesions in the obvious face of lack of follow-up as evidenced from the cited studies?"

Hedin described a persistent association between both entities which tends to persist until after 3 years of smoking cessation[9]. It has been suggested that smoking stimulates melanocytes to higher activity leading to melanosis[10] and one study reported an actual hypermelanocytosis in addition to melanosis[11].

The researchers observed that malignant lesions did not develop in sites with pre-existing melanosis. De-pigmentation and epithelial thinning were associated with malignancy melanin is in fact protective against intra-oral chemical aggression just as in intact epithelium. In their report, the presence of smokers' melanosis was indeed protective[7].

The question that immediately arises is, "if melanosis is as protective as reported, what were the early lesions reported to have pre-existed before the development of intra-oral malignant melanoma?" Again, why the synergistic potentiation of intra-oral melanosis in smokers who also drank alcohol? If "93.3% of alcoholics showed a high degree of pigmentation"[11], the relationship appears to be more than a casual finding or a coincidence.

Conclusion

Although melanin pigmentation is known to increase with smoking, it is also important to note that pigmentations involving the oral cavity may be associated with various other factors apart from smoking. If such lesions are thought to be irrelevant to smoking then they require clinical and pathological correlations for definitive diagnosis, which will be expected to reflect the underlying cause.

At present, it appears impossible to conclusively distinguish between melanosis related to smoking and that from other causes without biopsy and histopathological categorization, universal biopsy of all cases of smokers' melanosis is therefore advocated.

References

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