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Ganglioneuroma: Clinicopathological study with emphasis on the histologic features and differential diagnosis

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- Objective** : *Ganglioneuroma is a rare benign tumor and there has been no previous paper focusing on the histologic criteria that is essential for diagnosis and also for differential diagnosis. This study includes the clinicopathological features of ganglioneuroma and its differential diagnosis which may be mistaken.*
- Setting** : *Department of Pathology, Faculty of Medicine, Chulalongkorn University*
- Design** : *Retrospective descriptive study*
- Subject** : *Patients diagnosed with ganglioneuroma from January 1989 to December 1998.*
- Methods** : *Determination of clinical features including sex, age, location, presenting and associated symptoms, treatment and follow-up time. Determination of pathological features consisting of number of masses, size, gross appearance, nerve association, light microscopic examinations and including immunohistochemistry studies.*
- Results** : *Five cases of ganglioneuroma were recruited into the study. The female to male ratio was 3:2. The ages ranged from 14 to 51 years (mean 32.5 and median 35 years). Masses localized at the posterior mediastinum were 40%, retroperitoneum (extraadrenal) 40 % and neck 20 %. The lesions were all resected and patient were alive after follow-ups ranging from 3 to 77 months.*

The pathological features included gross appearance, microscopic examination and immunohistochemistry study. The majority of masses appeared as solitary (80%). All cases (100%) showed solid, fibrous encapsulation masses with 40% grey white and whorl-like cut surfaces. The remaining displayed grey, slimy and a few small cystic cut surfaces (60%). There was no obviously diffuse hemorrhage, necrosis, calcification or association with nerves. The microscopic features of ganglioneuroma consisted of mature elements that contained schwann cells, ganglion cells, and stromal collagen. Our study disclosed compact features (80%) and edematous features (20%). The number of ganglion cell nuclei varied from one to three. None showed atypia. The lymphocytic cells were diffusely distributed (60%), infiltrating surrounding blood vessels (20%), or paucicellular (20%). The blood vessel patterns was neither prominent or proliferate. Hyalinization of blood vessel walls was not demonstrated. Melanin pigment disclosed in 40% of cases. The collagenous stroma was presented as intervening of spindle cells. There was no evidence of thick collagen bundles. One case (20%) showed microscopic calcification. An immunohistochemistry profile was applied and revealed that all lesions were reactive for Neurofilament and S-100 protein. The neurofilament appeared in both ganglion and spindle cell stroma but the S-100 protein was localized at the spindle cells.

Conclusions : *The size of our sample was very small since this tumor is very rare. However, we determined the real incidence of these cases of King Chulalongkorn Memorial Hospital for a ten year period. We propose that the combination of clinical and pathological features is the most useful for diagnosis and differential diagnosis. Furthermore, we emphasise all the histologic features that may cause confusion. In addition, the utility of neural markers for this tumor was the conjunction tool but it was not very helpful for differential diagnosis.*

Key words : *Ganglioneuroma, Ganglioneuroblastoma, Immunohistochemistry of ganglioneuroma.*

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วรรณข บัญญาวรรุณี, พิเชฐ สัมปทานุกุล, ปรีชา เรืองเวชวรชัย. Ganglioneuroma: การศึกษาลักษณะทางคลินิกและพยาธิวิทยา โดยมุ่งเน้นเรื่องลักษณะทาง histology และการวินิจฉัยแยกโรค. จุฬาลงกรณ์เวชสาร 2542 ส.ศ; 43(8): 545-60

- วัตถุประสงค์** : Ganglioneuroma เป็นเนื้องอกที่พบน้อยมากและยังไม่มีรายงานซึ่งศึกษา มุ่งเน้นถึงลักษณะทางฮิสโตโลจี ซึ่งใช้เป็นเกณฑ์ในการวินิจฉัย และใช้แยกออกจากโรคอื่น การศึกษานี้ได้ศึกษาถึงลักษณะรวมของทางคลินิกและทาง พยาธิวิทยาและนำเสนอการแยกวินิจฉัยออกจากโรคอื่นซึ่งอาจพบมี ความผิดพลาดเกิดขึ้นได้
- สถานที่ที่ทำการศึกษา** : ภาควิชาพยาธิวิทยา คณะแพทยศาสตร์ จุฬาลงกรณ์มหาวิทยาลัย
- รูปแบบการวิจัย** : การศึกษาเชิงบรรยายแบบย้อนหลัง
- ผู้ป่วยที่ได้ทำการศึกษา** : ผู้ป่วยที่เคยได้รับการวินิจฉัยโรค ganglioneuroma ทั้งหมดในช่วงระยะเวลา 10 ปีโดยเริ่มตั้งแต่ มกราคม 1989 ถึง ธันวาคม 1998.
- วิธีการศึกษา** : ศึกษาลักษณะทางคลินิกของผู้ป่วย ได้แก่ เพศ, อายุ, ตำแหน่งของก้อน, อาการนำและอาการร่วม, การรักษา และระยะเวลาการติดตามผล ศึกษาลักษณะทางพยาธิวิทยา ซึ่งประกอบด้วย จำนวนของก้อนเนื้องอก, ขนาด, ลักษณะภายนอกก้อน และผิวหน้าตัด รวมทั้งศึกษาว่ามีความ สัมพันธ์กับเส้นประสาทหรือไม่ นอกจากนี้ยังศึกษาลักษณะที่ตรวจพบทาง กล้องจุลทรรศน์รวมถึงการนำอิมมูโนฮิสโตเคมีมาใช้ศึกษา
- ผลการศึกษา** : ผู้ป่วย Ganglioneuroma 5 ราย พบอัตราส่วนของผู้หญิงต่อผู้ชายเท่ากับ 3:2 โดยพบในช่วงอายุตั้งแต่ 14 ถึง 51 ปี (ค่าเฉลี่ย 32.5, ค่ากึ่งกลาง 35 ปี) ก้อนเกิดที่ Posterior mediastinum 40%, retroperitoneum (extra-adrenal) 40%, neck 20%. ผู้ป่วยได้รับการผ่าตัดเอาก้อนออกทั้งหมดผลหลังผ่าตัด ผู้ป่วยยังมีชีวิตอยู่และแข็งแรงดี โดยใช้ระยะเวลาติดตาม 3 ถึง 77 เดือน ลักษณะทางพยาธิวิทยาซึ่งดูลักษณะภายนอก, กล้องจุลทรรศน์, อิมมูโน ฮิสโตเคมีพบเนื้องอกเป็นก้อนเดี่ยว 80 % โดยทุกก้อนมี Fibrous capsule ล้อมรอบและมีผิวหน้าตัดแข็ง, สีขาวและมี Whorl-like (40 %) นอกจากนี้ พบผิวหน้าตัดสีเทา, นุ่มและเส้นเป็นเมือก, ถุงน้ำขนาดเล็ก (60%) ทุกก้อนไม่ พบมีเลือดออก, เนื้อตาย, แคลเซียม รวมทั้งไม่มีความสัมพันธ์กับเส้น ประสาทใด ๆ ลักษณะทางกล้องจุลทรรศน์ของ Ganglioneuroma ประกอบ

