CASE REPORT

Small cell lung cancer presenting as unilateral rhinorrhoea

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SUMMARY

The metastatic spread of infraclavicular malignancies to the nasal cavity is rare. We describe the case of a 58-year-old man who presented with a 4-month history of right-sided rhinorrhoea, maxillary hypoesthesia, hyposmia and hypogeusia. Clinical examination revealed an irregular mass within the right nasal cavity. Immunohistochemical analyses of biopsies were consistent with small cell carcinoma of indeterminate origin. A positron emission tomography scan demonstrated extensive mediastinal lymphadenopathy with collapse-consolidation of the right lung's middle lobe and no other sites of metastasis. Following discussion at the lung multidisciplinary team meeting, a diagnosis of metastatic small cell lung cancer (SCLC) was made; the patient was staged with N3, M1b disease and palliative chemo-radiotherapy was started. To the best of our knowledge, this report represents the first documented case of a solitary nasal cavity metastasis arising from a SCLC.

BACKGROUND

Primary nasal cavity malignancies are rare and account for less than 3% of all tumours of the upper aerodigestive tract.¹ The metastatic spread of infraclavicular malignancies to the nasal cavity is rarer still.

Small cell lung cancer (SCLC) is a high-grade neuroendocrine malignancy distinguished from non-SCLCs by its rapid doubling time, high growth fraction and the early development of widespread metastases.² The most common sites of metastatic spread are to the contralateral lung, bone, brain and adrenal glands. Very rarely SCLC can present as a metastasis involving the head and neck.

We describe the case of a patient who presented with a solitary nasal cavity metastasis from an undiagnosed SCLC. To the best of our knowledge, this represents the first such case and thus adds to the spectrum of differentials for a mass within the nasal cavity.

CASE PRESENTATION

A 58-year-old man was referred to the Head & Neck clinic with a 4-month history of persistent unilateral right-sided rhinorrhoea. He also reported a history of hyposmia, hypogeusia and right maxillary hypoesthesia. He had not experienced any weight loss, night sweats or other constitutional symptoms. He was otherwise fit and well, having no significant medical history and was not taking

any regular medications. He was an ex-smoker of 20 pack-years, having successfully ceased 6 months prior to presentation.

Clinical examination with flexible nasendoscopy demonstrated a large, ulcerated, friable, irregular mass originating from the lateral wall of the right nasal cavity. The osteomeatal complex and maxillary sinus were clear bilaterally and the left nasal cavity was macroscopically normal. A full head and neck examination was otherwise unremarkable.

INVESTIGATIONS

A contrast-enhanced CT scan of the head and neck demonstrated a large enhancing mass within the superior aspect of the right nasal cavity extending into the posterior ethmoidal region ([figure 1](#)). There was evidence of bony erosion of the cribriform plate bilaterally and soft tissue extension into the anterior cranial fossa.

The patient underwent examination under general anaesthetic with rigid nasal endoscopy and multiple biopsies were taken from the lesion in the lateral wall of the right nasal cavity ([figure 2](#)). Histopathological analysis demonstrated a necrotic tumour composed of sheets of pleomorphic epithelioid cells showing nuclear moulding and numerous apoptoses ([figure 3A](#)). The cells stained positive for CK7 ([figure 3B](#)), CD56, synaptophysin ([figure 3C](#)), TTF-1 ([figure 3D](#)), chromogranin and negative for CK20, CD3 and CD20, consistent with a diagnosis of small cell carcinoma (SCC). The primary origin of the lesion could not be delineated based on immunohistochemistry alone; thus, further radiological investigations were conducted.

A whole-body positron emission tomography (PET) CT scan was performed which demonstrated extensive mediastinal and bilateral hilar lymphadenopathy with collapse-consolidation of the middle lobe of the right lung ([figure 4](#)). No other sites of metastases were seen. Based on the immunohistochemistry, radiology results and after discussion in the lung multidisciplinary team (MDT), the patient was diagnosed with stage 4 (N3, M1b) SCLC.

