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Mesenchymal chondrosarcoma of the vagus nerve

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Abstract
Mesenchymal chondrosarcoma is a rare, aggressive, malignant neoplasm, which arises from extraskeletal sites in 30–40 per cent of cases. It is extremely rare in children. We present a novel case of childhood mesenchymal chondsarcoma arising from the vagus nerve in the neck, resulting in paralysis of the right vocal fold. The clinicopathologic features and management of this case are described along with a brief discussion on the aetiology of vocal fold paralysis in this age group. Current literature on extraskeletal presentation of mesenchymal chondrosarcoma is reviewed.

Key words: Chondrosarcoma, Mesenchymal; Cranial Nerve Neoplasms; Vagus Nerve

Case report

A 12-year-old female presented with a one-year history of progressively increasing hoarseness of voice. She was otherwise asymptomatic with no evidence of dysphagia or history suggestive of thyroid dysfunction. Her appetite was normal and her weight remained steady. There was no other past medical history or family history of note.

Examination of the neck revealed a smooth, firm mass situated above the right sternoclavicular joint, and extending below the sternum. The mass was non-tender to palpation and did not move with swallowing. There was no associated cervical lymphadenopathy. She was clinically euthyroid and a full systemic examination was otherwise normal.

Laryngoscopy demonstrated a right vocal fold paresis and a plain X-ray showed a soft-tissue mass on the right side at the base of the neck. Contrast-enhanced CT scan revealed a rounded, well circumscribed mass measuring 2.5 cm in its maximum horizontal dimension, lying adjacent to the lower pole of the right thyroid lobe (Figure 1). Two small calcified densities were present within the soft-tissue mass. Technetium 99 scan was performed and did not show increased uptake in the thyroid gland.

At operation, exposure was gained via a low skin crease incision and division of the strap muscles. The mass was hard and irregular, measuring $7 \times 3 \times 2$ cm, lying between the internal jugular vein and the common carotid artery. The vagus nerve entered the mass from above and emerged from its lower pole. The thyroid gland and thymus gland were found to be normal.

The tumour was resected along with the involved area of vagus nerve and the specimens were sent for histology. The patient made an excellent recovery and was discharged home on the third post-operative day. Follow-up at one year showed no evidence of local recurrence or metastatic disease.

Histopathological assessment revealed a well-circumscribed tumour with an interrupted fibrous pseudocapsule at the periphery (Figure 2). The tumour was biphasic with admixed cellular sheets merging into irregular cartilage nodules throughout the mass. The tumour and its cellular component showed the presence of focal haemangiopericytoma-like foci with well developed irregularly branching blood vessels. The majority of cells were small and round with hyperchromatic nuclei, small nucleoli and little cytoplasm. These merged with ill-defined bundles of spindle cells throughout the tumour along with a round to elliptical cell component. Occasional mitoses were seen, approximately one per 10 high-powered microscope fields. The round cells merged into islands of cartilage, which appeared benign with no obvious malignant features. Some of these islands were densely calcified. Immunoperoxidase staining of the tumour revealed strong diffuse

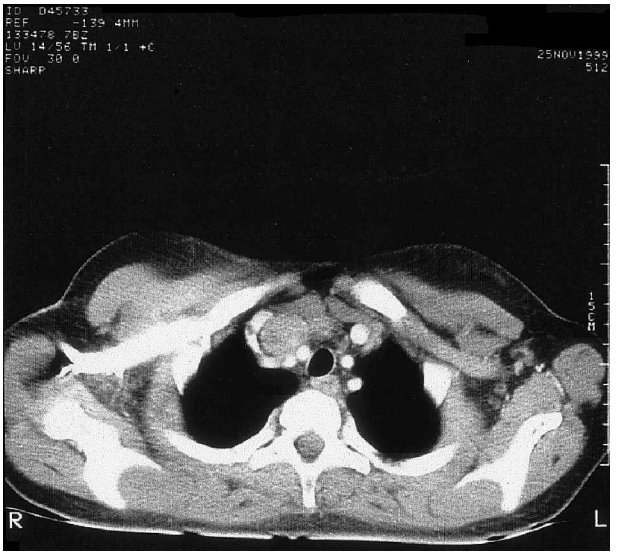

Fig. 1
Contrast-enhanced CT scan showing a well-circumscribed tumour lying anterior to the carotid vessels on the right.

