Annals of Diagnostic Pathology 20 (2016) 24–28

Contents lists available at ScienceDirect

Annals of Diagnostic Pathology

# Schwannomas with pseudoglandular elements: clinicopathologic study of 61 cases

Nasir Ud Din, MBBS, FCPS *, Zubair Ahmad, MBBS, FCPS, Arsalan Ahmed, MD

*Department of Pathology and Laboratory Medicine, Aga Khan University Hospital, Karachi Pakistan*

ARTICLE INFO

*Keywords:*
Schwannoma
Pseudoglandular elements
Spinal nerve roots
S100
EMA

ABSTRACT

Schwannomas are benign neoplasms of peripheral nerve sheath. A number of morphologic variants of schwannoma have been described. The pseudoglandular variant is very rare. We retrieved and reviewed hematoxylin and eosin slides of all cases of schwannoma reported between 2007 and 2014 to look for pseudoglandular elements. Pseudoglandular cystic spaces were seen in 61 (6.3%) of 971 schwannomas diagnosed during the study period. Of these 61 cases, 56 (91.8%) were located in the spinal nerve roots. The majority (60.6%) were male. Mean age in these 61 cases was 41 years. Mean tumor size was 3.5 cm. All 61 cases showed typical Antoni A and Antoni B areas with multiple pseudoglandular cystic spaces scattered throughout. These areas were lined by flat to cuboidal cells which showed positivity for immunohistochemical stain S-100 and were negative for epithelial membrane antigen. An average of 7 pseudoglandular cystic spaces was noted per case. In conclusion, pseudoglandular cystic spaces are lined by Schwann cells and most likely represent degenerative changes in schwannoma probably degenerated Verocay bodies. They are rare albeit well-defined features seen in a significant though small number of schwannomas. It is important not to mistake them for other neoplasms. Larger studies are required to determine predilection of these changes in spinal nerve root schwannomas as seen in our series.



## 1. Introduction

Schwannomas (or neurilemmomas) are benign, encapsulated neoplasms of the peripheral nerve sheath and arise from Schwann cells [1]. Schwannomas are common, accounting for 85% of cerebellopontine angle neoplasms and almost 30% of spinal nerve root neoplasms [2]. Classically, they demonstrate a biphasic pattern on histology, that is, cellular Antoni A areas alternating with hypocellular Antoni B areas and characteristic Verocay bodies [1]. They often show, especially in longstanding cases, degenerative changes which can be quite marked. These include nuclear atypia (without increased mitotic activity), prominent hyalinized blood vessels, and sheets of foamy histiocytes and others [3].

Schwannomas do not show any predilection for males or females, they are most common in the fourth to sixth decade of life, and more than 90% are sporadic and solitary [1,4]. Most common locations include peripheral nerves in skin and subcutaneous tissue of head and neck and extremities and spinal nerve roots forming intradural, extramedullary tumors [1].

Apart from the classic biphasic pattern, a number of morphologic variants are described which include cellular, plexiform, epithelioid, glandular, and ancient variants [1,3,4]. The last mentioned is now termed *schwannoma* with degenerative changes. A very rare pseudoglandular variant has also been described in which gland-like structures or cystic spaces are formed which are lined by neoplastic Schwann cells. Columnar or flat cuboidal Schwann cells line variable-sized microcystic spaces which sometimes contain a secretion-like eosinophilic substance [5,6]. These cystic or pseudoglandular structures are scattered throughout classic cellular Antoni A or hypocellular Antoni B areas [7]. This pseudoglandular variant was first described by Ferry and Dickersin in 1988, and later, 3 cases were reported by Chan and Fok in 1996 [5,6]. Since then, this extremely rare variant has been reported in a few case reports. To our knowledge, the largest series of 16 cases was reported by Robinson et al in 2005 [7].