DIFFERENTIAL DIAGNOSIS

The nasal cavity is composed of a variety of tissues which carry the potential for malignant differentiation; as such, the differential for a mass within the nasal cavity is extensive. Primary malignancies of the nasal cavity are rare and account for less than 0.5% of all cancers.¹ Squamous cell carcinoma is the most common histological diagnosis, but

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Figure 1 Contrast-enhanced axial CT image demonstrating right-sided nasal cavity mass.

non-squamous tumours (including adenocarcinoma and its variants, neuroendocrine tumours and mucosal melanoma) display a predilection for the nasal cavity over other regions of the head and neck. In a Dutch population-based study of 3329 patients with sinonasal malignancies, squamous cell carcinoma, adenocarcinoma, melanoma and olfactory neuroblastoma accounted for 48%, 15%, 8% and 3% of cases, respectively.³

The spread of metastases from infraclavicular tumours to the nasal cavity is rarer still; the total number of reported cases was only 169 in 2001, with renal cell carcinoma and breast carcinoma being the most common primary source, representing 40% and 10%, respectively.⁴ A thorough literature search could not identify any other reports of SCLC metastasising to the nasal cavity.

SCCs most commonly arise in the respiratory tract; however, these tumours can uncommonly arise in non-pulmonary sites as the histologically identical but clinicopathologically distinct entities of extrapulmonary small cell carcinomas (EPSCC). These are

Figure 2 Rigid nasendoscopy image demonstrating an irregular, ulcerated, friable mass within the right nasal cavity.

rare neuroendocrine tumours thought to originate from totipotent stem cells present in all tissues; consequently, they have been reported in multiple sites throughout the body, including the head and neck. The larynx is the most frequently affected site, followed by the salivary glands and sinonasal region.^{5–7} Primary sinonasal EPSCC is very rare, with less than 65 published reports in the literature.⁵

Histologically, EPSCCs are identical to SCLC, appearing as uniform small cells with sparse cytoplasm, dense nuclei and inconspicuous nucleoli under light microscopy. A haematoxylin and eosin stain is usually sufficient to establish the diagnosis of SCLC and EPSCC; however, immunohistochemistry can be a helpful adjunct in problematic cases. The most useful neuroendocrine markers include CD56, chromogranin and synaptophysin. SCC can stain diffusely and strongly with all three markers, focally and weakly with only one or two, or negatively with all three in <10% of cases. In the latter context, a diagnosis can still be established if the morphology is diagnostic.⁸

Further differentials of EPSCC include other neoplasms composed of small round blue cells under light microscopy: malignant lymphoma, other neuroendocrine pulmonary neoplasms (including carcinoids and large cell neuroendocrine carcinoma), malignant amelanotic melanoma, metastatic carcinoma of the breast or prostate and metastatic neuroendocrine carcinomas from other sites. In virtually all cases, however, the diagnosis of SCLC can be made reliably based on cell morphology.⁸

TREATMENT

The case was discussed extensively at the lung oncology MDT. Based on the aforementioned histological and radiological investigations the lung mass was deemed most likely to represent a SCLC primary with metastatic spread to the nasal cavity. The patient was staged with N3, M1b SCLC and offered palliative chemo-radiotherapy.

OUTCOME AND FOLLOW-UP

The patient initially demonstrated an excellent response to treatment with near total resolution of the nasal cavity and chest mass. He remained in remission for 12 months, after which time an aggressive nasal cavity recurrence was demonstrated on a follow-up PET scan. Further palliative chemotherapy was declined and the patient died 2 months later, 14 months after diagnosis.

DISCUSSION

The metastatic spread of infraclavicular malignancies to the nasal cavity is extremely rare. Renal cell carcinoma and breast carcinoma are the most commonly reported primaries.⁴ Published reports of other primary tumours metastasising to the nasal cavity include: tracheal adenoid cystic carcinoma,⁹ hepatocellular carcinoma,¹⁰ rectal carcinoma¹¹ and testicular choriocarcinoma.¹² There are no reported cases of SCLC metastasising to the nasal cavity in the literature.

