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An unusual case of laryngeal spindle cell carcinoma metastasising to the orbit and heart

N Mani, D Lowe, L Pope, H El-Daly*, A Pfleiderer

Abstract

We report the first case in the world literature of laryngeal spindle cell carcinoma metastasising to the orbit. A 65-year-old woman was previously treated for T_3 N_0 M_x laryngeal spindle cell carcinoma, with laryngectomy and post-operative radiotherapy. Five months following this treatment, she developed proptosis, diplopia and reduced right visual acuity, secondary to an enlarging mass within the right orbit. This was biopsied, and subsequent histology confirmed a diagnosis of metastatic spindle cell carcinoma. Subsequent post-mortem examination demonstrated additional pulmonary, hepatic and cardiac metastatic disease, in the absence of any other primary tumour or locoregional disease. The radiological investigation of patients with laryngeal spindle cell carcinoma is discussed and contrasted with that of laryngeal squamous cell carcinoma.

Key words: Larynx Neoplasms; Spindle Cell Carcinoma; Neoplasm Metastasis; Orbit

Introduction

Laryngeal carcinoma is the commonest head and neck cancer in the western world,[1] and accounts for 200 000 deaths annually worldwide. Typically, large tumours give rise to direct extra-laryngeal or regional lymph node spread, the latter being perceived as the single most important determinant of prognosis. It is known that glottic tumours rarely give rise to nodal metastases due to sparse lymphatic drainage; however, after direct spread to either the subglottis or supraglottis, the propensity increases.[2] Distant metastases are unusual – one retrospective study demonstrated an overall rate of distant metastases from glottic tumours of 4.4 per cent.[3] Such distant metastases impact adversely on patient survival and may significantly affect patient management. When laryngeal carcinoma does metastasise, distant metastases arise mainly in the lung (45 per cent), followed by the bones (25 per cent) and liver (6 per cent).[4]

Spindle cell carcinoma has previously been described as a 'sarcomatoid' tumour, as histological appearances may resemble sarcoma. It is now considered by most authorities as a variant of squamous cell carcinoma, although the precise histogenesis remains a source of debate.[5] Spindle cell carcinoma typically presents as an ulcerated tumour, which on histological examination contains mesenchymal elements including spindle cells. While spindle cell carcinoma may have a comparable prognosis to squamous cell carcinoma of the same stage, one case series demonstrated a relatively high incidence of distant metastasis from laryngeal spindle cell carcinoma, albeit from a small number of cases (14 per cent; three of 26 cases).[6]

We present a case of primary spindle cell carcinoma of the larynx, with multiple distant metastases to the orbit, heart and bone, the former having never been previously reported in the world literature. In addition, we discuss the management of these unusual tumours.

Case report

A 65-year-old woman presented to the out-patient ENT department with a two-month history of hoarseness of voice, associated with left-sided otalgia and a left-sided sore throat. She had also lost one and a half stone in weight over the preceding 12 months. She was a lifelong heavy smoker of 40 cigarettes per day, and drank more than 40 units of alcohol per week.

Initial microlaryngoscopy demonstrated an extensive glottic tumour extending into the subglottis, with a fixed left vocal fold (clinically T_3 N_0 M_X). Histological analysis of the initial biopsy demonstrated spindle cell carcinoma (shown in Figure 1a and 1d). No areas of conventional squamous cell carcinoma or carcinoma in situ were present. A computed tomography (CT) scan of the thorax and neck excluded any primary or metastatic disease in the chest or cervical lymphadenopathy.

The patient underwent a total laryngectomy with primary tracheoesophageal puncture two weeks after histological diagnosis. At the time of surgery,

From the Departments of Otolaryngology, Head and Neck Surgery, and *Histopathology, Peterborough Hospitals NHS Trust, UK.

