Case Report

Masquerading Spitz naevi on the upper lip: A case report with a brief review of the literature

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Abstract

In a scenario where there is an increased incidence of oral squamous cell carcinoma (OSCC) in younger age groups, the diagnosis of pseudo-malignant lesions that mimic the histopathology of a moderate or even high-grade carcinoma becomes imperative for oral pathologists. Though paediatric malignancies such as melanomas and thyroid carcinomas and even OSCCs have been reported in young children, they are rare in the pre-pubertal age group. Melanocytic naevi such as Spitz naevi (SNs) or atypical SNs is, however, more common in this age group and could create some difficulty in diagnosis due to its histological variations that could mimic a malignancy. Hence, the need for a cautious correlation between clinical and histopathological features becomes manifold. Adjunct tools that use diagnostic and molecular techniques such as immunohistochemistry (IHC) and comparative genomic hybridisation (CGH) help in diagnosis and in differentiating certain types of SNs from Spitzoid melanomas or melanomas. A case that histopathologically resembled a moderately differentiated squamous cell carcinoma without any evidence of melanocytic content proved to be a melanocytic naevus after clinical correlation of both age and immunohistochemical analysis. This case report with review brings to light the importance of being aware of such pseudo-malignant lesions in our daily practice.

Keywords: Atypical Spitz tumour (ATS), immunohistochemistry, melanocytic neoplasms, melanoma, OSCC, pseudo-malignant, Spitz naevi

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INTRODUCTION

As encountering overlapping features amongst lesions is very frequent in histopathology, the awareness of certain pseudo-malignant lesions that could mimic the histopathology of moderate or even high-grade carcinomas becomes imperative for oral pathologists.

Head and neck squamous cell carcinoma (HNSCC) is common in adults and despite reports of a change in subsite predilection and age of onset, the Surveillance Epidemiology End Result (SEER) database and National Cancer Statistics in the United States cite the age-adjusted incidence to be only 0.24% and around 16.8 cases per 100,000 under 20 years, respectively.[1,2] Even melanomas and thyroid carcinomas that are common in young children are rare in the 1st decade of life/before puberty.

Despite these statistics, there have been cases of HNSCC reported in young children,[3-5] and the average annual age-specific incidence of all carcinomas in the age group 5

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to 9 has an increased female incidence (F:M = 3.1:2.3 per million) according to SEER and Elango *et al*.[6,7] Among the many pseudo-malignancies seen in children, SN, a benign melanocytic neoplasm is quite commonly encountered. It can show altered melanocytes that are epithelioid/spindle in nature along with pseudo-malignant features. As it could easily mimic an squamous cell carcinoma (SCC) or a melanoma, cautious reporting with correlation of both clinical and histopathological features becomes imperative in its diagnosis.

CASE

The gross tissue specimen after an excisional biopsy from a 6-year-old girl was submitted to the Department of Oral and Maxillofacial Pathology. As per the clinical record, the lesion, a small growth on the upper lip at the angle of the mouth, had slowly increased to the present size of 0.5 × 0.5 × 0.75 mm over a period of 6 months. A history of injury at the site during cavity preparation of carious tooth was given. On palpation and observation, the lesion was firm with a colour resembling normal mucosa. The surface was smooth and dome-shaped with focal slight speckling of brown pigmentation [Figure 1]. A provisional clinical diagnosis of 'traumatic fibroma' was given. The other differentials that were taken into account based on the clinical features are naevi, haemangioma, pyogenic granuloma, viral wart, molluscum contagiosum and dermatofibroma. After grossing and routine processing of the received specimen, the histopathological examination showed hyper-keratinised stratified squamous epithelium of variable thickness with acanthosis and some areas showing pseudo-epitheliomatous hyperplasia. The underlying connective tissue showed invasion by dysplastic epithelial cells in the form of cords, nests and islands with intra-epithelial keratin pearl-like formations [Figure 2a-c].

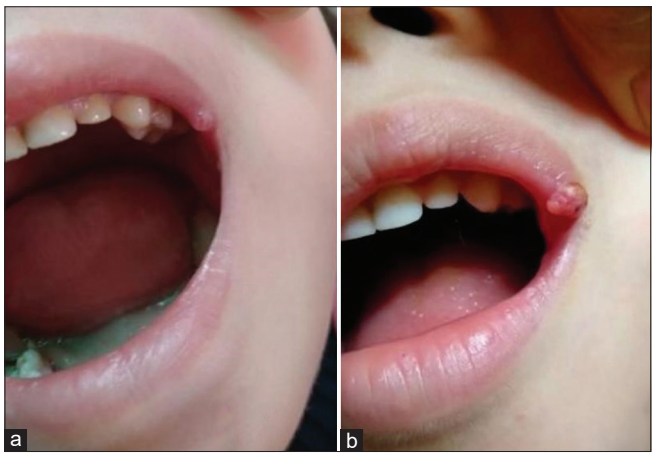

Figure 1: Clinical presentation. (a) Small nodular growth of less than 6 mm on the left corner of the upper lip. (b) Increase in size to greater than 1 cm after a period of 6 months

