CASE REPORT

Diagnosis and treatment of a rare sinonasal neuroendocrine tumour: adding to the evidence

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SUMMARY

Sinonasal neuroendocrine tumours (NETs) are rare, aggressive neoplasms with a high recurrence potential. There are no robust protocols for the management of these tumours. An 81-year-old man presented with an incidental sinonasal mass visualised on CT scan of head. Over the next few weeks he developed new onset, progressively worsening headache, right eye ptosis and restricted extraocular movements. Imaging confirmed a rapidly enlarging tumour involving the right nasal cavity and the orbit. Biopsy showed a large cell neuroendocrine carcinoma of the right ethmoidal sinus. The patient was treated with concurrent cisplatin chemotherapy and radiation. Repeat imaging showed decrease in tumour volume. The patient continues to do well and follows up regularly with our oncology service. Current protocols comprising chemotherapy after radiation are based on limited studies. A regimen involving concurrent chemoradiation also appears to aid in tumour volume reduction. Additional studies are required to formulate robust clinical protocols for management of sinonasal NETs.

BACKGROUND

Neuroendocrine tumours (NETs) are a diverse group of neoplasms that can arise from several different anatomical sites, but most commonly originate from the gastrointestinal and bronchopulmonary system.¹ NETs of the sinonasal and orbital regions are rare, aggressive and have a high recurrence potential.²⁻³ Owing to their rarity, there is limited data regarding the management of sinonasal NETs.

In this report, we describe a case of sinonasal NET, which presented as an incidental finding after head trauma. We will discuss the patient's rapid clinical evolution, treatment strategy and response to therapy.

CASE PRESENTATION

An 81-year-old man initially presented to the emergency department (ED) after he was involved in a motor vehicle accident. A CT scan of head (figure 1) incidentally found a right posterior ethmoid mass, which was asymptomatic at the time. One month later, at an initial ear, nose and throat evaluation, the patient's extraocular muscle movements (EOMs) were grossly intact without any ptosis. A flexible nasopharyngoscopy demonstrated an area of thick mucosal erythema that was not able to be biopsied. A subsequent endoscopic biopsy was planned. Over the next 2 weeks, the patient progressively developed dull headaches, severe right eye pain, severe extraocular muscle limitation and worsening ptosis of the right eye, which resulted in a visit to the ED.

Figure 1 CT scan on presentation.

INVESTIGATIONS

The MRI (figure 2) showed a large nasal passage mass that demonstrated significant growth compared to a CT scan performed 2 months prior. The mass extended into the right orbit, right maxilla, cribriform plate and into the right intracranial fossa without extension into the overlying right frontal lobe. The patient received high-dose glucocorticoids, and an endoscopic biopsy was performed. The biopsy result showed high-grade large cell NET (figure 3).

Figure 2 Axial T2-weighted MRI on presentation.

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Figure 3 Histopathology of the right ethmoidal sinus mass.

TREATMENT

Concurrent chemotherapy (cisplatin) with radiation was initiated. A repeat positron emission tomography scan following completion of concurrent chemoradiation showed a decrease in size and metabolic activity in the mass, with no evidence of distal metastasis. A decrease in tumour mass was also seen on a repeat MRI ([figure 4](#)).

OUTCOME AND FOLLOW-UP

The patient completed 7 weeks of concurrent chemoradiation with significant reduction in tumour volume. He continues to follow-up with our oncology service. Further treatment will be administered if necessary.

Figure 4 Coronal T2-weighted MRI during chemoradiation.

DISCUSSION

Epidemiology

The term NET is used to describe epithelial malignancies that show characteristic cytological patterns on light microscopy. Sinonasal NETs commonly present with headache, visual loss and nasal discharge.⁴ Other less common symptoms include nasal obstruction, epistaxis, local pain and tenderness.^{4 5} In the USA, the overall annual incidence of NETs has been estimated to be between 3.65 and 5.25 per 100 000 with a median age of diagnosis of 63.^{6–8} Common sites of presentation include the small intestines and lung. Primary NETs of the sinonasal and orbital regions are rare. In the USA, nasal cavity and paranasal sinus tumours account for 0.2%–0.8% of all malignant neoplasms with an annual incidence of 1.0–1.5 cases per 100 000.^{6 7 9} The incidence of sinonasal NETs is markedly lower. The rarity of these tumours can be demonstrated by one case series study that was capable of accruing only 19 patients with sinonasal tract NETs over a span of 6 years.⁶