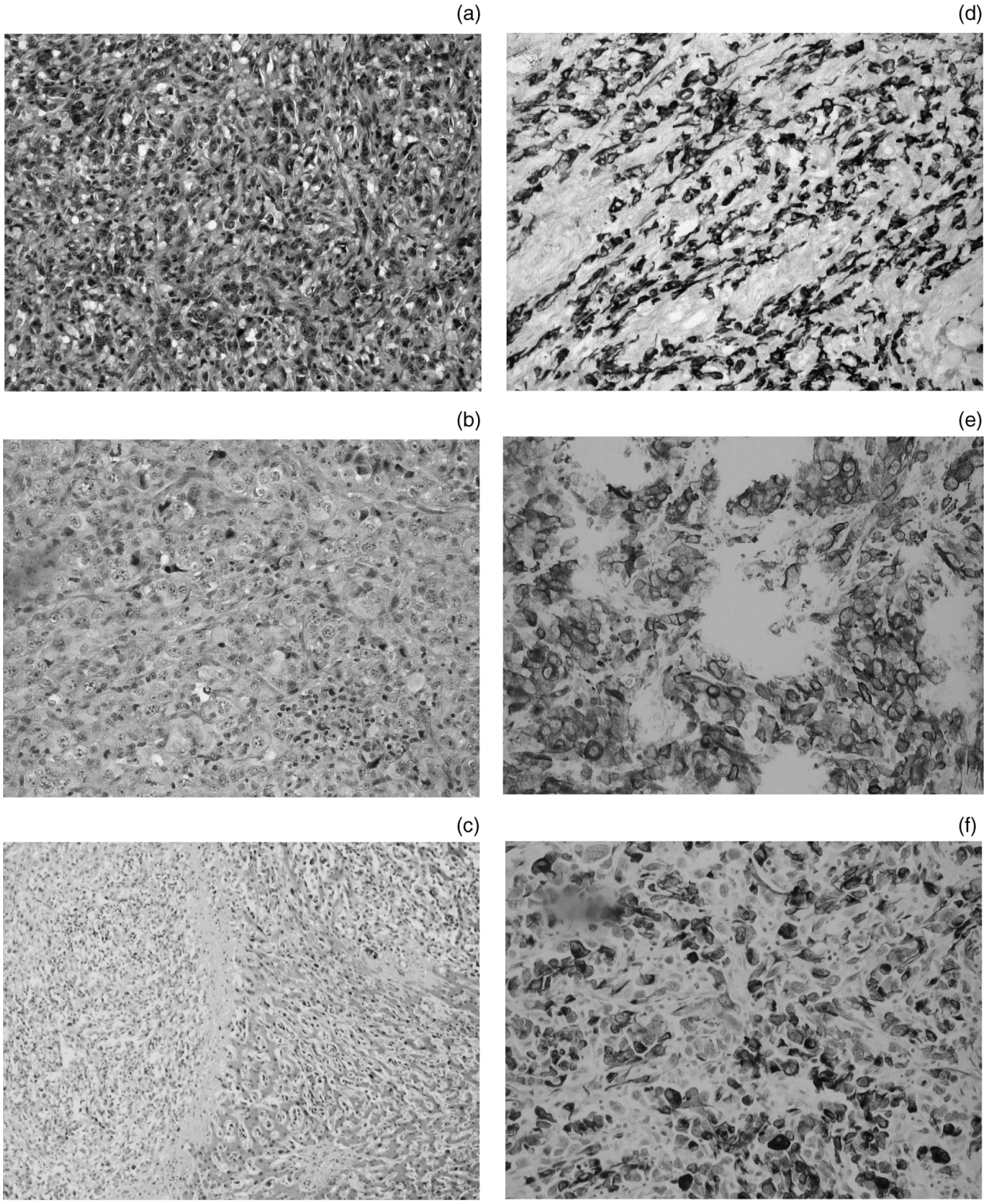

FIG. 1

Photomicrographs showing sections of the tumour, stained both with haematoxylin and eosin and with immunochemical stain (i.e. MNF-116 (Monoclonal mouse anti-human cytokeratin antibody which detects kevatins 5, 6, 8, 17 and 19. The antibody shows an especially broad pattern of reactivity with human epithelial tissue from simple glandular to stratified squamous epithelium) positive), from the larynx (a and d), orbit (b and e) and liver (c and f), respectively. (Figures 1a and d: x 40. Figures 1 b,c,e and f: x 100).

the tumour was seen to extend at least 1.5 cm into the subglottis.

