Angiosarcoma Arising in a Vagal Schwannoma - Report and Literature Review

Case Report

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Abstract

Schwannoma and angiosarcoma are rare occurrences. Angiosarcoma's occurrence in a preexisting schwannoma is a very rare event with only fifteen cases reported in the literature. We report the sixteenth case of angiosarcoma arising in a schwannoma, a 30-year-old male patient with a long-standing (15 years) history of right neck lump. The lump measured around 10x7 cm at the time of presentation and all cranial nerves were intact. We performed a fiberoptic laryngoscopy and a computed tomography scan of the head and neck with contrast. Our provisional diagnosis was a parapharyngeal space neoplasm, most likely a salivary gland malignancy. The tumor was excised surgically. On histopathology it contained two distinct tissue architectures representing a schwannoma and epithelioid angiosarcoma, also confirmed on immunohistochemistry. Literature review of these limited cases implicates a poor prognosis of the disease. The pathogenesis is uncertain, but the theories put forward suggest chronic vascular stasis or vascular endothelial proliferation as possible etiologies. The main takeaway of our report is to consider the potential of malignancy in long standing cases of schwannomas. Prompt surgical treatment should be offered, and the patient and their family be counselled for postoperative adjuvant treatment for better prognosis.

Keywords: Angiosarcoma, schwannoma, malignant peripheral nerve sheath tumors, neck, surgery, immunohistochemistry, case report

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Introduction

Schwannomas are slow growing, painless benign peripheral nerve tumors with a distinct morphology on microscopy. It is extremely rare for schwannomas to undergo malignant transformation. Among these, malignant peripheral nerve sheath tumors (MPNSTs) are the most common variety with angiosarcoma being the least common (1). Peripheral nerve sheath tumors are more commonly associated with neurofibromatosis type 1 (2, 3).

The majority of MPNST cases and all cases of angiosarcoma arising in schwannoma have an epithelioid morphology (4). There still is no explanation for this finding. Throughout the literature so far, only fifteen cases have been reported. To the best of our knowledge, this is the sixteenth such case and the seventh case arising in a vagal nerve schwannoma.

Case Presentation

A 30-year-old male patient was referred to our ENT outpatient department with a long-standing (15 years) history of a right neck lump. It was insidious in onset with gradual progression. He started experiencing a change in voice (hot potato voice) about eight years back. One year later, he started experiencing dysphagia. Examination showed a huge right-sided neck mass approximately 10x7 cm. A scar mark was seen on the most prominent part of the lump due to an incisional biopsy attempted at another center, which was inconclusive. Fiberoptic laryngoscopy showed a bulge in the nasopharynx, but the gag reflex and bilateral vocal cord mobility were normal. All cranial nerves were normal on examination. Computed tomography (CT) scan (Figure 1) showed a soft tissue density mass measuring 8.0x8.5 cm extending from the skull base to the level of cervical vertebrae C5, causing partial luminal narrowing of the airway and lateral displacement of the carotid sheath. We considered various parapharyngeal space tumors in differential diagnosis based on the findings.

A surgical excision was performed, and the mass was removed in toto. Perioperatively the mass was well encapsulated (Figure 2), displacing contents of the carotid sheath laterally but was not adherent to any surrounding structures. Postoperatively, the patient had an uneventful recovery.

On gross histopathological examination, the tumor measured 11.5x9x6 cm with the overlying skin ellipse measuring 9x3 cm. It was well-circumscribed, reddish, hemorrhagic, and friable. On microscopic examination two distinct different components were seen. Several sections of the tumor revealed necrotic tissue exhibiting spindle cell lesion arranged in sheets with wavy and hyperchromatic nuclei (Figure 3). These cells stained positive with S-100 on immunohistochemistry (IHC) (Figure 4). Verocay bodies, diagnostic for schwannoma were also seen.

The second component exhibited polygonal cells that had a moderate amount of eosinophilic cytoplasm with round to oval, hyperchromatic nuclei with mitotic figures raising the suspicion of a vascular tumor (Figure 3). IHC on epithelioid cells showed high proliferative activity (Ki-67 >10%), positive CD-31, and erythroblast transformation specific related gene (ERG)-which are markers for vascular tissue-however, negative CD-34, P63, S-100 and Cytokeratin 5/6. Hence, the diagnosis of epithelioid angiosarcoma arising in a schwannoma was made.

Based on the diagnosis, postoperative positron emission tomography/CT scan was advised to plan the patient for adjuvant concurrent chemoradiotherapy. Despite repeated efforts to contact the patient and his family, he was lost to follow up.

Written consent was taken from the patient after histopathology report was finalized to report this case.

