Cavernous hemangioma within a schwannoma: A case report of a rare amalgamation of two entities

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ABSTRACT

Schwannoma occurring in peripheral nerves is a common tumor. Cavernous hemangiomas are also common vascular malformations. Although both of these lesions occur quite frequently, an amalgamation of both lesions is rare. Here, we present one such case. An adult male presented with a chief complaint of swelling over the left arm for 20 years. On histopathology, a diagnosis of schwannoma with cavernous hemangioma was made. A total of 36 cases have been reported in the literature, which showed cavernous hemangioma associated with neoplastic lesions of the nervous system; 24 cases were of Schwann cell origin. Furthermore, only 26 cases have been found in conjoint association. Overall, the association of cavernous hemangioma with neoplastic lesions of the nervous system is rare.

Key words: *Hemangioma, Peripheral nerves, Schwannoma, Tumor*

Schwannomas are common benign tumors occurring in peripheral nerves. Cavernous hemangiomas are also common vascular malformations occurring in different organs of the body. However, the association of cavernous malformations, also referred to as cavernous angiomas or cavernous hemangiomas of the nervous system, with neoplastic lesions of the nervous system is rare [1]. In the literature, a total of 36 cases have been published [1]. Schwannomas and neurofibromas were the most common tumors associated with cavernous malformations, accounting for 26 of 36 cases (72%). Here, we describe a case report of a patient harboring cavernous hemangioma in a schwannoma occurring within a peripheral nerve.

CASE REPORT

A 30-year-old male presented with a chief complaint of swelling over the left arm for 20 years. The patient was a non-smoker. Family history was unremarkable. On general examination, his vitals were stable. Local examination of the left arm revealed a 5 cm×3 cm×2 cm swelling which was firm, mobile, non-pulsatile, and non-tender. The skin over the swelling was stretched and non- erythematous. The patient's blood counts, coagulation profile, urinalysis, liver function, and renal function tests were within normal limits.

Excision of the swelling was performed. Gross examination of the swelling showed a single grey-white soft-tissue piece measuring 4.5 cm×2.5 cm×1.5 cm. On the cut, it was cystic and filled with a blood clot (Fig. 1). Some focal grey-white areas were identified close to the cyst walls.

On microscopic examination of these grey-white areas, distinct hypercellular and hypocellular areas suggestive of Antony A and Antony B areas were identified. Verocay bodies were also identified. Adjacent to these areas was large vascular channels lined by endothelial cells (Figs. 2 and 3). Immunohistochemistry (IHC) confirmed both components. The schwannoma showed tumor cells which were positive for S100. The endothelial cells lining the cavernous spaces were positive for CD34 (Fig. 4). Based on histopathology and IHC, a final diagnosis of schwannoma with vascular malformation was made. After the surgery, the patient was lost to follow-up.

DISCUSSION

Peripheral nerve sheath tumors (PNSTs), both benign and malignant, commonly involve the upper extremity. The most common PNSTs of the upper extremity are schwannomas, which are benign tumors arising from Schwann cells [2]. The majority of schwannomas occur in the distal upper limb. They occur more often in mixed nerves than pure sensory or motor nerves. Fascicular involvement is also common [3].

Magnetic resonance imaging is useful in characterizing soft-tissue masses of the upper extremity. Nerve sheath tumors are homogeneously hypointense centrally, with a peripheral hyperintensity. However, this "target sign" is non-specific [2].

Management of benign PNSTs of the extremity is conservative if they remain stable in size and remain asymptomatic. Surgical management of benign PNSTs involves excision. Extremity

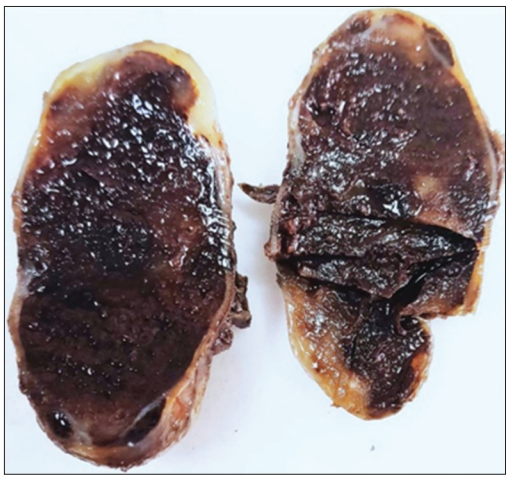

Figure 1: Cystic areas filled with blood and focal grey-white areas in the periphery

