CASE REPORT

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Never too young for a salivary gland carcinoma ex-pleomorphic adenoma



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Abstract

Background Carcinoma ex-pleomorphic adenoma (CXPA) can either arise primarily as a de novo or from the malignant transformation of a benign pleomorphic adenoma (PA). CXPA mostly occurs in adults aged 50 to 70 years; hence, the occurrence of CXPA in younger ages is not common.

Case presentation We report a 27-year-old female who had a history of submandibulectomy for pleomorphic adenoma, and presented with recurrent left submandibular swelling for 4 months. The mass was rapidly increasing in size and was associated with occasional throbbing pain. Examination showed a multilobulated, firm left submandibular swelling with no overlying skin changes. FNAC was performed twice, by conventional and ultrasound-guided techniques, and both concluded as benign salivary gland tumours. CT scan and MRI revealed a well-demarcated tumour with an area of necrosis within, with no obvious invasion into surrounding soft tissue and no significant lymphadenopathy. Having high suspicion of a malignant transformation, the tumour was resected with a concurrent modified radical neck dissection. The histopathological examination confirmed a carcinoma ex-pleomorphic adenoma with the myoepithelial malignant component. The patient subsequently received adjuvant radiotherapy. This case demonstrated that CXPA, although rare, can occur in young adults. Pre-operative FNAC and radiological imaging may mimic a pleomorphic adenoma.

Conclusion The presence of recurrent tumours with rapid growth should alarm the clinician about a possible malignant transformation of a benign parotid tumour.

Keywords Carcinoma ex-pleomorphic adenoma, CXPA, Pleomorphic adenoma, Malignant transformation, Salivary gland neoplasms, Submandibular glands

Background

Carcinoma ex-pleomorphic adenoma (CXPA) is an uncommon malignant salivary gland tumour, which only accounts for 12% of salivary malignancies and 4% of all salivary tumours [1]. It most commonly originates from the parotid glands (67%), followed by minor salivary

¹ Department of Otorhinolaryngology Head and Neck Surgery, Hospital Canselor Tuanku MuhrizUniversiti Kebangsaan Malaysia Medical Centre, Kuala Lumpur 56000, Malaysia glands (18%), submandibular glands (15%), and sublingual glands (less than 1%) [1]. CXPA mostly occurs in the 6th and 7th decades of life and is rare in young adults [2]. In untreated patients, the majority of reported malignant transformations of a pleomorphic adenoma (PA) took 15 to 20 years [3, 4]. We present an atypical case of recurrent submandibular mass in a young female that resembles a pleomorphic adenoma but is later ascertained to be a malignant tumour.

Case presentation

A 27-year-old female presented with a recurrent left submandibular swelling that had rapidly enlarged over 4 months of duration. It was associated with intermittent throbbing pain but no discharge from the swelling



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or skin discoloration. There were no other related ear, nose, or throat symptoms. On further questioning, she revealed that she previously had a similar left submandibular swelling, for which she had undergone a surgical excision 7 months ago in another hospital. However, unlike the current mass, the first submandibular swelling was smaller in size, gradually enlarged, and had been present for 1 year before the surgery. She was told that the mass was of benign salivary gland origin. Subsequently, she noticed recurrent swelling at the same site 7 months after the surgery.

A current examination of the neck showed a large mass extending from the left submandibular region to level II of the neck posteriorly and level IV inferiorly (Figs. 1 and 2). The mass measured 8×12 cm in size, with a multilobulated surface and firm consistency. It was not fixed to the underlying structures, and there was no tethering of the skin. There was no other palpable neck mass. Examination of the tongue and other oral cavity subsites revealed no abnormalities. Endoscopic examination of the pharynx and larynx was normal. Facial nerve function, especially the marginal mandibular branch, was normal.

Fine needle aspiration cytology (FNAC) of the mass showed multiple clusters of rounds to plasmacytoid cells

Fig. 1 A large multilobulated mass at the left submandibular region extending to the lateral side of the neck



Fig. 2 From side view, a large multilobulated mass at the left submandibular region extending to the lateral side of the neck

and some spindle-shaped myoepithelial cells admixed with ductal cells. The myoepithelial and ductal cells display bland nuclei, minute conspicuous nucleoli, and a moderate amount of cytoplasm. No atypical or malignant cells were seen. These features are favourable for of pleomorphic adenoma (PA). In view of the high suspicion of malignancy, a repeated FNAC was performed with ultrasound guidance but yielded a similar result suggestive of a PA.

