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Salivary duct carcinoma of submandibular gland with trigeminal nerve invasion to intracranium

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Abstract
Salivary duct carcinoma is a rare and invasive malignant tumour with rapid distant metastasis and dismal prognosis. Clinically, perineural invasion of the salivary duct carcinoma is commonly noted. Here, we present a case of salivary duct carcinoma of submandibular gland origin with perineural invasion of the trigeminal nerve proximal to the intracranium, that was well demonstrated by a magnetic resonance image (MRI) and was consistent with the clinical presentation. This case received radical resection and radiotherapy with inclusion of the skull base within the field. There was no tumour recurrence and distant metastasis 24 months post-operatively.

Key words: Carcinoma; Salivary Duct; Submandibular Gland; Trigeminal Neuropathy; Neoplasm Invasiveness

Introduction

Salivary duct carcinoma is a rare high-grade adenocarcinoma of salivary gland origin, which arises from excretory duct reserve cells,[1] first described by Kleisaser *et al.* in 1968. It is histologically similar to intraductal and infiltrating ductal carcinoma of the breast. This neoplasm occurs mainly in the parotid gland in the elderly male. Furthermore, it is associated with aggressive biological behaviour with early lymph node metastasis, local recurrence, distant metastasis and signficant mortality. Quicker recurrence and poor survival have been reported for a salivary duct carcinoma arising in the submandibular gland rather than the parotid gland.[2] Since 1968, few cases of salivary duct carcinoma arising from the submandibular gland have been reported. Here, we present a salivary duct carcinoma arising from the submandibular gland with intracranial invasion via the trigeminal nerve, proven by magnetic resonance image (MRI) and consistent with the clinical presentation. Such findings have not been described in previous studies. The patient received surgery and subsequent radiotherapy incorporating the skull base within the field. There has been no evidence of tumour recurrence or distant metastasis for 24 months.

Case report

A 49-year-old man was referred in October 2000 complaining of intermittent tender swelling over his left neck for four months. On physical examination, a 2.5 × 2.5 cm mildly tender mass over the left submandibular area was noted. Bimanual palpation revealed that there was no stony hard nodule deep in the floor of mouth. Computed tomography (CT) showed a homogenous enhanced swelling of the left submandibular gland with equivocal calcification in the duct (Figure 1). Nevertheless, calculi-related inflammatory disease of the submandibular gland was suspected. Excision of the submandibular gland was performed. During this operation, the submandibular gland was found adhesive to the surrounding tissue. There were some small (1.5 × 1 cm) hard lymph nodes surrounding the submandibular gland, which were confirmed by frozen section to contain metastatic carcinoma. One week later, salivary duct carcinoma was diagnosed by permanent sections (Figure 2). The patient then received a more radical operation including wide excision of the tumour, segmental mandibulectomy, left modified radical neck dissection and free fibula osteocutaneous flap reconstruction. Lymph node metastasis and nerve invasion were also confirmed by pathologic examination. Two weeks after surgery, he complained of headache and left facial progressive numbness over the distribution of the

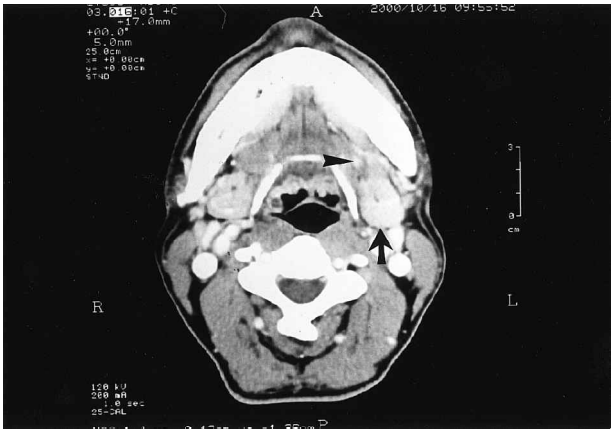

Fig. 1
Axial CT scan with enhancement demonstrating homogenous enhanced swelling of left submandibular gland (arrow) and an equivocal calcification in duct (arrowhead) were noted.

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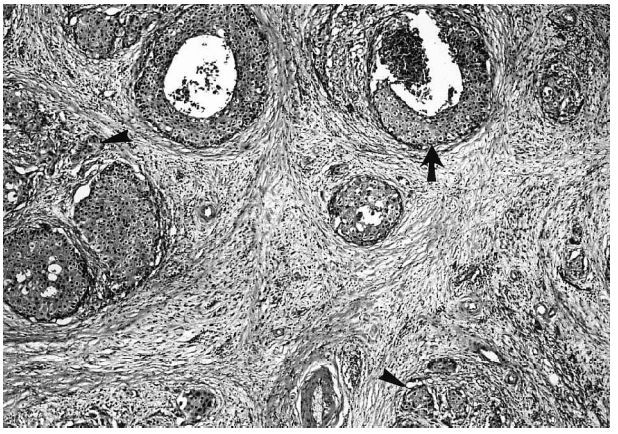

