

A Study on Schwannomas: Morphology Alone is Insufficient

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Rec Date: Aug 01, 2016, Acc Date: Aug 28, 2016, Pub Date: Aug 30, 2016

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Abstract

Schwannomas constitute one of the most common benign peripheral nerve sheath tumors. Schwannomas can occur anywhere in the body occasionally with unusual presentation. FNB does not appear to provide an accurate preoperative diagnosis. Complete excision of the mass should be the goal of surgical excision. In this case series, we studied various clinicomorphological features of schwannomas for duration of one year. Immunostaining were done using anti-S100 protein and a panel of antibody to confirm the diagnosis cases as well as in cases whose histological picture simulated schwannoma. Out of the 9 cases in our study, two cases showed unusual presentations. Schwannoma often gives a differential diagnosis of similar benign soft tissue tumors. All cases were benign schwannoma except one case with rectal growth turned out to be gastrointestinal stromal tumor on immunohistochemistry. Herein, we are discussing about the various histological pictures of schwannoma, diagnostic difficulties encountered in histopathology and the indispensable role of immunohistochemistry in confirmation. Classic schwannoma picture in histology is insufficient to confirm the diagnosis. Cellular schwannoma often posed a differential diagnosis of other tumors in histology such as spindle cell tumor. Palisading of nuclei is not unique to schwannoma as seen in the case of gastrointestinal stromal tumor. It can also occur in leiomyoma, leiomyosarcoma, gastrointestinal stromal tumor, calcifying aponeurotic fibroma, and even in non-neoplastic smooth muscle lesion. Gastrointestinal stromal tumor may harbor a picture of classic schwannoma and should be careful in gastro intestinal site.

Keywords: Schwannoma; S100; Immunohistochemistry

Introduction

Background

Schwannoma (neurilemoma) is one of the few truly encapsulated neoplasms of the human body and is almost always solitary (unless seen as a component of Recklinghausen disease type 2) [1]. It constitutes one of the most common benign peripheral nerve sheath tumors. It's most common locations are the flexor surfaces of the extremities, neck, mediastinum, retroperitoneum, posterior spinal roots, and cerebellopontine angle [2]. The presence of a noninvasive tumor next to a peripheral nerve suggests the diagnosis of schwannoma. The great majority of cases occur sporadically, while a small percentage of cases are associated with neurofibromatosis type 2. Occasionally, isolated cells with bizarre hyperchromatic nuclei are observed [3]; they are particularly common in so-called ancient schwannomas and are of no particular significance [4]. Mitoses are usually absent or extremely scanty. Blood vessels can be of such prominence as to simulate a vascular neoplasm. Thrombosis and hyaline thickening of the adventitia are common.

It is generally agreed that the neoplasm originates from Schwann cells, hence the current preference for the term schwannoma [5]. By electron microscopy, the tumor cells have a continuous and often reduplicated basal lamina; numerous, extremely thin cytoplasmic processes; aggregates of intracytoplasmic micro fibrils; peculiar intracytoplasmic lamellar bodies; and extracellular long-spacing collagen [6-10].

Objectives

A retrospective study of clinical, morphological, characteristics of schwannoma and to correlate and confirm with immunohistochemistry for a period of one year.

Materials and Methods

Data were retrieved from the archives of Pathology with information correlated with medical record department of our Institution. Paraffin blocks of all cases, histologically diagnosed as schwannoma, were collected and Hematoxylin and Eosin stained slides were reviewed under light microscope. The cases diagnosed as schwannoma microscopically were included and features were analyzed.

Immunostaining (IHC) was done using anti-S100 protein antibody to confirm diagnosis of Schwannoma as well as those cases with differential diagnosis of schwannoma. In cases where picture were not classic, additional markers were done. The primary antibodies and secondary detection system containing horse radish peroxidase belonged to FDA approved company were used (Table 1).

The markers used in IHC were S100, CD117, Desmin, Calretinin, Smooth muscle antigen and Vimentin. Approximately 3 mm to 4 mm tissue sections were taken in 3-aminopropyl triethoxysilane coated slide along with control slide.