Discussion

Schwannomas are benign peripheral nerve sheath tumors. Approximately 25-45% occur in the head and neck region with parapharyngeal space being the most common site extracranially involving the vagus, the glossopharyngeal and phrenic nerves more commonly (5). These are slow growing tumors with evidence of degeneration in long standing cases. Malignant transformation is a rare occurrence and should be documented as a case report. The dominant presenting feature in these patients is a painless mass with hot potato voice in only one patient.

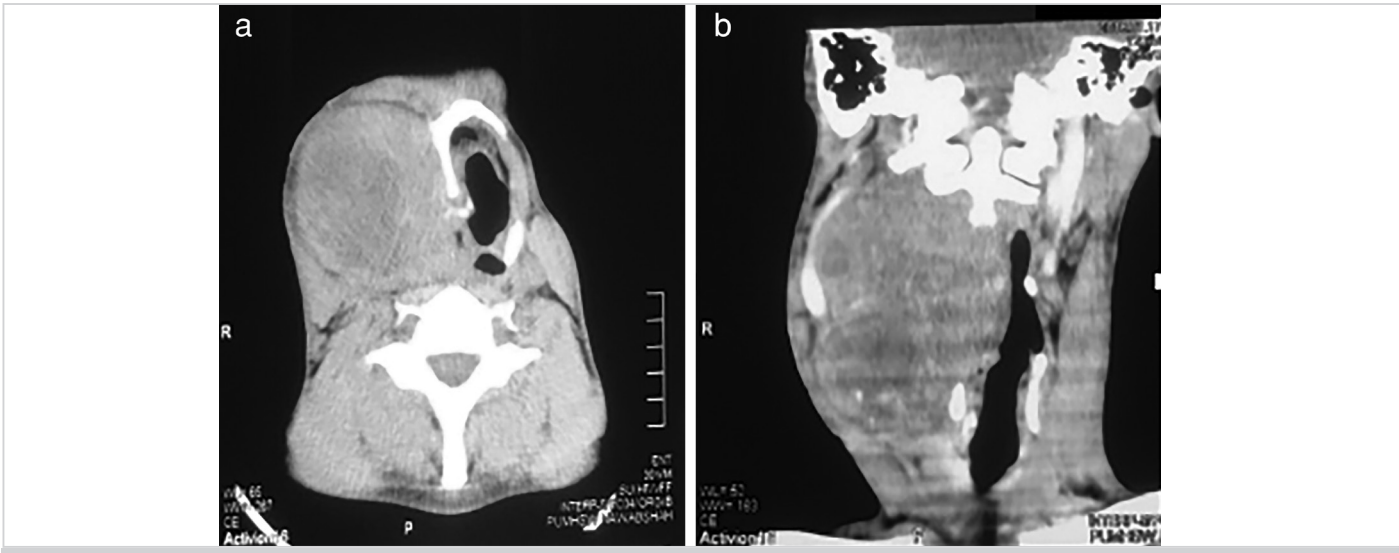

Figure 1. Computed tomography scan showing a large, heterogeneous mass with intact surrounding fat planes. a) Axial image at the level of hyoid bone, b) coronal image

The histogenesis of angiosarcoma arising in a schwannoma remains indistinct. Since the epithelioid component also stains positively for S-100, it is hypothesized to arise from the malignant transformation of differentiated neoplastic Schwann cells (6). Various theories have been put forward to explain its origins. Chronic vascular stasis in longstanding cases of schwannoma was proposed as a means of pathogenesis of angiosarcoma by Rückert et al. (7). On the other hand, Trassard et al. (8) found Weibel-Palade bodies in the cytoplasm of epithelioid cells by means of electron microscopy. They suggested that these could have arisen from pre-existing vascular tissue in schwannoma. The presence of vascular endothelial growth factor in Schwann cells on IHC has been implicated in another study (3).

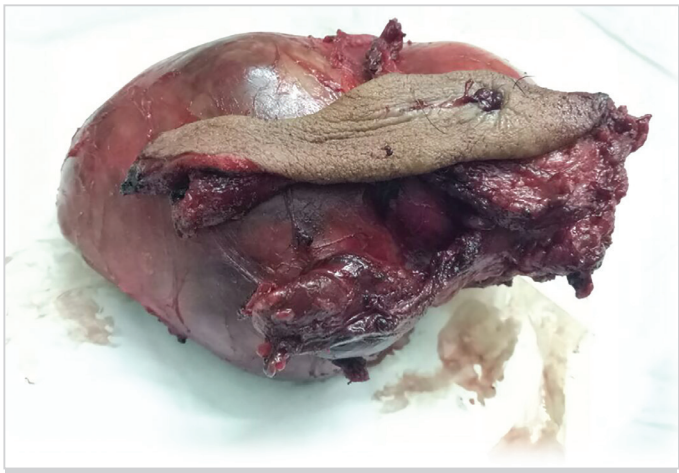

Figure 2. Tumor specimen postoperatively with overlying skin

Since 1996 when the first case was described by Trassard et al. (8), only 15 patients of angiosarcoma in a schwannoma have been reported. None of these had an association with NF 1 or 2. Among these, six were reported in the neck, making it the most common site. All of these originated on the right side of neck except one and all arose in vagus nerve except one from phrenic nerve. The mean age is 55 years, the size of the tumor ranges from 2.5 to 11 cm with median at 6 cm. Interestingly, in our case, the patient belonged to a younger age group with a larger tumor size at 11.5 cm in comparison to other reported patients (Table 1).