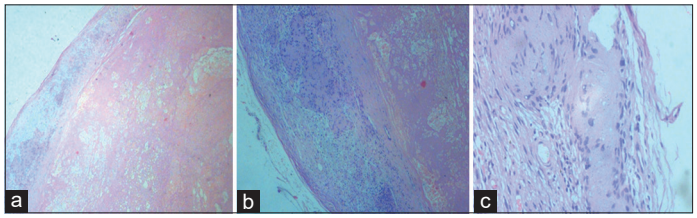

Figure 2: (a) Rim of cellular areas and vascular areas with dilated blood vessels (×4, H and E); (b) Hypercellular areas with Verocay bodies (×10, H and E); (c) Verocay bodies (×40, H and E)

schwannomas, being encapsulated, can be managed by enucleation or intraneural dissection; this allows salvage of the associated nerve. Sometimes, fascicles cannot be safeguarded, as they are also involved [2]. Neurofibromas, on the other hand, blend with the underlying nerve; thus, intraneural dissection and fascicular salvage may not be possible [2]. The excision of fascicles with the tumor can result in functional deficits [3].

On histology, schwannoma is an encapsulated neoplasm containing Antony A and Antony B areas. Antony A is cellular and consists of spindle-shaped Schwann cells. These cells commonly show nuclear palisading and Verocay bodies. Antony B areas are also composed of Schwann cells, but their cytoplasm is inconspicuous, and their nuclei are suspended in a copious myxoid matrix. On IHC, schwannomas show strong S100 positivity. Cavernous hemangiomas consist of poorly circumscribed, irregularly dilated blood vessels lined by flat endothelium.

An extensive literature search yielded only 36 cases showing an association between a nervous system tumor and hemangioma [1,4-25] (Tables 1 and 2). However, the amalgamation of schwannoma and hemangioma is rare. The cavernous malformation was found within the tumor (conjoint association) in 25 cases and at some distance from the tumor (discrete association) in 11 cases. Schwannomas and neurofibromas were the most common tumors associated with cavernous malformations, accounting for 26 of 36 cases (72%). Five of these cases were patients with neurofibromatosis. Glial tumors were the next most common tumor type.

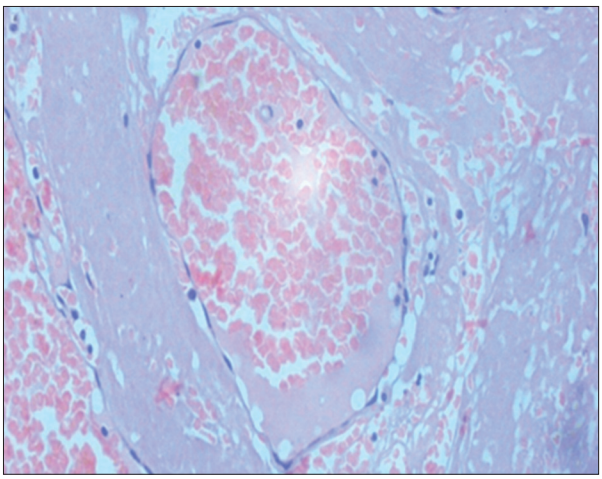

Figure 3: Endothelium-lined cavernous spaces (×40, H and E)

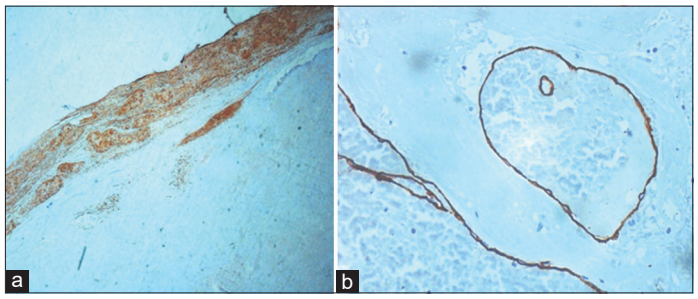

Figure 4: (a) Immunohistochemistry (IHC) showing tumor cells positive for S100; (b) IHC with CD34 showing endothelium-lined cavernous spaces

In our review of literature, a conjoint association between schwannoma and hemangioma was found in 20 cases (Table 1). The incidence was eight for cranial nerves and ten for peripheral nerves. Two cases were intracranial, of which one was intracerebral. The largest case series describing the conjoint association included seven cases. With this background, our case could be the 11th case to occur in peripheral nerves. Other cases showed a conjoint association of hemangioma with various entities such as ganglioglioma, anaplastic astrocytoma, and oligodendroglioma [1,4-16].

A total of 11 cases showed a discrete association [17-25] (Table 2). With a discrete association, six cases had both components intracranially, four cases had one intracranial component, and one had extracranial component, and one had both components extracranially. Neurofibroma was the most common tumor showing such discrete association, with five cases reporting association.