The route taken by metastases of distant primaries to the nasal cavity is not well characterised. The spread of metastases around the body can follow either a haematogenous or lymphogenous route.¹³ One such postulated haematogenous route is via the vertebral venous plexus (Batson plexus). This is a low-pressure, valveless plexus which permits communication between the deep pelvic veins, intercostal veins, vena cava and the azygos system, thereby providing a route for the spread of primary malignancies in the pelvis, abdomen and thorax.¹⁴ Once tumour cells have entered the circulation, they may then reach the sinonasal area

Figure 3 Haematoxylin and eosin stain (x400) demonstrating round blue cell tumour infiltrating around nerve fibre and blood vessel (A). Immunostain (x400) weakly positive for CK7 in tumour cells compared with surface epithelium (B). Immunostain (x200) positive for synaptophysin in tumour and negative in surface epithelium (C). Immunostain (x400) showing diffuse nuclear positivity for TTF-1 (D).

via the arterial system of the pterygoid plexus and cavernous sinus.¹⁵ Alternatively, a postulated lymphogenous route involves tumour emboli from regional lymph nodes entering the thoracic duct and thence via retrograde flow to the head and neck via intercostal, mediastinal or supraclavicular lymph vessels.^{16 17} In our case, a right-sided lung primary presented as a right-sided nasal cavity metastasis; due to the common drainage pathways

these postulated routes of spread use, such a mirroring of laterality is likely to be purely coincidental.

The clinical presentation of metastases to the nasal cavity is similar to that of a primary sinonasal tumour.¹⁸ Signs and symptoms are usually non-specific and include recurrent unilateral epistaxis, nasal obstruction and facial pain. Proptosis, diplopia, visual acuity impairment and ptosis may also be noted as the nose and paranasal sinuses are closely related to the orbit.¹² A high index of suspicion is needed when patients present with recurrent epistaxis and metastatic disease should be included in the list of possible differential diagnoses. The patient in our case presented with persistent unilateral rhinorrhoea and nasal blockage, explained by the presence of a large, obstructing, friable mass within his nasal cavity. His symptom of hyposmia is explained by the bilateral erosion of the cribriform plate, and thus destruction of his olfactory neuroepithelium, noted on imaging. The complaint of hypogeusia is more difficult to explain, taste being mediated by components of the facial, glossopharyngeal and vagus nerves, none of which appear to have been involved with tumour. The sensation of altered taste our patient experienced is likely a secondary consequence of his hyposmia and thus represents a subjective alteration in how he perceived flavours of food rather than reflecting involvement or

Figure 4 Axial positron emission tomography CT image demonstrating widespread bilateral lymphadenopathy.

destruction of neural pathways. He also experienced hypoaesthesia of the right cheek suggesting involvement of the infraorbital nerve (a branch of the maxillary division of the trigeminal nerve) as it traverses the maxillary sinus.

In our case, the tumour stained positively for the three most relevant neuroendocrine markers for SCLC (CD56, chromogranin and synaptophysin) as well as displaying a characteristic morphological appearance. However, in a case such as ours, the only way to differentiate between SCLC and EPSCC is by obtaining radiological imaging to confirm the presence or absence of chest involvement; the diagnosis of EPSCC by definition requires radiological evidence of no involvement of the chest. To this end, whole-body PET CT scanning is recommended as it is associated with nearly 100% sensitivity for SCLC and proved a useful adjunct in our case.

The distinction between SCLC and EPSCC is, however, clinically less important for determining management as the treatment of head and neck EPSCC is based on that of disseminated SCLC, that is, a platinum-based chemotherapy regimen including etoposide. Successful use of irinotecan combined with cisplatin has also been described in a case of primary nasal cavity EPSCC.¹⁹ Similarly with SCLC, prophylactic cranial irradiation is also recommended in head and neck EPSCC due to the relatively high incidence of brain metastases (41%) from primaries in this location in contrast with EPSCC of other locations.²⁰

Learning points

- Primary nasal cavity malignant neoplasms are rare and the metastatic spread of an infraclavicular malignancy to the nasal cavity is rarer still.
- Small cell lung cancer (SCLC) is a high-grade neuroendocrine malignancy distinguished from other lung cancers by its early development of widespread metastases. Very rarely SCLC can present as a solitary metastasis involving the head and neck.
- The diagnosis of extrapulmonary small cell carcinoma (EPSCC) should be considered in the context of unusually located small cell carcinoma without evidence of lung involvement. The treatment of EPSCC is similar to that of SCLC.
- The clinical presentation of metastatic lesions within the nasal cavity is similar to that of primary tumours and most often includes recurrent epistaxis, nasal obstruction and facial pain.

Contributors AH performed the literature search and drafted the case report. SM assisted in the drafting of the case report. ATH and SM performed revisions. NC

was the consultant overseeing the patients care, reviewed revisions and gave final approval of the published version.

Competing interests None declared.

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