The step was followed by deparaffinization in descending grades of alcohol, which was followed by antigen retrieval with TRIS buffer. Dedicated antigen retrieval (EZ-Retriever system v.3) was used for optimum retrieval of epitopes in a standardized laboratory condition.

The nonspecific sites were blocked by peroxidase and power block inside a humidity chamber. Primary antibodies were incubated for duration of one hour. Finally, secondary antibody, super enhancer polymer-HRP and DAB chromogen was used in multiple steps. It was then counterstained with iron free hematoxylin.

Name of antibody, ready to use		Reference
Anti-S100	Mouse Monoclonal antibody in PBS with carrier protein and preservative	
Anti-Desmin	-do-	AM072-2M
Anti-Calretinin	-do-	AM583-5M
Anti-Vimentin	-do-	AM074-5M
Anti-CD117	-do-	AM423-2M
Secondary antibody	Super Sensitive Polymer-HRP IHC Detection System	QD400-60KE

Table 1: IHC antibodies.

No. of cases	Sex	Age (yrs)	Site	No. of swellings	Size (cm ²)	Histology Impression	Diagnosis
1	M	45	Lt. 2nd intercoastal space	1	1 × 1	Schwannoma	Schwannoma S100 +
2	F	30	Submandibular region	2	2 × 2.5	Schwannoma/ leiomyoma	Cellular Schwannoma S100 +
3	M	40	Level III cervical region	1	Small bits	Benign soft tissue tumor	Schwannoma S100 +
4	F	26	Right leg	1	Small bits	Neurofibroma	Schwannoma S100 +
5	M	20	Right forearm	1	2 × 2	Dermatofibroma-	Schwannoma S100 +
6	F	48	Forearm	1	2 × 2	Ulnar nerve schwannoma	Schwannoma with hyaline degeneration S100 +
7	M	45	Rt. Upper arm	1	5 × 4	Spindle cell Sarcoma/ Schwannoma	Cellular schwannoma S100 +
8	M	Day 23	Wedge resected specimen of mesenteric cyst with attached small bowel	1	3 × 2	Cystic lesion with schwannomatous areas	Congenital (Cellular) schwannoma S100 +, Vimentin+
9	M	46	Biopsy of rectal growth	1	Small bits	Schwannoma	GIST S100-, CD117+, Desmin-

Table 2: Case presentations.

Results

There were total of 9 cases in the duration of one year with various presentations, age range and sizes are shown in the above table 2. The age ranged from 20 years to 48 years except one in newborn as congenital. There were 6 males and 3 females. The sizes were from 1 cm to 5 cm and sites are mostly in extremities. IHC for S100 stained showed positive in 8 cases and in case of rectal schwannoma, it was diagnosed as gastro intestinal stromal tumor (GIST) (Table 2).

Out of 9 cases, 3 cases were diagnosed as cellular schwannoma. They all showed S100 protein immunoreactivity (Figure 1).

The rectal growth was diagnosed as schwannoma microscopically but some areas simulated leiomyoma and gastrointestinal stromal tumor (GIST). So immunohistochemistry (IHC) panel with CD 117, Desmin along with S100 were done which showed positivity for CD 117 while the other two was negative (Figures 2-4).

Thus it was diagnosed as GIST. Grossly, the schwannomas often contain cystic areas (Figure 5).

Histologically, it contains two types of tissue. First, Antoni type A tissue, which is highly cellular consisting of spindle-shaped cells and surrounding an ovoid mass of eosinophilic cytoplasm (Verocay bodies) with nuclear pallasading. Second, Antoni type B, which consists of Schwann cells arranged haphazardly in very loose vacuolated reticular stromal tissue. The cellular schwannomas are highly cellular and exclusively composed of Antoni A areas but lack Verocay bodies (Figures 6-9).

