Primary Ewing sarcoma of the larynx with distant metastasis: a case report and review of the literature

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ABSTRACT

Extraosseous Ewing sarcoma is a rare, poorly differentiated round-cell tumour that is part of the Ewing sarcoma family of tumours. Here, we present an extremely rare case of primary extraosseous Ewing sarcoma arising in the larynx, with distant metastases.

A 53-year-old man with a history of Hodgkin lymphoma treated 4 years earlier with 8 cycles of chemotherapy presented to our medical centre with a 2-week history of hoarseness. On physical examination, he was found to have a right supraglottic mass together with a fixed right vocal cord. Computed tomography imaging of the patient’s neck showed a heterogeneously enhancing lesion measuring 5.0×3.8×3.8 cm, centred on the right thyroid cartilage and invading the right true vocal cord. Imaging by integrated fluorodeoxyglucose positron-emission tomography and computed tomography showed active subcarinal and axillary lymph nodes, multiple scattered lung nodules, and multiple bony metastases. Needle core biopsy of the laryngeal mass was diagnostic for Ewing sarcoma. The patient received radiation to the laryngeal area and then alternating cycles of vincristine–actinomycin-D–cyclophosphamide and etoposide–ifosfamide. The patient remains in remission 1 year after completing therapy.

As demonstrated in the present report, these tumours can behave very aggressively both locally and by metastasizing to distant organs. Our treatment approach provided favourable results for the patient; however, future reports are needed to further elucidate optimal management.

Key Words Ewing sarcoma, pNETs, laryngeal cancer, larynx, metastases

INTRODUCTION

Extraosseous Ewing sarcoma (ees) is a rare, poorly differentiated round-cell tumour that is part of the Ewing sarcoma family of tumours (esft), which also includes classical Ewing sarcoma (ews) of bone, peripheral neuroectodermal tumour (pNET), and Askin tumour1,2. Evidence of ees can be traced back to 1969, when Tefft, Vawter, and Mitus were the first to describe four extraosseous tumours that bore an uncanny resemblance to Ewing sarcoma and that could not be classified otherwise3.

Primary ees in the head-and-neck region is very rare, representing between 8.5% and 12% of all ees tumours according to some studies4,5. The prognosis and outcome of ews tumours in the head and neck in general is better than in other anatomic locations; however, the age of the patient and the stage of the disease at diagnosis play important roles as prognostic factors6. Primary ees of the larynx is even rarer, and to the best of our knowledge, only 6 cases have been reported in the literature thus far7–12. Because of the small number of cases, it is unclear whether, in the long run, primary ees of the larynx behaves like other ews tumours of the head and neck.

Treatment of ees generally takes a multimodal approach that can include any or all of local resection, chemotherapy, and radiotherapy. However, a set protocol has yet to be established, and most treatment regimens are extrapolated from skeletal ews13. When ees arises in the larynx, it poses an additional challenge for treatment because of its location and proximity to vital structures.
Here, we present an extremely rare case of primary EWS arising in the larynx, with distant metastases. A review of the relevant literature is also presented.

CASE DESCRIPTION

A 53-year-old man, a heavy smoker and recovering alcoholic with a history of Hodgkin lymphoma treated 4 years earlier with 8 cycles of doxorubicin–bleomycin–vinblastine–dacarbazine, presented to our medical centre with a 2-week history of hoarseness. On physical examination, he was found to have a hard right-sided level II neck mass. Flexible laryngoscopy was performed and showed a right supraglottic mass together with a fixed right vocal cord.

Computed tomography imaging of the patient’s neck showed a heterogeneously enhancing lesion measuring 5.0×3.8×3.8 cm centred on the right thyroid cartilage and invading the right aspect of the pre-epiglottic fat, right paraglottic space, and the right true vocal cord (Figure 1). It appeared inseparable from the right strap muscles. Prominent right cervical lymph nodes were seen, the largest (at level 2A) measuring 13 mm in the shortest axis. Subsequently, whole-body integrated positron-emission tomography and computed tomography imaging with fluorodeoxyglucose showed active subcarinal and axillary lymph nodes, multiple scattered lung nodules, and multiple bony metastases. Notably, the patient’s original lymphoma did not involve the bones or lung parenchyma.