The patient subsequently received a post-operative course of radical radiotherapy totalling 60 Gy, in 30 fractions. Histological analysis again confirmed spindle cell carcinoma, completely excised with clear resection margins and no evidence of lympho-vascular invasion or nodal involvement. The patient

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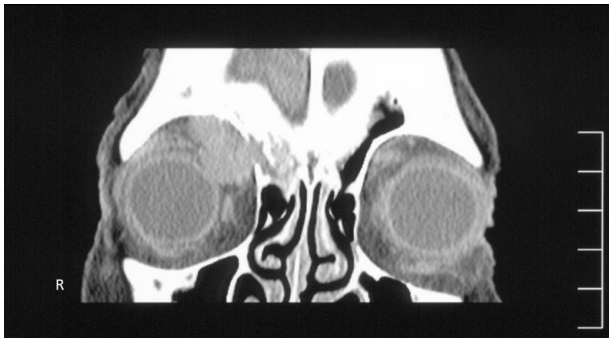

FIG. 2
Coronal computed tomography scan demonstrating right orbital metastasis.

made an uneventful recovery and developed good speech. She remained under regular follow up in the multidisciplinary head and neck clinic.

Five months following laryngectomy, the patient presented with diplopia, reduced right visual acuity and also bilateral hip pain. Clinical examination showed marked proptosis of the right eye, with lateral and inferior displacement of the globe. There was a palpable mass at the superomedial aspect of the right orbit. There was no evidence of involvement of overlying skin. Superior gaze was restricted in the right eye.

Computed tomography of the orbits confirmed a 2 cm mass in the right orbit, with bony orbit wall erosion (demonstrated in Figure 2). Biopsy of this mass indicated a carcinoma with a morphology and immunohistochemical pattern analogous to that of the primary laryngeal neoplasm (i.e. spindle cell carcinoma). Despite this, the histological appearance of the orbital metastasis (see Figure 1b) was perhaps more typical of poorly differentiated squamous cell carcinoma (SCC), when compared with the primary. While unproven in this case, distant metastases may be derived from elements of SCC within the primary neoplasm. Immunohistochemical staining was positive only for monoclonal anti-cytokeratin (clone MNF-116). The tumour cells showed negative staining for marker for malignant melanoma (anti-S100), markers for gastrointestinal, lung, ovarian breast, as well as endometrial epithelial tumors (anti-CK7, anti-CK20, anti-TTF1), marker for neoplasms arising from endothelial cells and haematopoietic and lymphoid tumors (CD34) as well as marker for neuroendocrine tumors, NK/T lymphomas, small cell lung carcinoma (anti-CD56).

Neurological examination of the lower limbs showed reduced muscle strength in both quadriceps, with absent knee jerks but present ankle jerks. A magnetic resonance imaging scan of the spine revealed multiple thoracic vertebral deposits in T5, T6, T7 and T9 and para-vertebral soft tissue masses at levels T5/6 and L2/3, in keeping with metastasis. Computed tomography scanning of the thorax and abdomen showed multiple lesions, consistent with pulmonary and hepatic metastases.

A post-mortem was carried out, which confirmed the radiological findings of multiple chest and hepatic metastases. No other primary neoplasm was identified. In addition, a previously undiagnosed metastatic deposit to the heart was demonstrated in the wall of the left ventricle. Histological analysis from the pulmonary, hepatic, spinal and heart metastases confirmed similar histological appearances to the primary tumour.