A contrast-enhanced CT scan of the neck showed a large heterogenous mass epicentre at the left submandibular area with central necrosis, measuring $6.3 \times 6.6 \times 7.2$ cm (Fig. 3). In keeping with the previous excision, the normal left submandibular gland was not visible. The mass extends from the angle of the mandible to the level of the thyroid gland inferiorly. Medially, it extended into the parapharyngeal space, abutting the common carotid artery and hypopharyngeal wall. An MRI of the neck was subsequently performed for better delineation of the extent of the mass in relation to the vital structures. The tumour is fairly well circumscribed, appeared predominantly isointense on T1W sequence, and heterogeneous enhancing in T2W and post-contrast studies (Figs. 4 and 5). There are some areas within the tumour that showed mildly restricted diffusion in DWI/



Fig. 3 The CECT neck shows a multilobulated, heterogenous mass over the left submandibular region with multiple necrotic areas seen within



Fig. 5 MRIT2 (coronal cut) of the neck shows a left submandibular mass extending superiorly until the angle of the mandible and inferiorly up to the level of the



Fig. 4 MRIT2 (axial cut) of the neck shows a large lobulated solid mass at the left submandibular region



Fig. 6 The excised tumour was multilobulated and well encapsulated. Received one fragment of fibrofatty tissue measuring $22 \times 20 \times 12$ mm

ADC mapping. The tumour displaced the sternocleidomastoid muscle laterally, but no obvious intramuscular extension was seen. It compressed the internal jugular vein, causing a slit-like narrowing and lying in close proximity to the common carotid artery, resulting in less than 90 degrees of the encasement. There was no significant enlarged cervical lymph node seen on the radiological imaging.

The clinical features and radiological imaging were suggestive of a malignant tumour in spite of the FNAC

result. However, CXPA cannot be totally excluded as the aspiration sample may not have targeted the malignant component of the tumour. The patient subsequently underwent tumour excision via a transcervical approach. A well-encapsulated multilobulated tumour was found intraoperatively, which was firm to hard in consistency (Fig. 6). The tumour extended from the body of the mandible to the level of cricoid cartilage (Fig. 7). It could be separated from the great vessels and laryngopharynx, except for part of the sternocleidomastoid muscle that was infiltrated by the tumour, thus had to be removed



Fig. 7 The intraoperative picture shows the submandibular tumour posteriorly to the angle of the mandible and inferiorly to the level of the cricoid cartilage



Fig. 9 Malignant cells seen adjacent to the paucicellular stroma of pleomorphic adenoma (H&E, × 20)



Fig. 8 Section shows the tumour with multilobulated architecture that consists of pleomorphic adenoma infiltrated by malignant cells arranged in sheets, cribiform, and



Fig. 10 Malignant cells exhibit mild pleomorphism, hyperchromatic to vesicular nuclei, with inconspicuous nucleoli, and moderate amount of cytoplasm. Few mitotic

together with the tumour. Ipsilaterally modified radical neck dissection was performed with preservation of the spinal accessory nerve and internal jugular vein. Besides, part of the parotid gland was removed to achieve an oncological clear margin.

Histopathological examination (HPE) of the tumour revealed malignant cells with myoepithelial differentiation forming trabeculae, cribriform, and sheets patterns, infiltrating the stroma of the surrounding pleomorphic adenoma (Figs. 8, 9 and 10). Areas of tumour necrosis and haemorrhage were seen. There was no perineural or lymphovascular invasion, but extracapsular infiltration into the muscles was evident. From the neck dissection specimen, 6/35 lymph nodes showed malignant cell infiltration with no extranodal extension. The final diagnosis was CXPA stage pT3N2bM0. The patient made an uneventful recovery from the surgery, and subsequently, she received adjuvant chemotherapy (paclitaxel and carboplatin) for 6 cycles.

Discussion

Carcinoma ex-pleomorphic adenoma (CXPA) is a malignant salivary gland tumour that can either arise de novo or result from the malignant transformation of a recurrent benign pleomorphic adenoma (PA).

