CASE REPORT

Intractable hiccups: A rare presentation of phrenic nerve schwannoma

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KEYWORDS
Hiccups;
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Schwannoma;
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Phrenic nerve

Summary

Introduction: Schwannoma rarely involves the phrenic nerve. We report a unique case of schwannoma as a cause of chronic hiccups due to the involvement of phrenic nerve.

Case presentation: A 72-year-old male presented with 20-year history of hiccups. He underwent multiple esophagogastroduodenoscopy procedures, all of which were negative. A computed tomography (CT-scan) of soft tissue of the neck was remarkable for left retrosternal mass with central calcification, located adjacent to the thyroid gland. He underwent surgery and this mass was found to be originating from the left phrenic nerve. Resection of the portion of phrenic nerve with mass was performed. Grossly, the specimen was a pale-tan piece of soft tissue, 4.8 cm in maximum dimension with an attached portion of nerve. Microscopically, it showed a well-circumscribed spindle cell lesion with hypercellular and hypocellular areas and multiple Verocay bodies. There was no atypia or significant mitotic activity. On immunohistochemical staining, the spindle cells were positive for S-100, supporting the diagnosis of schwannoma.

Conclusion: Postoperatively, the patient showed marked improvement in his symptoms and the hiccups were almost completely resolved. Although they are very rare, schwannomas of the phrenic nerve should be considered in the differential diagnosis of chronic hiccups.

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Introduction

Schwannoma is a nerve sheath tumor, which is also called neurilemmoma. Phrenic nerve schwannomas are rare. A few cases of phrenic nerve schwannoma have been reported in the literature. They can involve both the cervical [1,2,3] and intrathoracic portion of the nerve. We describe a very rare presentation of schwannoma, associated with chronic intractable hiccups, arising from left phrenic nerve.

Case report

A 72-year-old male presented with a longstanding history of hiccups for over 20 years. The symptoms started off being occasional and became more persistent lasting for longer periods of time with shorter intervals between exacerbations. He had history of cerebrovascular accident (CVA) in 2009 and since then his symptoms exaggerated. A computed tomography (CT-scan) of the soft tissue of the neck was done, which revealed a 4 × 3 cm mass with central calcification located adjacent to the thyroid gland. The patient underwent surgical resection. Intraoperatively, the lesion was seen to be arising from the phrenic nerve. Resection of the mass and portion of the phrenic nerve was performed.
Grossly, it was a pale tan oval piece of soft tissue with an attached piece of nerve. Serial sectioning revealed a yellow to brown calcified cut surface (Fig. 1). Histological examination showed an encapsulated variably cellular neoplasm composed of spindle shaped cells with extensive hyalinization (Fig. 2). In the more cellular areas, there was nuclear palisading with the formation of Verocay bodies. Immunohistochemical staining with S-100 was positive (Fig. 3). The diagnosis of Schwannoma was made. There were no postoperative complications. The patient was discharged after few days postoperatively and he is doing well with a marked decrease in hiccups.

**Discussion**

There are many causes of hiccups, of which schwannoma is a very rare one. It can cause hiccups by the involvement of the phrenic nerve (afferent pathway). The involvement of phrenic nerve is very unusual. Tanaka et al. reviewed 138 mediastinal tumors and only one originated from phrenic nerve [3]. The majority of phrenic nerve schwannomas

![Figure 1](image1.png) Schwannoma. Yellow to brown cut surface with area of calcification in the middle and an attached piece of phrenic nerve at the periphery (gross picture).

![Figure 2](image2.png) Schwannoma. Sections shows spindle cell lesion with hypercellular and hypocellular areas (H & E, original magnification × 100).

![Figure 3](image3.png) Schwannoma. Sections show diffuse staining with S-100 stain (S-100 stain × 400).

**Table 1** Differential diagnosis of schwannomas.

<table>
<thead>
<tr>
<th>Schwannoma</th>
<th>Neurofibroma</th>
<th>Solitary fibrous tumor</th>
<th>Malignant peripheral nerve sheath tumor</th>
<th>Ganglioneuroma</th>
</tr>
</thead>
<tbody>
<tr>
<td>Myxoid background, Antoni A (with Verocay bodies) &amp; B areas, thick wall blood vessels</td>
<td>Bland spindle cells arranged in fascicles, mast cells can be seen but no Antoni A &amp; B areas</td>
<td>Monotonous bland-appearing spindle cells with characteristic intermixed “ropey” collagen</td>
<td>Infiltration within nerve, hypercellularity, nuclear pleomorphism, spindle cells with tapered ends</td>
<td>Spindle cells population, encapsulated, well-formed ganglion cells</td>
</tr>
<tr>
<td>S-100 and calretinin [8] are positive and negative for pEMA</td>
<td>Positive staining for Neurofilament, S-100 and pEMA negative</td>
<td>Neoplastic cells stain for CD34, CD99 and BCL-2 but usually negative for pEMA</td>
<td>Decreased expression for S-100 and overexpression for p53</td>
<td>Ganglion cells are positive for synaptophysin</td>
</tr>
</tbody>
</table>

* EMA: epithelial membrane antigen.
Phrenic nerve schwannoma

are benign but rarely can be malignant [4]. They may be asymptomatic, however patients may present with cough, hoarseness, or weight loss. Some investigators have also reported cases of diaphragmatic eventration [5] and involvement of accessory phrenic nerve [6]. Schwannoma is a slowly growing tumor that is usually present for several years before diagnosis. Imaging studies are helpful in the early recognition of the disease [7]. Grossly, the tumor has pale tan yellow appearance. Large tumors are more likely to undergo calcification and degeneration. Microscopically, schwannoma consist of spindle cells with hypercellular and hypocellular areas, called as Antoni A and Antoni B areas respectively. Antoni A areas show nuclear palisading, whorling appearance and Verocay bodies. In Antoni B areas, the tumor is less cellular and there is loose meshwork of cells with myxoid changes. Immunohistochemically, S-100 protein is positive in schwannoma particularly in Antoni A areas. There are different histological variants of schwannoma depending on the cell type, cellularity and atypia. The differential diagnosis includes neurofibroma, malignant peripheral nerve sheath tumor, solitary fibrous tumor and ganglioneuroma (Table 1). Neurofibromas show a mixed population of cells, with a predominance of Schwann cells admixed with perineurial-like cells and fibroblasts. They do not have Antoni A and B areas. Fine et al. demonstrated that calretinin is usually stain positive in schwannoma and is a useful marker for differentiating schwannomas from neurofibromas [8]. Microscopically malignant peripheral nerve sheath tumor shows features of spindle cell with fascicular pattern and varying degrees of mitosis, necrosis and tumor calcification. Solitary fibrous tumor has characteristic "ropey" collagen admixed with neoplastic spindle cells. Ganglioneuroma usually occurs in childhood and the major histologic difference from other lesions is the presence of well-formed ganglion cells. These features are not present in schwannoma.

Surgery is usually required to improve the symptoms and quality of life of the patients. Some investigators have suggested a conservative approach with preservation of the nerve [9] and others favor surgery, depending on the symptoms, size and all clinical parameters. Regular clinical follow-up is required after surgery.

Conclusion

Although they are very rare, schwannomas of the phrenic nerve should be considered in the differential diagnosis of chronic hiccups. In our patient, a few months’ postoperative follow-up showed that the hiccups were markedly diminished and there were no postoperative complications.

Disclosure of interest

The authors declare that they have no conflicts of interest concerning this article.

References