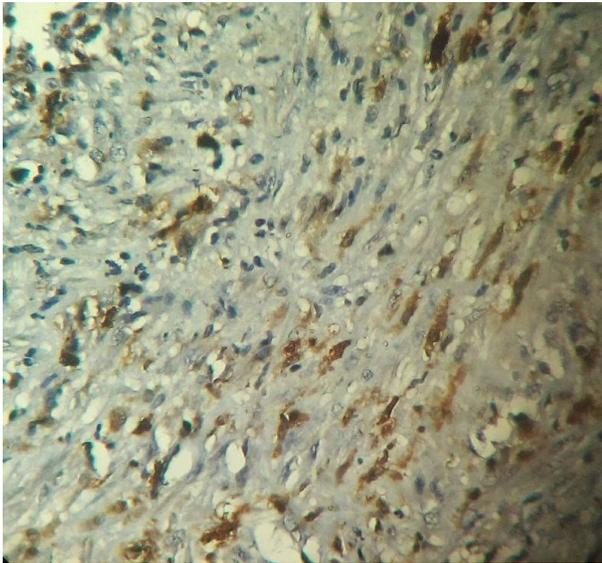


Figure 1: Showing immunostaining with S100 protein antibody which shows dark brown immunostained characteristic of Schwannoma cells. 40X.

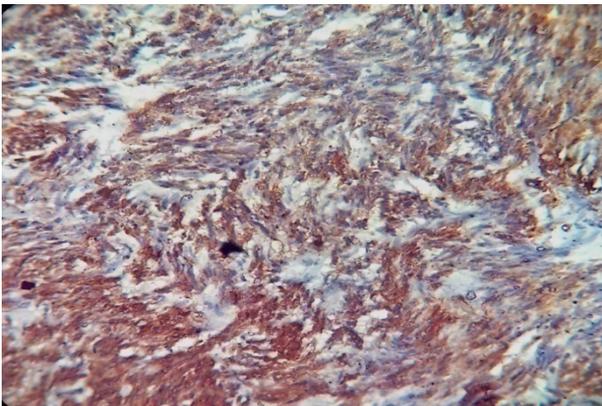


Figure 2: Showing CD117 positivity characteristic of GIST which was diagnosed initially as Schwannoma on the basis of histomorphological picture. IHC; 40X.

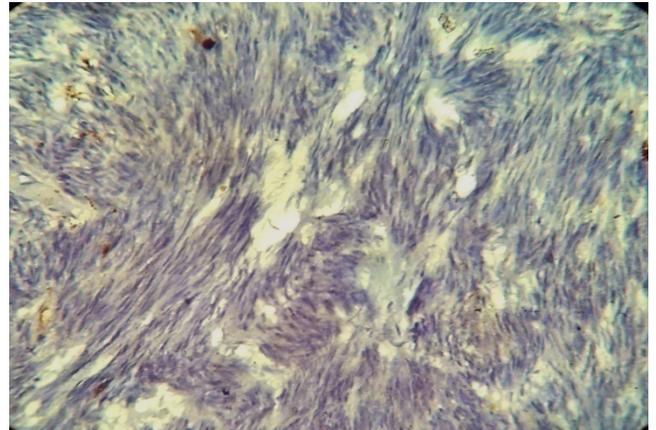


Figure 3: Showing Desmin negativity. IHC; 40X.

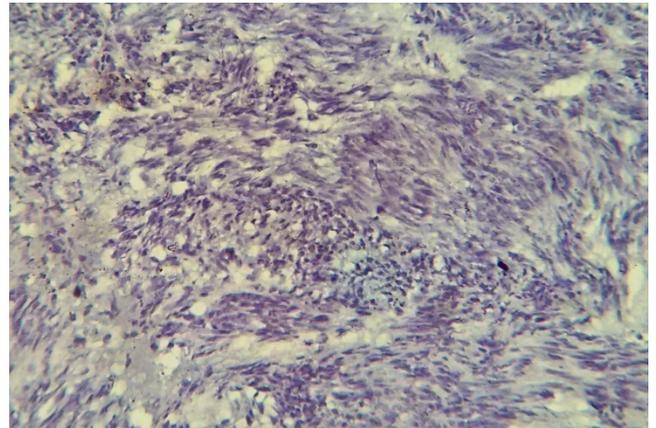


Figure 4: Showing S100 negativity. IHC; 40X.