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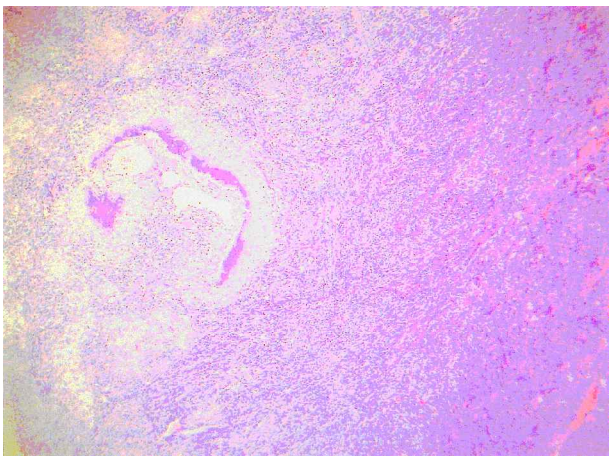

FIG. 2
Low power view of tumour showing small round cells merging into osteoid and cartilage. H&E; × 150.

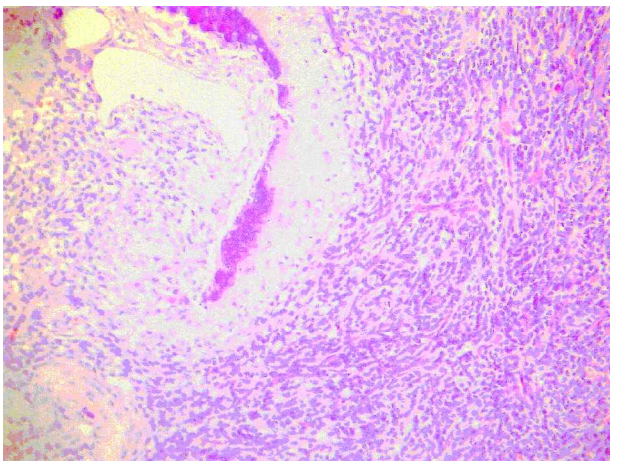

FIG. 3
High power view showing the characteristic biphasic pattern of small round cells merging into islands of cartilage and osteoid. H&E; × 400.

positivity for vimentin and CD99 in a membrane pattern. Reactivity for cytokeratin, S-100, HMB45, EMA, carcinoembryonic antigen, neurofilament, chromogranin, desmin, smooth muscle actin was absent in the majority of cells. Only small numbers of spindle cells at periphery where the tumours merges with nerve bundles from the vagus nerve were immunoreactive for S-100. Based on these findings a diagnosis of mesenchymal chondrosarcoma was made.

Discussion

Voice change in children has a diverse aetiology and may be an early symptom of serious local or systemic disease.[1] Vocal fold paralysis is well recognized as a significant cause of hoarseness in children and may be due to dysfunction of brain stem nuclei, the vagus nerve or the recurrent laryngeal nerve.[2] When this is unilateral, the most common cause is reported as idiopathic (including viral illness) in up to 50 per cent of cases. Other causes of unilateral vocal fold paralysis in children include neoplasms of the head, neck and mediastinum, trauma following endotracheal intubation, surgery in the neck or mediastinum and cardiovascular defects.[3] In adults, malignancy and surgical trauma account for the majority of causes of unilateral vocal fold paralysis, with idiopathic cases accounting for only 13 per cent.[4]

Neoplasms of the vagus nerve are rare in adults and even rarer in children.[5] They may be benign or malignant with vocal fold palsy frequently being observed in benign neoplasms. It is generally agreed that vagal tumours arise from the nerve sheath cells and not from the neural cells themselves. Histopathological examination of these neoplasms reveals paragangliomas in 50 per cent of cases and schwannomas account for approximately 30 per cent of cases. Neurofibromas and neurofibrosarcomas are infrequent findings and usually occur in association with von Recklinghausen's disease. Mesenchymal chondrosarcoma involving the vagus nerve has not previously been reported in the literature and this is the first case of its kind to our knowledge.

