Research Paper

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CLEAR CELL SCC: UNCOMMON VARIANT OF COMMON MALIGNANCY IN HEAD AND NECK

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ABSTRACT Clear cell squamous cell carcinoma (SCC) is an extremely rare and incompletely understood entity. Clear cells change occurs due to cytoplasmic accumulation of glycogen, water, intermediate filaments, immature zymogen granules, or a paucity of cellular organelles. We, hereby present a case of clear cell variant of squamous carcinoma on lower gingivo buccal mucosa in 59-year-old male patient. Histopathology showed sheets of clear cell separated by fibrous septa and foci showing squamous cells with malignant features. Histochemical findings showed Periodic Acid-Schiff (PAS) negative and immunohistochemistry (IHC) revealed CK positivity. We concluded by emphasizing on the need of further analysis of all clear cell tumours in head and neck with histochemistry and IHC investigations to arrive at the proper diagnosis. To establish the biological nature, significance and clinical course of clear cell SCC more number of case reports are expected to be published in future.

KEYWORDS

Clear Cells, Squamous Cell Carcinoma, Oral Cavity, Histochemistry

ARTICLE HISTORY

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INTRODUCTION

Clear cells, as the name suggests, are microscopic clearance of cytoplasm due to failure to stain with hematoxylin and eosin. It occurs due to cytoplasmic accumulation of glycogen, water, intermediate filaments, immature zymogen granules, or a paucity of cellular organelles. Clear cell change in malignancy is not an uncommon phenomenon, but when a tumour is designated as clear cell tumour or a variant of some primary tumour, it is limited in numbers. Though WHO has not categorised clear cell variant in squamous cell carcinoma, there are available literature mentioning their occurrence, nature and predicting their behaviour. After literature search, we could analysed 7 such cases involving the skin and 2 cases of oral cavity squamous cell carcinoma to compare with our case.

CASE REPORT

A 59 year old man came to head and neck opd with a swelling in right upper jaw for past 4 months and complained of pain which was insidious in onset. His intra oral examination revealed an exophytic growth in the right upper jaw, and extra- oral examination revealed multiple bilateral cervical lymph nodes largest measuring 3.5x3.0 cm. CT scan showed a heterogeneously enhancing lobulated soft tissue density lesion measuring 50x38x35 mm in the right upper alveolus, upper lip and right nasolabial fold. Incisional biopsy report was given as moderately differentiated squamous cell carcinoma. The patient has undergone maxillectomy along with extended radical neck dissection .

On gross examination , a large ulceroproliferative growth measuring 5x4cm seen in upper jaw extending upto the upper lip and right nasolabial fold. Cut section of the growth was gray white and lobulation was noted. Microscopy showed sheets of predominantly clear cells invading into underlying connective tissue stroma. The cells were round to polygonal with clear cytoplasm having nuclear hyperchromasia and atypia. Underlying maxillary bone was involved by the tumour cells. Foci of tumour cells showed squamoid differentiation with the presence of keratin pearls.PAS stain was done to know the nature of clearing artefact and it was negative. To rule out the differentials of clear cells in head and neck lesions, immunohistochemistry of CK, S100, EMA was done. Except CK, all other markers were negative.

A diagnosis of squamous cell carcinoma –clear cell variant has been reported with a pathologic staging of pT4aN2b M0

DISCUSSION

There are very few case reports of clear cell variant of SCC. Kuo[1] was the first one to report the clear cell subtype of cutaneous SCC in 1980 and kiran kumar[2] was the first one to mention the same in the oral cavity. Since maximum number of the cases were mentioned from cutaneous part, we could observed few of the valuable findings to compare our case with them. Though, most of the cases were reported in head and neck region, there were 2 cases reported in axilla and torso too.[4]

