Hyalinizing clear cell carcinoma of the base of tongue


Abstract. Hyalinizing clear cell carcinoma is a rare, low-grade neoplasm of the minor salivary glands. It is composed exclusively of epithelial cells with optically clear cytoplasm. There are only a few isolated cases reported in the literature involving the base of tongue. The treatment of choice is wide excision and selective neck dissection, with or without radiotherapy. The prognosis of these tumours is good. A 57-year-old male patient presented with a lesion in the base of tongue, which was well enhanced on contrast computerized tomography scan. Once confirmed by biopsy, the hyalinizing clear cell carcinoma was resected via a transcervical approach. The patient underwent postoperative radiotherapy. There was no evidence of locoregional recurrence or distant metastasis at 18 months of follow up.

Case report

A 57-year-old male presented with a history of foreign body sensation in the throat for 1 month. There was no history of smoking or intake of alcohol. On examination by indirect laryngoscopy, a 3 cm × 3 cm smooth submucosal mass towards the left side of the base of tongue, extending to the tonsillolingual sulcus and vallecula (Fig. 1). On palpation, the mass was firm, not tender and did not bleed. The tongue movement was normal. There was no palpable cervical lymphadenopathy.

The computerized tomography scan of the neck (axial cuts) with contrast showed a well defined heterogeneously enhancing mass at the base of tongue towards the left (Fig. 2). It involved the ipsilateral mylohyoid muscle and bilateral genioglossus muscles. The lesion was extending to the left vallecula and abutting the epiglottis, displacing it posteriorly. There was no evidence of enlarged cervical lymph nodes. A chest radiograph was normal. A biopsy was taken under general anaesthesia, which was suggestive of clear cell carcinoma. An ultrasound of the abdomen was normal. The patient was taken up for excision of the mass via a transcervical approach under general anaesthesia following nasotracheal intubation. On exposure of the hyoid bone, the muscles attached to its superior border were cut and retracted to expose the tumour. The tumour was removed in toto by blunt dissection. An extended supraomohyoid neck dissection was done. The wound was closed after achieving haemostasis and placing a vacuum drain.
Grossly, the tumour was partly circumscribed, measuring 3 cm x 2 cm x 1.5 cm. It was solid and grey white on cut surface. Microscopically, the tumour was partly encapsulated with infiltrative margins, and was composed of large polygonal cells with clear cytoplasm and distinct cell borders (Fig. 3a). In some areas, these cells were admixed with smaller cells having amphophilic cytoplasm. The nuclei were large, oval to slightly irregular with coarse chromatin. The neoplastic cells were arranged in nests and trabeculae, surrounded by fibrous stroma showing hyalinization (Fig. 3a). Periodic acid–Schiff (PAS) stain with and without diastase showed intracytoplasmic glycogen in some of the tumour cells (Fig. 3b). There was no evidence of intracytoplasmic mucin or fat. No atypical mitosis or necrosis was seen. Immunohistochemistry showed the tumour cells to be positive for cytokeratin (AE1/AE3; Dako) (Fig. 3c). S-100 (Dako) and vimentin (Dako) were negative. The light microscopic and immunohistochemical features were diagnostic of hyalinizing clear cell carcinoma. The resected margins and the lymph nodes were free of tumour.

Three weeks after surgery, the patient received postoperative radiotherapy of 60Gy in 30 fractions over 6 weeks. When seen on follow up after 18 months there was no evidence of recurrence or distant metastasis.

Discussion

Hyalinizing clear cell carcinoma (HCCC) is a distinct clinico-pathological entity. Microscopically, it is composed exclusively of a monomorphic population of undifferentiated cells with optically clear cytoplasm. It is a rare entity accounting for less than 1% of all salivary gland tumours. They arise from the minor salivary glands within the oral cavity and are commonly located in the palate, lips and buccal mucosa. Base of tongue, hypopharynx, larynx, nasal cavity and jaw bones are the other rare documented sites of tumour occurrence. The tumour is more common in women between the fifth and seventh decades of life. Clinically, as in this case, HCCC presents as a slow growing and painless submucosal mass.