These entities pose certain challenges to pathologists, radiologists, and clinicians. Inadequate sampling, i.e., sampling one of the two components, may lead to misdiagnosis on fine- needle aspiration cytology. Pathologists also need to ensure adequate sectioning during grossing; otherwise, a thin rim of schwannoma is likely to be missed. Clinicians ought to know that nerve sheath neoplasms that comprise mesenchymal tissues are usually malignant and more frequently occur in peripheral nerves [11].

Table 1: Cases of conjoint association

Study	Year	Cases	Tumor type	Location of tumor
Wilson [4]	2016	1	Schwannoma	Left temporal lobe
Feiz Erfan [1]	2006	1	Schwannoma	Cranial nerve VIII
Kogler *et al.* [5]	2000	1	Ganglioglioma	Occipitoparietal lobe
Acciarri *et al.* [6]	1994	1	Anaplastic astrocytoma	Parietal lobe
Asari *et al.* [7]	1992	1	Schwannoma	Cranial nerve V
Kasantikul *et al*. [8]	1987	1	Schwannoma	Parasellar
Chee *et al.* [9]	1985	1	Oligodendroglioma	Frontal lobe
Kasantikul *et al.* [10]	1984	1	Schwannoma	Parapharyngeal
Kasantikul *et al.* [11]	1982	1	Schwannoma	Cranial nerve V
Fischer *et al.* [12]	1982	2	Oligodendroglioma Glioma (not specified)	Frontal lobe Temporoparietal lobe
Pasquier *et al.* [13]	1980	1	Schwannoma	Mediastinum
Kasantikul and Netsky [14]	1979	7	Schwannoma	Cranial nerve VIII (4), spinal cord C1-2, peroneal nerve, ulnar nerve
Bojsen-Moller and Spaun [15]	1978	5	Schwannoma	Intraspinal (3), cranial nerve VIII, brachial plexus
Willis [16]	1967	1	Schwannoma	Posterior mediastinum

Table 2: Cases of discrete association

Study	Year	Site of cavernous malformation	Cases	Tumor type	Location of tumor
Gupta *et al.* [17]	2017	Right orbit	1	Schwannoma	Left orbit
Tews *et al*. [18]	1998	Right parieto-occipital lobe	1	Oligodendroglioma	Right parieto-occipital lobe
Mitsuhashi *et al.* [19]	1991	Intrasellar	1	Neurofibromatosis	Peripheral nerve
Lindboe and Nordal [20]	1985	Thoracic spinal cord	1	Neurofibromatosis	Cauda equina
Savoiardo and Passerini [21]	1978	Left occipital lobe, Right frontal lobe	2	Meningioma Astrocytoma	Left parietal lobe and right frontal lobe
Chapman *et al.* [22]	1959	Cerebellum,medulla oblongata	2	Neurofibromatosis	Peripheral nerve
White *et al.* [23]	1958	Temporal lobe	1	Astrocytoma	Septum pellucidum
Mandeville and Sahyoun [24]	1947	Fourth ventricle	1	Neurofibromatosis	Peripheral nerve
Lafora [25]	1911	Pons	1	Ependymoma	Fourth ventricle

Cases of vestibular schwannoma associated with cavernous hemangioma reported in the literature have shown a high incidence of hemorrhage. This finding is attributed to "vascular instability" caused by elevated levels of matrix metalloproteinase-2 and 9, whose release is thought to be promoted by tumor cytokines [26]. The abnormal vessels are friable and vulnerable to thrombosis and hemorrhage [7]. Hemorrhages, including subarachnoid hemorrhages, have also been reported when such mixed lesions have occurred in the central nervous system. To the radiologist, vascular malformations and PNSTs can look alike on imaging. PNSTs might be mistaken for vascular malformations, as they may also appear hypointense on T1 and hyperintense on T2-weighted imaging, and enhance with contrast [27].

Various theories have been proposed for the development of such mixed lesions. Some authors explain the presence of both neurilemmoma and angioma components on the basis of their common origin in ectomesenchyme [14]. Other theories have relied on a genetic basis. Krev-1 (= Rap-1A, whose expression is controlled by *KRIT1* on chromosome 7) operates as a tumor-suppressor protein binding to a number of Ras oncogene effectors. *KRIT1* loss escalates Ras-dependent tumor growth [1]. Another theory proposes that the angiomatous component develops as a sequel of the angiogenic stimulation produced by tumor cytokines. The most notable, among the angiogenic cytokines, is vascular endothelial growth factor (VEGF). Cytokines, including VEGF, are known to be induced and promoted by tumors of the nervous system [1].

CONCLUSION

The amalgamation of two entities (schwannoma and cavernous hemangioma) could increase the chances of bleeding during excision. A malignant component should be excluded from the study.

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