Figure 5: Gross picture of Schwannoma.

Discussion

Most of the cases of schwannoma included in the study were asymptomatic except for congenital schwannoma case which presented with subacute intestinal obstruction symptoms like vomiting and abdominal distension for which emergency exploratory laparotomy was done, and another case which presented as rectal growth with rectal bleeding. The large size of the tumors in these cases had led to frequent clinical suspicion of malignant growth. Though histomorphological resemblance to schwannoma were seen but the presence of high cellularity, atypical cells, adipose tissue, cystic changes led to differential diagnosis. Radiology had not shown any significant role in diagnosis.

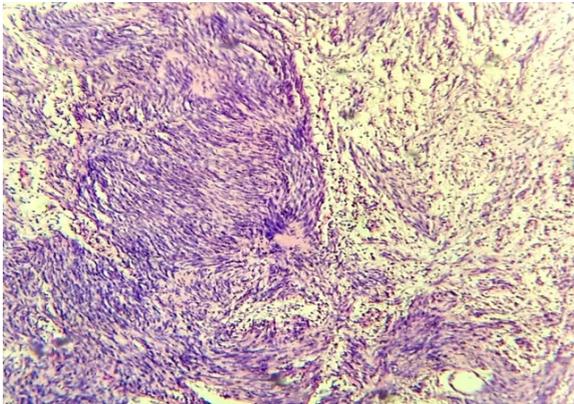


Figure 6: Histological picture of Schwannoma showing both type of tissues, Antoni type A and B. H&E; 10X.

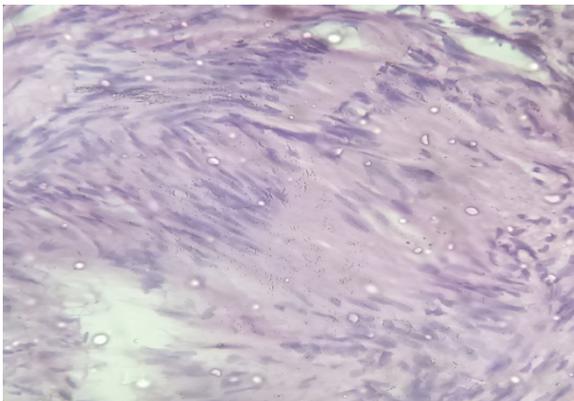


Figure 7: Histological picture showing Antoni A consisting of spindle-shaped cells and surrounding an ovoid mass of eosinophilic cytoplasm (Verocay bodies). H&E; 40X.

Genetically, schwannoma, whether sporadic or associated with neurofibromatosis type 2, is characterized by somatic mutation (sporadic form) or germline mutation (neurofibromatosis type 2) of the NF2 gene in one allele, and loss of NF2 in the remaining allele through deletion or monosomy 22 [11,12].

Schwannoma may affect any location in the course of the peripheral nervous system (i.e., cranial and spinal nerve roots, cranial and peripheral nerves, end organ receptors, small nerve twigs). They are common in paravertebral locations and the flexor regions of the extremities (especially near the elbow, wrist, and knee) and occasionally involve the skin. The presence of a noninvasive tumor next to a peripheral nerve suggests the diagnosis of schwannoma.

Palisading of nuclei is not unique to schwannoma as seen in our last case (Case 9). It can also occur in leiomyoma, leiomyosarcoma, GIST, calcifying aponeurotic fibroma, and even in non-neoplastic smooth muscle lesion. The rare occurrence of plexiform areas in schwannoma may cause them to be mistaken for neurofibroma [13,14]. Some schwannoma can be very cellular, somewhat pleomorphic, and mitotically active, and thus be confused with sarcoma [15,16].