The World Health Organization has not included HCCC as a separate entity in its classification of salivary gland neoplasms. Prior to its description by MILCH-GRUB et al., a few cases of the same tumour had been reported in the literature under various synonyms, such as clear cell carcinoma, glycogen-rich clear cell adenocarcinoma and glycogen-rich clear cell carcinoma. At present, it has the status of a distinct clinico-pathological entity, with the behaviour of a low-grade neoplasm with a low propensity towards recurrence, nodal and distant metastasis. A few cases of the tumour metastasizing to the regional lymph nodes and two cases with metastasis to the lungs have also been reported in the literature. Although increased mitosis was found in these cases, it is not a reliable feature in predicting tumour behaviour, as this feature was also seen in tumours with no metastasis.

Histologically, the tumour has infiltrative borders, with the neoplastic clear cells arranged in thick trabeculae, nests, cords or solid sheets with a hyalinizing stroma. Eosinophilic cells, as seen in the present case, may also be a component of the tumour. The clear cells have distinct cell borders.
borders with uniform small nuclei, which may show mild nuclear pleomorphism, as in this case. The special stain, PAS with and without diastase, shows variable amounts of PAS-positive diastase-sensitive material, representing glycogen, in the cytoplasm of the tumour cells. The tumour cells do not contain mucin. Immunohistochemistry shows expression of epithelial markers especially cytokeratins, and negativity for vimentin, S-100 and SMA. The differential diagnosis of HCCC on histopathology includes mucoepidermoid carcinoma, acinic cell carcinoma, clear cell oncocyteoma, epithelial myoepithelial carcinoma, malignant myoepithelioma, sebaceous carcinoma, odontogenic tumours and metastatic renal cell carcinoma, all of which show a significant proportion of clear cells. The use of special stains and immunohistochemistry, along with careful histological examination of the tumour, for identifying the typical features found in each of these neoplasms, help in arriving at a correct diagnosis. The clear cells of mucoepidermoid carcinoma contain cytoplasmic mucin highlighted by mucicarmine stain. In sebaceous carcinoma, the presence of cytoplasmic lipid which is lost in routine histological processing accounts for the optically clear cytoplasm, and is demonstrated by fat stain on frozen tissue. The clear cells in a clear cell oncocyteoma contain glycogen, while the oncocytes cells contain abundant mitochondria, which stains with phosphotungstic acid haematoxylin. The tumour cells in acinic cell carcinoma contain zymogen granules, which are PAS positive and diastase resistant. Neoplastic myoepithelial cells in epithelial/myoepithelial carcinoma and malignant myoepithelioma express S-100 protein and SMA, which are not expressed by HCCC. The odontogenic tumours show a biphasic growth pattern with expression of cytokeratin and S-100 protein. Neoplastic cells in renal cell carcinoma co-express cytokeratin and vimentin, whereas neoplastic cells in HCCC are negative for vimentin. Radiological imaging studies are also helpful in ruling out the possibility of a metastatic renal cell carcinoma. Clinical differential diagnosis of the lesion at the base of tongue would include epithelial malignancies, granulomatous conditions, lingual thyroid, prominent lingual tonsils and cysts.

As these tumours are rare, there is no standard treatment protocol. There is controversy as to the appropriate surgical margins, the role of radiotherapy and the management of the neck. The indolent clinical course suggests that wide local excision is the treatment of choice. Large tumour size and nodal metastasis may alter the prognosis. An aggressive variant has been reported. Postoperative radiotherapy is reserved for large tumours (>3 cm) and for positive surgical margins.

In conclusion, HCCC is a rare minor salivary gland tumour exhibiting the behaviour of a low-grade malignancy. It has a better prognosis than the other salivary gland tumours showing clear cells. Wide local excision achieves adequate locoregional control of small primary tumours.

References
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