Malignant salivary gland tumours are not common and account for less than 1% of all cancers and 3–5% of head and neck cancers. Approximately 41–50% of submandibular gland tumours are malignant, and CXPA accounts for 12.9% of all submandibular malignancies [5]. The incidence of CXPA in the submandibular glands is less common than in the parotid glands [6].

The most common presenting symptom of CXPA is a chronic salivary gland mass that is often painless, before

an accelerated increase in size, which may cause some discomfort or pain. However, the clinical presentation may mimic a benign PA, which makes the diagnosis of CXPA challenging [3].

A recurrent swelling in patients who previously had surgical resection of a PA should raise suspicion of CXPA.

Fine needle aspiration cytology (FNAC) is a quick, cost-effective, and widely used tool for the diagnosis of salivary gland lesions. It is highly accurate in distinguishing non-neoplastic lesions from neoplasms. The sensitivity of FNAC for salivary gland tumours varies from 62 to 97% [7]. The diagnostic accuracy is higher in benign than in malignant tumours. The reported sensitivity and specificity of FNAC for the diagnosis of CXPA were low, with less than 50% diagnostic accuracy [7].

The malignant component could be missed during the procedure in cases where it is small in a heterogeneous tumour. In our case, FNAC was performed twice, using the conventional method followed by an ultrasound-guided approach, but both did not identify any malignant cells.

Even if FNAC had detected the malignant component of CXPA, it could not distinguish the invasive nature of the tumour. Therefore, it is important to have a radiological investigation to assess the characteristics of the tumour. A CT scan and MRI are helpful to delineate the border and extent of the tumour [8]. However, a CT scan has poor soft tissue resolution, especially to determine the extracapsular extension of the tumour. MRI is superior in terms of assessing tumour extent, soft tissue invasion, and nerve involvement. Features of malignancy in MRI include heterogeneous contrast enhancement, local soft tissue invasion, poorly defined margins, hypointensity on T2-weighted imaging, and lymphadenopathy. Salivary gland malignancies have a significantly lower apparent diffusion coefficient (ADC) than benign tumours in diffusion-weighted (DW) MRI [5].

Surgical resection remains the mainstay of treatment for CXPA. Radiotherapy following surgery is considered a standard treatment for CXPA, particularly the invasive subtype, which helps reduce the incidence of local recurrence [9]. However, a study reported no recurrence at 6 years post-resection without any adjuvant treatment [3]. There is limited literature regarding adjuvant chemotherapy post-surgery in CXPA patients with mixed treatment responses [10]. The addition of chemotherapy to adjuvant radiotherapy post-surgery, especially in recurrent tumours, offers a good response and enhances the survival rate of the patient [10, 11].

CXPA is generally an aggressive tumour with a poor prognosis [3]. However, the prognosis of CXPA

depends on the stage of the tumour and complete tumour resection. High-grade tumours carry a poorer prognosis compared to low-grade tumour, whilst submandibular CXPA carries the least favourable prognosis [12, 13]. The reported overall 5- and 10-year survival rates for CXPA were 63.2% and 44.6%, respectively [14].

Conclusion

CXPA of the submandibular gland is not common and is rare in young adults. The diagnosis of CXPA is quite challenging, as FNAC, either conventional or ultrasound-guided, may miss the malignant component of CXPA, rendering the procedure non-diagnostic. A well-circumscribed tumour with no obvious local soft tissue invasion and no significant lymphadenopathy on radiological imaging does not necessarily exclude CXPA. The presence of recurrent tumours with rapid growth over a short period of time should raise a high clinical suspicion of a malignant transformation and should be addressed early to improve the patient's outcome.

Abbreviations

CXPA	Carcinoma ex-pleomorphic adenoma
PA	Pleomorphic adenoma
FNAC	Fine needle aspiration cytology
DWI/ADC	Diffusion-weighted imaging/apparent diffusion coefficient
CT	Computed tomography
MRI	Magnetic resonance imaging
HPE	Histopathological examination

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Declarations

Ethics approval and consent to participate

Ethical approval for this study was waived and inform and verbal consent to participate was obtained from all participants in this study.

Consent for publication

Informed and written consent to publish the patient's clinical details and clinical images was obtained from the participant in this study.

Competing interests

The authors declare no competing interests.

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