Differential diagnosis in our patient would include epithelioid MPNST and epithelioid malignant change (9). The presence of high proliferative activity as indicated by the Ki-67 index, is common in these tumors as is the presence of S-100 positivity. But the positive staining of CD-31 and ERG delineates the angiosarcoma on IHC.

The available literature on angiosarcoma arising in a schwannoma indicates poor prognosis due to rapid local growth, high rate of recurrence and early distant metastasis. Of the reported cases, three patients developed local recurrence, four developed distant metastasis and two patients died of the disease. The recognized causes of poorer outcomes are large tumor size, capsular penetration and incomplete resection (10). Understandably, there is no large

Table 1. Reported cases of angiosarcoma in a schwannoma

Sr No.	Case	Age (years)	Sex	Size (cm)	Site	Presentation	Treatment	Outcome
1	Mentzel and Katenkamp (3)	73	F	5x4.5x4	Rt. neck vagus nerve	Long standing mass	Surgery	NED at 43 months
2	Mentzel and Katenkamp (3)	63	M	4x3x2	Rt. neck vagus nerve	Bulge in oropharynx, long standing mass	Surgery + RT	Death with disease at 5 months
3	Rückert et al. (7)	50	M	4.5x3.5x3.5	Rt. neck vagus nerve	Neck mass for six months	Surgery	NED at 27 months
4	McMenamin and Fletcher (9)	74	F	5.5x4.5x4	Rt. neck vagus nerve	Neck mass for 30 years	Surgery	NED at 6 months
5	McMenamin and Fletcher (9)	17	F	6	Rt. neck phrenic nerve	Dyspnea on exertion for one year, swelling right neck for two weeks	Surgery + RT + CH	Death with distant metastasis at 14 months
6	Li et al. (10)	55	M	6x5x5	Lt. neck vagus nerve	Left neck mass for more than four years	Surgery	NED at 32 months
7	Mahajan et al. (1)	41	M	11x6.5x3.5	Lt. neck vagus nerve	Left neck mass for 12 years	Surgery + CH	Death with distant metastasis at 4 months
8	Current study	30	M	11.5x9x6	Rt. neck vagus nerve	Right neck mass for 15 years, change in voice for eight years, dysphagia for seven years	Surgery	Lost to follow up at 3 months

M: Male, F: Female, N/A: Information Not available, Rt.: Right, Lt.: Left, CH: Chemotherapy, RT: Radiotherapy, NED: No evidence of disease