## 2. Materials and methods

Slides of all cases reported as schwannoma between 2007 and 2014 in the Section of Histopathology, Department of Pathology and Laboratory Medicine, Aga Khan University Hospital, Karachi, and showing pseudoglandular elements were retrieved. All cases were surgically resected cases which were fixed in 10% buffered formalin and embedded in paraffin wax. Paraffin sections were cut at a thickness of 5 μm and were stained with hematoxylin and eosin (H&E). Multiple sections were submitted and examined in each case. The number of pseudoglandular cystic spaces was counted in each case. In those cases in which multiple slides were examined, counting was performed on the section with the highest number of cystic spaces. Representative

* Corresponding author. Tel.: +92 21 3486 4349; fax: +92 21 3493 4294.
*E-mail addresses:* nasir.uddin@aku.edu, nd176@yahoo.com (N. Ud Din), zubair.ahmad@aku.edu (Z. Ahmad), arsalan.ahmed@aku.edu (A. Ahmed).

http://dx.doi.org/10.1016/j.anndiagpath.2015.10.009
1092-9134/

**Table**
Schwannoma with pseudoglandular elements located at various spinal nerve root levels (n = 56).

| Spinal nerve root level | n | Percentage (%) |
|---|---|---|
| Cervical | 9 | 16.1 |
| Thoracic (or dorsal) | 23 | 41.1 |
| Lumbar | 11 | 19.6 |
| Sacral (including conus medullaris and filum terminale) | 2 | 3.6 |
| Exact spinal level not known | 11 | 19.6 |

blocks were selected for immunohistochemical (IHC) staining, and 5-μm-thick unstained sections were cut from these blocks. These unstained sections were deparaffinized in xylene followed by hydration in decreasing concentrations of alcohol solution and washing in Tris buffer. Immunohistochemical staining was performed using avidin-biotin-peroxidase (Sigma, St Louis, MO) method. The IHC antibodies used included polyclonal ready-to-use S-100 protein (1:1000; Dako Corporation, Carpinteria, CA), epithelial membrane antigen (EMA) (monoclonal, ready to use, Dako Corporation), and glial fibrillary acidic protein (polyclonal, ready to use, Dako Corporation). All data were recorded and analyzed using SPSS 19.0 software package.

## 3. Results

A total of 971 cases of schwannoma were reported in the 8-year period (2007-2014). Of these 971 cases, pseudoglandular structures or elements were seen in 61 cases (6.3%). Of these 61 cases, 56 (91.8%) were located in the spinal nerve roots, whereas 5 (8.2%) were located in extra nervous locations (1 each in scalp, retroperitoneum, thigh, popliteal fossa, and toe, respectively). The breakup of the 56 cases located in the nervous system is shown in the Table.

Of these 61 cases, 37 patients (60.6%) were male, whereas 24 (39.4%) were female. Ages ranged from 24 to 70 years with mean and median ages of 41 and 44 years, respectively. The size of the tumors ranged from 1.2 to 11 cm in maximum dimension. Mean size was 3.5 cm in maximum dimension. On histology, all 61 cases were composed of spindle cells with serpentine nuclei and demonstrated typical Antoni A (with Verocay bodies) and Antoni B areas with scattered pseudoglandular, microcystic foci associated with both. The Antoni A and/or B areas were seen abutting (bordering) the pseudoglandular areas. These pseudoglandular, microcystic areas were lined by flat to cuboidal to columnar cells (Figs. 1-3). These lining cells were positive and negative for the IHC stains S-100 protein and EMA, respectively (Fig. 4). The cystic areas variably showed intraluminal foamy and hemosiderin laden macrophages. The Antoni A and Antoni B areas were strongly positive for S-100 protein and negative for IHC stains EMA and glial fibrillary acidic protein. Elsewhere, the tumors showed presence of hyalinized blood vessels. Verocay bodies were seen in 57 (93.4%) of 61 cases, hyalinized vessels were seen in 58 (95%), whereas foamy and hemosiderin macrophages were seen in 29 (47.5%) and 45 (74%) cases, respectively. None of the 61 cases showed significant nuclear atypia, although very mild focal atypia was seen in a few cases. Mitotic figures ranged from 1 to 4 (mean, 1.3/10 high-power fields). The average number of pseudoglandular cystic spaces per case was 7. No statistical correlation was found between the tumor size and the number of pseudoglandular spaces in a given case.