Focal intracytoplasmic pigment and spindling of cells were seen along with blood vessels, extravasated red blood cells (RBCs) and chronic inflammatory infiltrates. The features resembled a moderately differentiated squamous cell carcinoma at first glance. Keeping in mind the age of the patient, lesional site and clinical appearance, the patient was referred to an oncology centre for further opinion and immunohistochemical (IHC) analysis. Cells were positive for SOX10 and HMB45 and negative for CD31, ERG-1 and CK; the Ki67 index was in the range of 2–3%. Therefore, malignancy was ruled out and a diagnosis of a Spitzoid melanocytic naevus was given.

DISCUSSION

There are many lesions such as angioma, viral wart, molluscum contagiosum, dermatofibroma, pyogenic granuloma and hypo/amelanotic SN that could be mimics of paediatric melanomas.[8] Some melanocytic naevi (especially the SN or an irritated naevus) are prone to misdiagnosis and misconstrued to be malignant when specimens present features of cytologic atypia, epidermal invasion and pseudo-epitheliomatous hyperplasia along with certain Spitzoid changes. SN cases where SCC or melanoma was considered as an initial diagnosis have been reported mainly due to an intimate admixture of a hyperplastic keratinocytic component with a neoplastic melanocytic component.[9,10]

Malignancies in paediatric patients are mainly dependent on the individual's relative genetic sensitivity (i.e., mutagenic factors and inherent deoxyribonucleic acid (DNA) damage repair capacity. Many high-risk factors implicated in paediatric malignancies range from Fanconi anaemia, graft-vs-host reactions in transplant recipients, human papillomavirus, blooms and keratosis ichthyosis deafness syndromes to connexion mutations.

The subsites usually involved in these young individuals are the tongue followed by gingiva and lip.[4,5] Our patient was a young girl of age 6 with demographics matching these estimates and histopathology that showed features similar to SCC. Another important differential was paediatric melanoma, which accounts for only 1% of all melanoma diagnoses and is usually seen above the age of 10 years. Melanomas can be categorised into three prevalent subtypes—congenital/adult-type melanomas, Spitzoid/atypical Spitz tumours (ASTs) and melanomas arising from a congenital melanocytic naevus.[11] The Spitzoid family of melanocytic tumours, especially in children, are usually benign. Some, however, consider it to be low-grade melanomas as it can show features akin

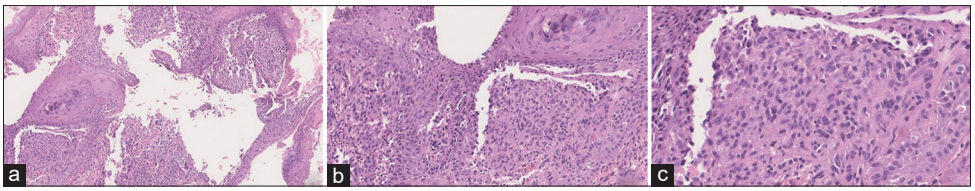

Figure 2: (a-c) H&E. (a) Photomicrograph showing areas of invasion and intra-epithelial Keratin pearl-like formation (H&E X10). (b) Photomicrograph showing cellular atypia and spindling of cells (H and E X20). (c) Photomicrograph showing areas of intermingling of both melanocytic and keratinocytic components (H&E X20)

to melanomas clinically and pathologically, thus creating difficulties in diagnosis.

SN and ASTs

The 'Spitz naevi' also called spindle/epithelioid cells/classic SNs were initially described by Darier and Civatte in 1910 and then by Sophie Spitz in 1948. They can arise de novo or from an already existing naevus. Though benign, the histological variations shown by some Spitzoid melanocytic naevus have resulted in the categorisation of these into SNs, Spitzoid melanomas and ASTs.[12] SNs can be of the junctional (65%), compound (75%) or intradermal (25%) variety. Another salient feature with regard to this not very uncommon benign tumour is its peak incidence in the 1st decade or prepubescent age of life with a ratio of 60:1 when compared to melanomas (occurrence—1st and 2nd decades). Age, hence, can be an adjunct clue in its diagnosis.[13] The features exhibited by an SN, an atypical Spitz tumour (ATS) and a Spitzoid melanoma can overlap requiring a proper correlation of clinical, histopathological and ancillary studies. This distinction is important because while the SN is completely benign, the Spitzoid melanomas are malignant and ASTs fall between the two with the outcome and prognosis varying greatly.