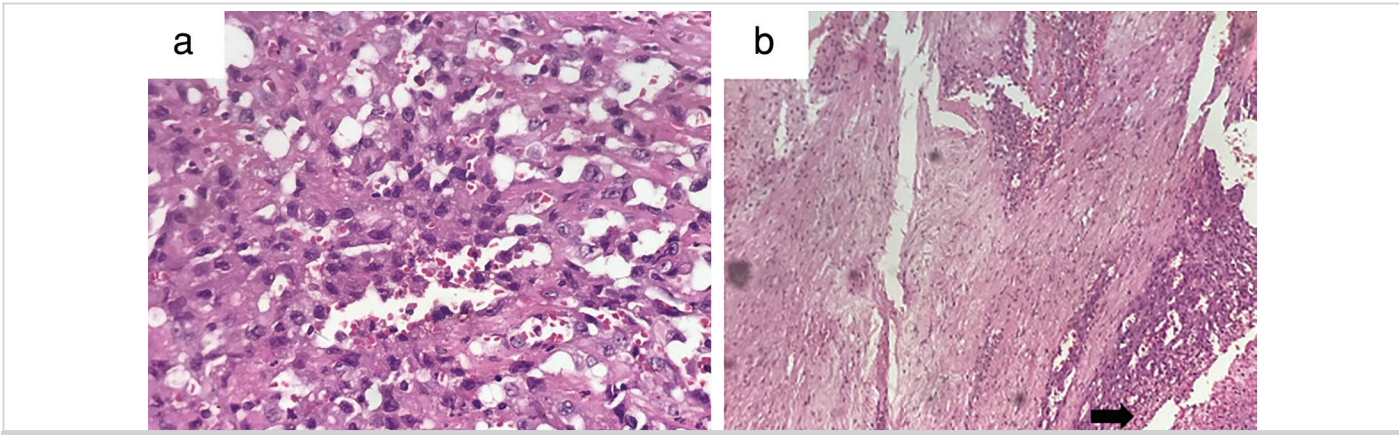

Figure 3. Hematoxylin and Eosin staining. Epithelioid angiosarcoma cells arranged in nest with marked vascularity. Cells are polygonal with moderate eosinophilic cytoplasm and round to oval nuclei (a) 40x. Spindle-shaped schwannoma cells lesion arranged in sheets, nuclei are wavy and hyperchromatic with Verocay body formation. Arrow indicates vascular lesion (b) 20x

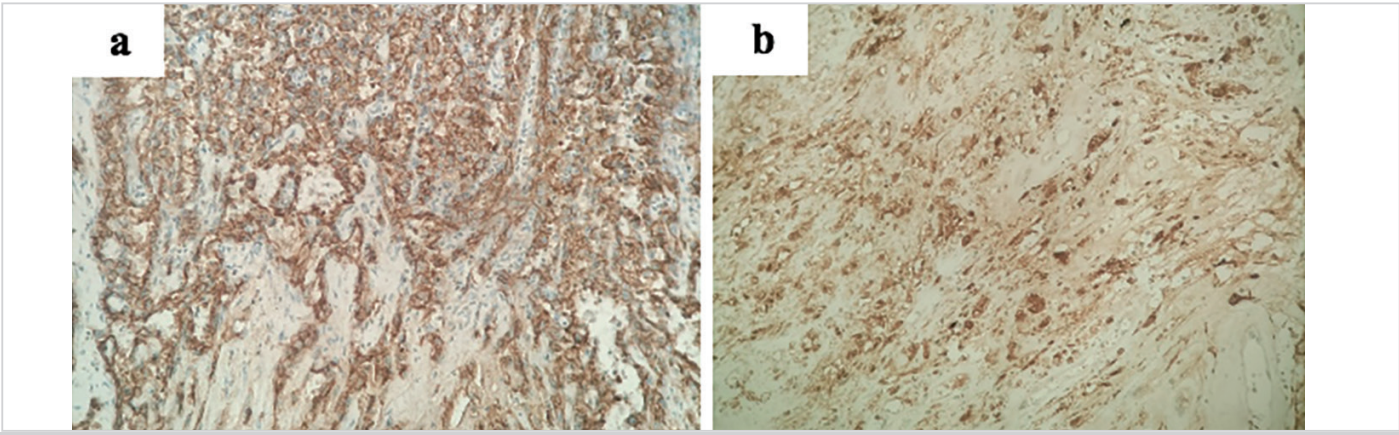

Figure 4. IHC. a) CD-31 was positive in endothelial cells, b) Cytoplasmic and nuclear components show S-100 positivity in Schwann cells
IHC: Immunohistochemistry

scale study to compare the various modes of treatment, but the most advocated approach is wide local excision followed by postoperative radiation +/- chemotherapy (7, 9).

Epithelioid angiosarcoma is a rare neoplasm with an unknown pathogenesis and a very poor prognosis. A painless lump causing dysphagia is the usual presentation in the neck. It is characterized by sheets of epithelioid endothelial cells that can imitate several epithelioid malignancies. Histopathological examination with IHC remains the gold standard of diagnosis. Early and complete surgical excision of the primary tumor is imperative. Adjuvant radiation therapy and chemotherapy may also contribute to prolonging survival. Patient and family should be counselled regarding the aggressive nature of the disease to ensure regular follow ups postoperatively.

Informed Consent: Written consent was taken from the patient after histopathology report was finalized to report this case.

Authorship Contributions

Surgical and Medical Practices: Z.A.S., I.A.M.K., Concept: Z.A.S., I.A.M.K., P.N., Design: Z.A.S., P.N., H.A., Data Collection and/or Processing: Z.A.S., A.D., P.N., H.A., Analysis and/or Interpretation: Z.A.S., I.A.M.K., A.D., P.N., Literature Search: Z.A.S., A.D., H.A., Writing: Z.A.S., A.D., P.N., H.A.

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Main Points

- Vagal schwannomas are rare entities and management is often delayed due to non-peculiar symptoms.
- Angiosarcomas are also rare vascular tumors and are seldom associated with vagal schwannomas; to date, only 15 cases have been reported in the literature.
- Surgical management is the mainstay of treatment along with adjuvant concurrent chemoradiotherapy.
- Long term outcomes indicate poor prognosis due to rapid local growth, high rate of recurrence and early distant metastasis.

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