In light of the imaging findings and the patient’s history of lymphoma, a needle core biopsy of the laryngeal mass was obtained under ultrasound guidance. Microscopically, the tumour exhibited cohesive cellular proliferation of small round blue cells growing in sheets, with patchy coagulative necrosis [Figure 2(A)]. The tumour cells showed a minimal-to-moderate amount of glycogen-rich clear cytoplasm. Numerous mitotic and apoptotic figures were noted. Immunostaining for CD99 showed diffuse membranous staining [Figure 2(B)]. The microscopic features and immunoprofile excluded a diagnosis of carcinoma and lymphoma, and was highly suggestive of EWS.

Given the patient’s advanced metastatic disease, surgical treatment was not pursued, and systemic therapy was favoured. The patient received radiation to the laryngeal area and then alternating cycles of vincristine–actinomycin-D–cyclophosphamide and etoposide–ifosfamide. Currently, at 1 year after the end of therapy, the patient has no evidence of active or metastatic disease.

DISCUSSION

Although Tefft, Vawter, and Mitus were the first to suggest the presence of extraosseous tumours that much resembled EWS in 1969, the first case of EWS of the larynx wasn’t published until 1983 by Abramowsky and Witt. In the present report, we have described the 7th case ever
reported of EES of the larynx, and the first to demonstrate distant metastases. Because such cases are few in number, conclusions about the behaviour of laryngeal EES cannot be accurately drawn. Table I summarizes the reported cases of laryngeal EES. Of those previously reported cases, 2 occurred in pediatric patients (1 day of age and 9 months of age); the other 4 occurred in adults between 45 years and 74 years of age. Of those 6 previously reported cases, 4 occurred in male patients, who presented with either hoarseness, stridor, or acute respiratory distress. It is interesting to note that the older published cases relied on histopathology to make the diagnosis; only the most recent report, by Lynch et al., confirmed the diagnosis through nuclear staining for EWSR1-FTII, which is now considered the “gold standard” for diagnosis.

Histologically, ESRF can present in one of several different variations, including typical rws, typical adamantinoma-like eesf, spindle-cell sarcoma-like eesf, sclerosing eesf, and large-cell or atypical eesf. Although those variations can differ in both their histologic and immunohistochemical features, typical ees is often described as having uniform sheets of small round cells in a lobular or diffuse arrangement, with a scant amount of pale, clear cytoplasm that might or might not be vacuolated. In addition, MIC2 (CD99) expression has been shown to be highly specific for both ees and pNET, and can be used to differentiate those tumours from other small round-cell tumours.

In recent years, the ESRF has been recognized as a spectrum of small round-cell entities that were previously classified separately, ranging in their extent of differentiation from the poorly differentiated rws to the more differentiated pNET. Before the use of molecular and cytogenetic techniques became prevalent, diagnosis of these small round-cell tumours had been based on clinical, radiologic, and histopathologic features, which posed a challenge because of their many similarities. Those features include CD99 staining and the classical t(11;22)(q24;q12) translocation, both of which are associated with most, but not all, cases of EES and pNET. In relatively recent years, the presence of chimeric transcripts involving the EWSR1 gene and a member of the ETS domain transcription factor family, with FLI1 being the most common, has been shown to be a defining characteristic that unifies all ESRF tumours. Other less-common fusions include EWSR1-ERG, EWSR1-ETV1, EWSR1-EIAF, and EWSR1-FEV.

Treatment of EES of the larynx in the literature has consisted of either surgical resection, chemoradiotherapy, or a combined approach. Total laryngectomy was used in 3 cases, and in 1 case, where the patient presented with a vocal cord lesion, treatment with microsurgery was used. A local recurrence was reported in only 1 case, in which the patient had been treated with a combination of surgery and chemotherapy. Our patient was not a candidate for surgery, given the advanced stage of his disease at presentation.

**SUMMARY**

To the best of our knowledge, we have presented the 1st reported case of primary EES of the larynx, with distant metastasis. Treatment consisted of chemotherapy and radiation. These tumours can present in a wide range of age groups, and as demonstrated in our report, can behave very aggressively both locally and by metastasizing to distant organs.

**CONFLICT OF INTEREST DISCLOSURES**

We have read and understood *Current Oncology’s* policy on disclosing conflicts of interest, and we declare that we have none.

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**REFERENCES**