Investigations

Imaging

In the workup of sinonasal NETs, initial radiological investigations include a CT scan and an MRI with and without contrast. A spiral CT scan or a three-dimensional (3D) MRI can help in constructing a 3D model of the tumour, which can assist in understanding the anatomical features and determining the surgical approach. It also aids in the delineation of pathology by providing means to distinguish between abnormal and normal tissues.¹⁰ On a CT scan, the lesions are usually isodense; however, they may also show mild hyperdensity ([figure 1](#)). Bone scan shows features of bone destruction including absorption, sclerosis or a moth-eaten appearance. On performing an MRI ([figures 2 and 4](#)), the lesions have been seen to be isointense on T1-weighted imaging and isointense or mildly hyperintense on T2-weighted imaging.⁴ Poor prognostic factors include tumor, node, metastasis (TNM) staging involvement of the fovea or orbit.¹¹

Histopathology and staging

Histopathological examination is essential for diagnosis. Cells show ultrastructural and immunohistochemical features such as dense core secretory granules, and staining for chromogranin, synaptophysin and keratin ([figure 3](#)).

The WHO classifies NETs as a typical, atypical, small cell and 'neuroendocrine carcinoma, not otherwise specified'.⁸ Despite the differences, there are some common themes, including distinction into well differentiated (low-intermediate grade), and poorly differentiated, including the small and non-small cell types. Well-differentiated NETs are associated with low metastatic rates, better survival and overall better prognosis.¹²

A staging system for olfactory neuroblastomas proposed by Kadish *et al*¹³ is the most frequent staging system applied to NETs. In addition, the American Joint Committee on Cancer Staging system of nasal cavity and paranasal sinus tumours (listed below) is also used for classification.¹⁴

Group A: tumour limited to nasal cavity.

Group B: tumour limited to nasal cavity and paranasal sinuses.

Group C: tumour extends beyond nasal cavity and paranasal sinuses.

Group D (proposed by Chao *et al* in 2001): cervical nodal metastases.

* Chemotherapy consists of Cisplatin 33 mg/m²/day for 3 days and Etoposide 100 mg/m²/day for 3 days. Initial chemotherapy is given in 2 cycles 15 days apart

Figure 5 Treatment protocol as per the 35th Congress of French Cervico-Faciale Carcinologic Society.

According to the WHO definition, our case was an atypical carcinoid (large cell neuroendocrine) tumour. According to AJCC, this patient possessed a group C tumour.

Treatment

Depending on the size and extent of involvement, treatment options include surgery, chemotherapy and radiotherapy. Owing to the rarity of NETs, these treatment modalities have not been systematically evaluated.⁷ Surgery is usually reserved for cases where complete tumour resection can be achieved with minimal morbidity or when the tumour is not responsive to chemoradiation.^{11 15 16}

Bhattacharya *et al* studied the administration of cisplatin and etoposide followed by stereotactic radiation. The team found the regimen to be effective, in which most patients achieved remissions without the need for surgery postchemotherapy and radiation.¹⁶ Fitzek *et al*³ used the same chemotherapeutic regimen of cisplatin and etoposide followed by radiation, which demonstrated a 5-year survival rate of 74%. In light of these findings, the 35th Congress of French Cervico-Faciale Carcinologic

Society developed a treatment protocol for NETs, which is described in figure 5.¹⁷

Several studies have shown good survival rates with initial resection of the tumour followed by postoperative chemotherapy.¹⁷ Additional studies have also shown that combined treatment with surgery is associated with better survival as compared to treatment without surgery.^{18–20}

However, as noted earlier, due to the rarity of these tumours, there is no consensus on the best method of treatment. Given the rapidity of developing symptoms in our patient, we chose cisplatin with concomitant radiotherapy. Our patient received seven cycles of chemoradiation, which caused a significant reduction in the symptoms and the tumour burden. The case emphasises the need for further research comparing concurrent chemoradiation with primary chemotherapy or surgical resection as the initial approach for the treatment of sinonasal NETs.

Learning points

- ▶ Sinonasal neuroendocrine tumours (NETs) are extremely rare and rapidly growing tumours.
- ▶ There is paucity of data regarding their treatment.
- ▶ Our experience with concomitant chemotherapy and radiotherapy has been positive with a definitive reduction in tumour burden. Further research is required to compare the efficacy of concurrent chemoradiation, primary chemotherapy or surgery as the initial approach for treatment of sinonasal NETs.

Contributors RD admitted the patient to the hospital, AG was the intern who cared for the patient daily, and YL was the medical student who cared for the patient daily. AD was the attending physician for this patient. All the authors collected the figures, performed literature search, wrote the article and edited the manuscript. AD performed the final edits of the manuscript.

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