FIG. 2

Typical cribriform growth pattern (arrow) with comedonecrosis and the infiltrating component of salivary duct carcinoma with irergular cell nests (arrowhead) (H&E; ×100)

second (V2) and third division (V3) of the trigeminal nerve. Retrospectively reviewing his history, these symptoms had already developed two months before. Because these symptoms were minimal, they were neglected by the physician and the patient himself at his first visit. Although there was no evidence of widening of foramina and canals on the previous CT images, MRI was performed to look for the possibility of trigeminal nerve invasion. It showed a perineural invasion of V3 with intracranial extension from the tumour bed. Post-operative radiotherapy was carried out with the field covering the skull base, tumour bed and neck. Although left hemifacial numbness persisted, the follow-up MRI showed regressive changes of V3. There has been no tumour recurrence or distant metastasis for 24 months after surgery.

- **This is a case report of a patient presenting with carcinoma of the submandibular duct**
- **Perineural spread in the trigeminal nerve was demonstrated radiologically and the case was treated with radical surgery and radiotherapy**
- **Intracranial spread was subsequently confirmed on the basis of the patient's symptoms and a MRI examination**
- **The authors conclude that the possibility of perineural invasion should be considered and that high resolution scanning and post-operative radiotherapy are important in the management of this disease**

Discussion

Salivary duct carcinoma is one of the most malignant neoplasms of the salivary gland, and has histological characteristics similar to ductal carcinoma of the breast, but it is frequently diagnosed at an advanced stage.[3] It occurs predominately in patients over 50 years old and is three times more common in males.[4] The most frequent occurrence is in the parotid gland that accounts for about 88 per cent of cases, eight per cent of cases arising in the submandibular gland and four per cent of cases in the minor salivary glands.[4] Salivary duct carcinoma arising in the submandibular gland appears to have a more aggressive behaviour than has been reported for the tumour arising within the parotid gland.[2]

The typical clinical presentation of salivary duct carcinoma at diagnosis is a rapidly enlarging mass,[1–7] 23 per cent patients have pain,[5] 29.3 per cent to 62.5 per cent patients present with a nerve palsy[3–6] and between 43 per cent and 72 per cent patients have cervical node metastasis respectively.[3,7] Because of its clinical manifestation of local pain and CT appearance, it may be misdiagnosed as an inflammatory process within the submandibular gland, as it was in our case.[4]

Although perineural invasion is frequently noted with salivary duct carcinoma, there was no reported evidence of this, either clinically or radiologically in the literature.[1–7] In general, other malignant salivary gland tumours, especially adenoid cystic carcinoma, which exhibit a similar clinical pattern of spread, metastases and perineural invasion usually develop later and are generally characterized by an indolent course.[3] In our case, the perineural invasion to the intracranial segment of the trigeminal nerve developed over a short time. Therefore the early and accurate detection of perineural invasion by a salivary duct carcinoma in the submandibular gland is necessary.

Patients with perineural invasion are initially asymptomatic, so imaging is crucial and contrast-enhanced fat suppression MRI is the method of choice.[8,9] In perineural invasion of trigeminal nerve in other malignancies, the tumour may invade intracranially along the extracranial V3.[8] When there is dysfunction of the trigeminal nerve, invasion of the intracranial segment of trigeminal nerve has often taken place.[8] In this case, the picture of intracranial trigeminal nerve invasion was identified by a coronal T1-weighted MRI scan. This corresponded well to the clinical presentation and explained the dysfunction of V2 and V3.

Histologically, the most peculiar features of salivary duct carcinoma are a striking resemblance to ductal carcinoma of the breast, with intraductal-like and invasive components.[1–7] The intraductal component grows in papillary, cribriform, or solid patterns often with central (commedo) necrosis (Figure 2). The infiltrating pattern is characterized by small ducts and cords of tumour cells associated with a marked desmoplastic stroma that is indistinguishable from that seen in scirrhous carcinoma of the breast. Perineural or intraneural infiltration is also a common finding, and the incidence of pathological nerve invasion (Figure 3) is higher than its clinical presentation.[4,6]

Because of the aggressive behaviour of salivary duct carcinoma, a combination of radical surgery for the primary site and neck with subsequent radiotherapy is warranted.[1–7] The frequent finding of pathological or clinical nerve involvement with possible rapid development of proximal perineural invasion intracranially means that the radiotherapy field may need to include the skull base.

Conclusion

Salivary duct carcinoma of the submandibular gland not only bears distinctive histopathological features and behaves clinically in an aggressive fashion, but also may have the propensity of perineural invasion proximally into the intracranium in a short time. To date, there is limited experience with it, but we suggest the high-resolution MRI evaluation and post-operative radiotherapy including the skull base may be important in the management of this disease.

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