SN normally is seen as a papule or nodule less than 6 mm, with pink/red/brown colouration. The ASTs, however, usually seem to have a size greater than 1 cm with raised or dome-shaped appearance and can be amelanotic and solitary. Though extremities are commonly involved in adulthood, 37% occur in the head and neck region in children.[14] It is typically seen in children before puberty or in their 1st decade of life, and it has a marked female predilection. The prognosis is most favourable in children compared with adults. While it is common on the skin of face, very few reports of lip involvement are present in the English literature. Our case reports Spitzoid naevi on the upper lip, which in itself is uncommon.[15] The histopathological variations seen between ATS and SN could be variegated to their symmetry, pleomorphism, migration, maturation or zonation. While the SN is characteristically symmetrical with epithelioid/spindle melanocytes and Kamino bodies (KBs), they show minimal dysplastic features. ASTs, however, can show asymmetry, ulceration, cytological atypia, increased mitotic (>2–6/mm^2) and proliferation indices (≥10%) along with single melanocytes instead of clusters, presence of zonation and no KB.

KBs are hyaline globules that are similar to but dull in appearance compared with a dyskeratotic cell and are localised more in the hyperplastic epidermal layer above the dermal papillae. They are found to contain collagen (type IV and VII) laminin and fibronectin. It can also be present in melanomas and other melanocytic naevi but can be differentiated from those by being PAS-D-positive.[16] An important observation of 'consumption of epidermis' (COE) where there is considerable effacement of rete ridges is usually seen in both melanomas and SNs leading to a diagnostic dilemma compounded further by atypia.[17] The feature of COE can explain the areas resembling invasion on histopathological examination in our case report. IHC becomes imperative in these situations to arrive at a diagnosis.

A panel of markers is suggested to differentiate an SN from melanomas. It usually consists of PAN CK, CD68 and P40 all carried out to rule out the list of differentials based on infiltrates (lymphocytic, histiocytic or melanocytic). P40 with its improved specificity is predominantly expressed in OSCC. A negative CK, CD31 and ERG-1 helped us to rule out epithelial tumours and those with endothelial differentiation, respectively. A negative synaptophysin dismissed thyroid carcinoma and neuroendocrine tumours. Markers sensitive for melanoma are Melan-A/MART-1, MIB-1, P16, (weak expression) SOX10 and HMB45. Our case was positive for SOX10, indicating a positive melanocytic lineage. MIB-1 showed only a low percentage (0–2%) of immunoreactivity in SN and ASTs as normal. The proliferation index of Ki67 was between 2 and 3% [Figure 3], indicating that it could be more in tune with an intermediate tumour such as ASTs as <2% favours benign SNs and an index >10% favours Spitzoid neoplasms. So, the case was reported as a benign Spitzoid melanocytic naevus.[18]

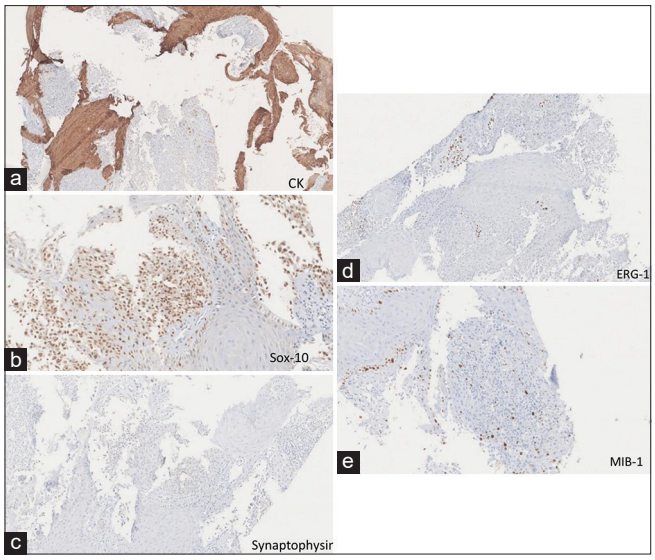

Figure 3: (a-e) IHC. (a) Photomicrograph showing CK-negative expression, X20. (b) Photomicrograph showing SOX10-positive expression, X20. (c) Photomicrograph showing synaptophysin-negative expression, X20. (d) Photomicrograph showing ERG-1-negative expression, X20. (e) Photomicrograph showing MIB weakly positive expression, X20

Management: Recurrence of SN is rare, and surgical excision is generally recommended. Conservative management with clinical and dermoscopic controls every 3–6 months can be taken up for relatively small lesions with a size less than 1 cm, provided there is no sudden change in size, colour, shape and size of the lesion.[8]

CONCLUSION

Cutaneous malignancies are a rarity except in the neonatal age group, and their diagnosis has to be dealt with very cautiously as many skin-related pathologies in children can mimic a malignant condition based on the presenting features. Therefore, a proper correlation of clinical, histopathological and clinical courses should be combined with adjunct tools such as diagnostic and molecular techniques such as IHC and comparative genomic hybridisation (CGH) to differentiate certain types of SNs from Spitzoid neoplasm, melanoma and carcinomas.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form the patient (s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initial s will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

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Conflicts of interest

There are no conflicts of interest.

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