The possible differentials for clear cell neoplasms in oral cavity region includes salivary gland origin (mucoepidermoid carcinoma, acinic cell carcinoma, epithelia- myoepithelial carcinoma, clear cell myoepithelial carcinoma and hyalinizing clear cell carcinoma) and odontogenic origin (clear cell odontogenic carcinoma and clear odontogenic ghost cell tumor) with rare occurrence of SCC and melanoma with clear cell changes[4,5]. In case of appearance of clear cells in cutaneous malignancies the differentials to be ruled out include the various adenexal tumours (, clear cell hidradenoma, eccrine

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spiradenoma, clear cell hidradenocarcinoma, tricholemmoma, Tricholemmal carcinoma, pilar tumor) melanocytic lesions (balloon cell nevus, balloon cell melanoma, amelanotic melanoma), clear cell acanthoma and metastatic carcinoma from (renal cell carcinoma, lung, liver, large bowel, prostrate,thyroid) and very rarely clear cell chondrosarcoma, liposarcoma, clear cell sarcoma etc.[4,5,6] Therefore, special stains like PAS with or without diastase (to rule out adenexal, salivary gland origin), sudan black (lipid), mucicarmine and alcian blue (mucin) along with various IHC markers like CK (epithelial origin), SMA (myoepithelial)S100(melanocytic),EMA and CEA (adenexal) are required to arrive at the proper diagnosis. Originally, Kuo described three types of clear cell SCC, namely, keratinizing (type I), nonkeratinizing (type II), and pleomorphic (type III). Type I tumors are described as neoplasms formed by sheets or islands of clear cells with empty appearing or "bubbled" cytoplasm with foci of keratinization and keratin pearl formation. TypemII tumors are described as predominantly dermal neoplasms with parallel and anastomosing cords of cells with central nuclei and finely reticulated clear cytoplasm, without keratinization and ductal or glandular differentiation. Type III demonstrates marked pleomorphism with extensive vascular and perineural invasion[7,1].A study from spain by Corbalán-Vélez R et al had highlighted few of the facts after studying 249 cases of cutaneous SCC that clear cells were common in SCCs, though only some SCCs present a large number of clear cells. The invasive SCCs derived from bowen disease presented a larger proportion of clear cells which showed presence of glycogen and explained as clearing because of adenexal involvement. In their study, observation of the histologic pattern of clear cells around keratin pearls practically ruled out adnexal differentiation where actinic keratosis was the prior lesion and showed p16 positivity. Hence, they suggested that the presence of HPV may be an essential factor for the development of this histologic pattern, whereas actinic keratosis or chronic solar damage would be additional factors[3]. The other possible various attributable factors include arsenic exposure, radiation, chronic ulceration, immune suppression etc.[1,7]

Most of the cases were seen in elderly female while our case was a middle aged male. Like all other reported cases, the present case also showed rapidly growing large ulcero- proliferative growth and showed aggressive behaviour. Except one case report, all other case of clear cell SCC were glycogen negative. Corbalán-Vélez R et al had suggested that development of clear cells in SCC is a progressive process that require time and occur only in advanced SCC.[7] Hence, we too support the theory of degenerative changes rather than intracellular accumulation. So, presence of any clear cells, the basic PAS stain should be done to predict the cause of clearing and also to rule out the possibility of adnexal and salivary gland origin neoplasms. Further IHC will help to confirm the diagnosis. Al-Arashi MY et al had studied cases of clear cell squamous carcinoma in situ (SCCIS) and found clear cell change in SCCIS was part of a spectrum which displayed Outer Root Sheeth differentiation.[9]

CONCLUSION

Clear cell change in any tumour may not be very uncommon but pure clear cell variant still might be rare incidence. Whenever evidence of primary neoplasm is missing, special stain and IHC will help to arrive at the diagnosis. Because clinical prognosis of these carcinomas may be different. The biological nature and clinical course of clear cell SCC needs to established. For that further case studies are required to consider it as a separate variant or just an usual phenotypic phenomenon.

LIST OF ABBREVIATIONS USED

SCC- squamous cell carcinoma
PAS- periodic acid schiff
IHC- immunohistochemistry
WHO- world health organization
CK-cytokeratin
EMA- epithelial membrane antigen
CEA-carcinoembryonic antigen

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