Mesenchymal chondrosarcoma is a rare tumour, which was first reported as a distinct histopathological condition in 1959.[6] Since then it has become well recognized as a malignant and aggressive tumour usually affecting bone, with the maxilla, mandible and skull base being common sites of presentation.[7] Extraskeletal mesenchymal chondrosarcoma occurs in 30–40 per cent of cases reported in the world literature.[8] The meninges, orbit and lower limbs are common extraskeletal sites, with other cases being reported in the brain,[9] parapharyngeal space,[10] nasal and sinus mucosa,[11] retroperitoneum[12] and lung.[13]

Extraskeletal mesenchymal chondrosarcoma has a slight female preponderance and occurs in two principal age groups.[14] In cases involving the central nervous system it characteristically affects the 20–30 age group; those occurring in the soft tissues outside the central nervous system commonly affect patients over 40 years of age. They are extremely rare in children; when they do occur, the central nervous system is usually affected and the meninges are often involved.[15]

Plain radiography was unhelpful in this case but demonstrates a soft-tissue mass with arc-ringed or stippled calcification in over 50 per cent of cases.[16] CT commonly demonstrates coarse calcification and predominantly peripheral enhancement following administration of contrast. MRI does not reveal any distinguishing features and therefore a definitive diagnosis of mesenchymal chondrosarcoma is based on histological features.

Microscopically, the tumour morphology is identical to that of intraosseous mesenchymal chondrosarcoma and is typically biphasic.[8] The cellular component consists of undifferentiated small neoplastic cells which vary in shape from round to spindle-shaped, interspersed with islands of well differentiated, sharply demarcated foci of cartilaginous tissue. Intervening zones of gaping vascular channels resembling findings in haemangiopericytomas are well recognized features. Immunohistochemistry is typically strongly positive for vimentin and CD99 and reactivity for cytokeratin is negative in 75 per cent of samples as in this case.[17] However, there is no specific immunohistochemical marker for mesenchymal chondrosarcoma and although chromosomal translocations have been reported,[15,18,19] there is no consistent cytogenetic abnormality that can help with diagnosis. There is no reliable correlation between histological appearance and biological behaviour but all mesenchymal chondrosarcomas are high-grade tumours due to the presence of small round cells. The individual grading of tumours is precluded on this basis.[20]

Treatment of mesenchymal chondrosarcoma requires wide surgical excision of the tumour. The role of adjuvant chemotherapy and radiotherapy remains obscure due to the absence of prospective randomized clinical trials.

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Although some series have shown a beneficial effect with adjuvant therapy in selected cases,[21] others have shown no effect on survival.[8]

The prognosis for mesenchymal chondrosarcoma is poor and the disease may follow a protracted course. In a series of 35 patients, Huvos *et al.* reported a 10-year survival rate of 28 per cent with a mean survival of 37.9 months.[21] There are no differences in survival between mesenchymal chondrosarcoma occurring in bone and extraskeletal sites.

Long-term follow-up is essential as local recurrence or metastatic disease may occur after a long quiescent period following treatment. Evidence of metastases can be found in over half of patients at some stage, with the most common site being the lungs.[8]

The differential diagnosis is monophasic synovial sarcoma or malignant peripheral nerve sheath tumour which often show focal immunopositivity for keratin and neural markers; these features were not present in this case.

Conclusion

We present the first known case of mesenchymal chondrosarcoma involving the vagus nerve. Mesenchymal chondrosarcoma is an extremely rare malignant aggressive tumour with a poor prognosis regardless of the site of occurrence. Diagnosis can only reliably be made by histological assessment. Surgical excision needs to be followed by long-term review for detection of local recurrence or distant disease. The role for adjuvant radiotherapy or chemotherapy remains controversial.

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