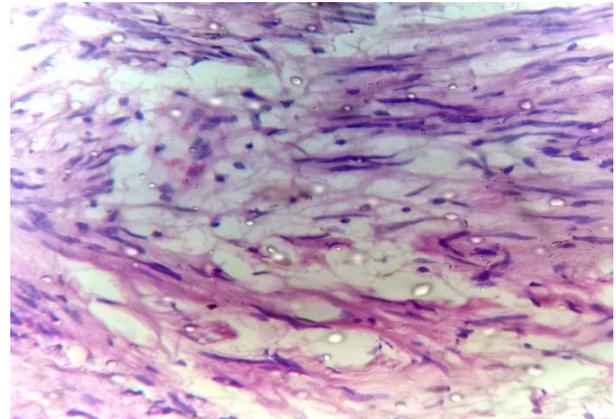


Figure 8: Histological picture showing Antoni type B, which consists of Schwann cells arranged haphazardly in very loose vacuolated reticular stromal tissue. H&E ;40X.

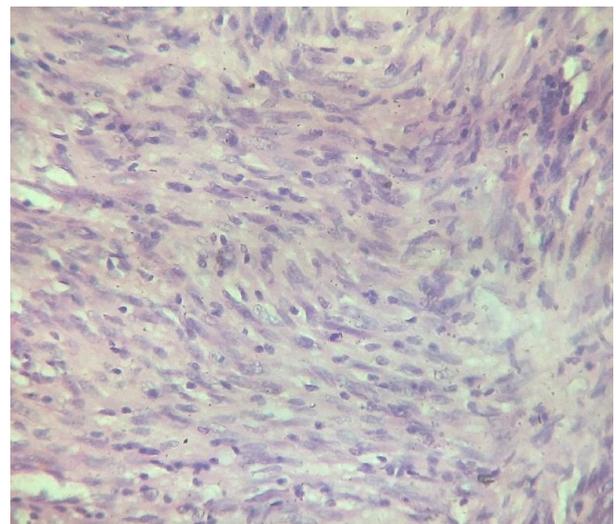


Figure 9: Histological picture showing highly cellular schwannomas composed exclusively of Antoni A areas but lack Verocay bodies. H&E; 40X.

In such cases, it is better to do panel of immunohistochemistry markers to arrive at correct diagnosis as different diagnosis will lead to different prognosis and protocol of treatment. Immunohistochemically, the tumor cells show immunoreactivity for S100 protein, Calretinin (in contrast to neurofibromas), calcineurin, basal lamina components (such as laminin, type IV collagen, and mersin), vimentin, nerve growth factor receptor, lipocortin-1, and sometimes glial fibrillary acidic protein and KP-1 (CD68) [17-29].

The signs, symptoms and disease course of schwannoma vary in duration and severity and depend on the site and in some cases nerve involved as seen in acoustic neuroma. Schwannoma can occur in any age but are most common in second to fifth decade. As schwannoma grow, they can cause pressure, irritation or damage to the nerve itself. Most patients with schwannoma have no symptoms at all as seen in

most of our cases. In our case 8, the patient presented with symptoms of subacute intestinal obstruction.

All our patients underwent complete excision of the tumor except our last case (Case 9) as the patient took discharge without further treatment. The nerve of origin often can be demonstrated in the periphery, flattened along the capsule but not penetrating the substance of the tumor. Given the benign nature of neurilemmomas, therapy is conservative and directed toward sparing the parent nerve when one is identified and is of any clinical significance (e.g., facial nerve or vagus nerve). Complete excision of the mass should be the goal of surgical excision. Malignant transformation is exceedingly rare in schwannoma; still incomplete excision may result in slow local recurrence.

The prognosis for schwannoma is excellent. All of our patients are enjoying good health. Although, incomplete excision may be associated with slow recurrence, and higher recurrence rates are noted with the intraspinal, sacral, intracranial, and plexiform variants. Locally aggressive behavior is observed in tumors with increased cellularity, higher mitotic rates (mean, 4 per 10 high-power fields), and underlying bone extension (observed in occasional cases of orbital neurilemmomas).

Conclusion

Classic schwannoma picture in histology is insufficient to confirm the diagnosis. GIST may harbor a picture of schwannoma and should be careful in gastro intestinal site. Therefore, for correct diagnosis, microscopic examination of the biopsy and clinico-pathologic correlation along with IHC remains the golden rule.

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