## 4. Discussion

Schwannomas may sometimes show glands and benign epithelial structures. These structures probably represent true epithelial differentiation. Intestinal and respiratory type epithelium is seen in such glands, and occasionally, these glands have been shown to be lined by ependymal cells [8-11]. Schwannomas with pseudoglandular elements are distinct from these true glandular structures and should not be confused with them because these cystic spaces are lined by

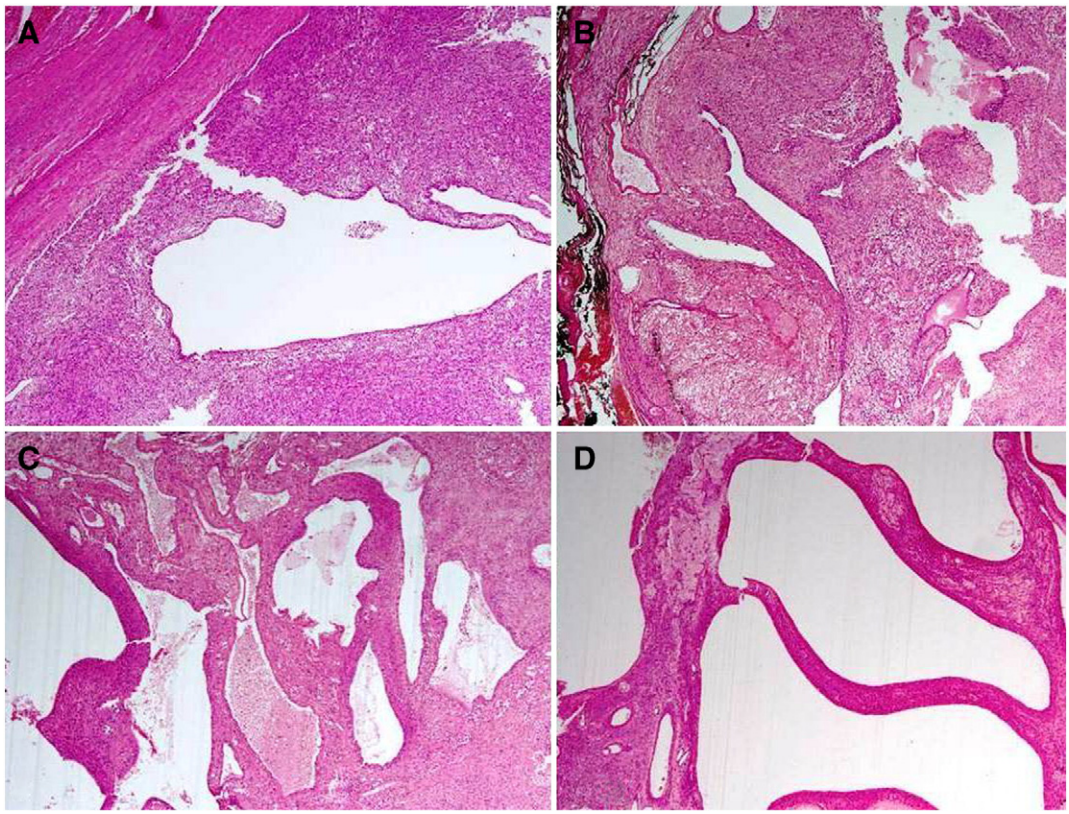


**Fig. 1.** Large irregular cystic spaces reminiscent of branching glands (H&E, original magnification ×40) (A-C). Sheets of foamy histiocytes can be seen within septae of cystic spaces (H&E, original magnification ×100) (D).