Discussion

Spindle cell carcinoma is an unusual and uncommon neoplasm. It has been described in various sites throughout the body, but has a predilection for the upper aerodigestive tract.[6] The histological origin of spindle cell carcinoma is controversial, and its appearances have been described using a number of terms, including pseudosarcoma, sarcomatoid carcinoma, carcinosarcoma and pleomorphic carcinoma. Two large case series of spindle cell carcinoma of the larynx both showed a particularly high male preponderance (more than 90 per cent),[6,7] as well as a high incidence of glottic tumours (more than 70 per cent).

Spindle cell carcinoma is said to behave in a similar manner, biologically, to squamous cell carcinoma of the larynx. Both may demonstrate local spread as well as metastatic capability to regional lymphatics and distant sites.[8] However, some studies[9,10] suggest that spindle cell carcinoma of the head and neck may represent a more aggressive neoplasm than typical squamous cell carcinoma. The pattern of metastatic spread in our patient would support this.

One study showed that, when predicting the metastatic potential of spindle cell carcinoma, the primary consideration is the site of origin, rather than histological characteristics.[11] The same authors noted that, in keeping with squamous cell carcinoma, glottic spindle cell carcinoma tumours have a low propensity for metastasis. The approximate metastatic rate in the cases reviewed was 15 per cent for glottic tumours, 30 per cent for supraglottic tumours and 60 per cent for hypopharyngeal tumours. In our case, the primary glottic spindle cell carcinoma was seen to extend markedly into the subglottis.

The importance of keratin immunostaining of the tissue has been highlighted by Olsen *et al.*,[5] who demonstrated that patients with negative keratin immunostaining had a significantly increased survival rate. Furthermore, in the series that they considered, all patients with metastases had tumours that stained positive for keratin. In another series of spindle cell carcinoma cases, 65 per cent of tumours showed keratin positivity.[6] In our case, keratin immunostaining was positive, as expected.

Clinical evidence of non-lymphatic distant metastases has been reported in approximately 10 per cent of cases of head and neck squamous cell carcinoma. A review of reports on metastatic orbital tumours revealed that most were from the lung, followed by the breast, liver, adrenal gland and stomach, in that order.[12] However, post-mortem examination did not demonstrate another primary tumour in our patient, and there was no evidence

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of locoregional spread, either before death or at post-mortem.

A previously published report described one case of adenoid cystic carcinoma of the larynx giving rise to a metastasis within the eye.[13] However, to our knowledge, the present case represents the first report in the world literature of laryngeal spindle cell or squamous cell carcinoma giving rise to an orbital metastasis. In addition, post-mortem examination confirmed that an intra-cardiac metastasis was present, which in itself represents a particularly unusual finding in a patient with laryngeal carcinoma.

Conclusion

This case represents the first reported example of spindle cell carcinoma of the larynx metastasising to the orbit and heart. We have also discussed the differences between spindle cell and squamous cell carcinoma of the larynx. In our case, given the relatively short time interval from presentation to death, it remains likely that such distant metastases may have originated early in the clinical course or at least prior to laryngectomy. Early and rapid distant metastases have been previously reported with spindle cell carcinoma from a T_1 N_0 tumour.[14] In this case, it is likely that the pre-operative CT scans of the chest failed to demonstrate metastatic disease; if available, positron emission tomography scanning might have offered an additional opportunity for detailed staging at presentation.

There is accumulating evidence suggesting that spindle cell carcinoma is more aggressive and carries a worse prognosis than other laryngeal squamous cell carcinoma because of its greater propensity for distant metastasis. This is demonstrated and supported by our case. As a result, we would recommend consideration of increased radiological screening, in order to exclude distant metastases, prior to treatment in such cases.

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Address for correspondence:
Mr David A Lowe,
Abbeystone House,
High Street,
Milton,
Cambridge CB4 6AJ, UK.

E-mail: dlowe@rcseng.ac.uk

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