ด้วยส่วนของ Schwann cells, ganglion cells, stromal collagen ซึ่งองค์ประกอบเหล่านี้มีการพัฒนาเต็มที่ (maturation) จากการวิเคราะห์พบ มีปริมาณของเซลล์รูปกระสวยมาก (spindle cell, schwann cell) และเรียงตัวแน่น (compact feature) 80 % ส่วนลักษณะเซลล์ซึ่งอยู่กันหลวม ๆ และมีพื้นโครงสร้างเป็น myxoid มากพบ 20 % จำนวนของนิวเคลียสของ Ganglion cell พบได้ตั้งแต่ 1 ถึง 3 นิวเคลียสโดยทั้งหมดนี้ไม่พบมีความผิดปกติของ นิวเคลียส (atypia) นอกจากนี้ lymphocyte มีการเรียงตัวกระจายทั่ว ๆ ไป 60 %, พบเรียงตัวรอบหลอดเลือด 20 %, และพบจำนวนของ lymphocyte น้อยมากในสไลด์ 20 % ลักษณะของหลอดเลือดในเนื้ออกไม่พบมีการเพิ่มปริมาณ และไม่มี hyalinization ของผนังหลอดเลือด สารนิวโรเมลา닌พบได้ 40 % ลักษณะของ Stroma ซึ่ง collagen จะแทรกอยู่และกระจายทั่วไป ไม่พบลักษณะของ collagen ที่หนาตัวขึ้นพบแคลเซียมเกาะในก้อนเนื้ออกทางกล้องจุลทรรศน์ 20 % การนำอิมมูโนฮิสโตเคมีมาใช้โดยเลือกตัวตรวจหาของระบบประสาท (Neural marker) ซึ่งพบผลบวกทั้งใน Ganglion cell และ Spindle cell จากการใช้ antibody ต่อ Neurofilament ส่วน S-100 protein พบติดในส่วนของ Spindle cell

สรุป

- : ขนาดตัวอย่างของการศึกษานี้มีขนาดเล็ก เนื่องจากเนื้ออกชนิดนี้พบได้น้อยมาก แต่อย่างไรก็ตามจากการศึกษาค้นคว้านี้ทำให้ทราบพฤติกรรมการเกิดโรคจริงในช่วงระยะเวลา 10 ปี ของผู้ป่วยในโรงพยาบาลจุฬาลงกรณ์ เราขอเสนอแนะให้นำลักษณะทางคลินิก ร่วมกับลักษณะทางพยาธิวิทยา มาใช้ร่วมกันในการวินิจฉัยโรคและวินิจฉัยแยกโรค ยิ่งไปกว่านั้นเรายังเน้นย้ำถึงลักษณะทางฮิสโตโลยี (Histology) ซึ่งอาจจะเกิดความสับสนขึ้นได้ในการวินิจฉัยแยกโรค ส่วนการนำอิมมูโนฮิสโตเคมีมาใช้นั้นเป็นเพียงตัวยืนยัน และใช้ร่วมในการวินิจฉัย แต่ไม่ได้มีประโยชน์มากนักโดยเฉพาะในการใช้แยกโรค

Ganglioneuroma is quite a rare benign neural tumor when compared with other benign neural tumors such as schwannoma and neurofibroma.⁽¹⁾ This tumor primarily consists of mature elements that contain schwann cells, ganglion cells and stromal collagen. It represents a fully differentiated member of the family composed of neuroblastoma, ganglioneuroblastoma and ganglioneuroma.^(2,3,4) However, diagnosis is difficult for among this group, especially the ganglioneuroblastoma. Ganglioneuroblastoma are malignant and the treatment is totally different. This study will focus on ganglioneuroma, which may be difficult for diagnosis in some cases, and will classify the clinicopathological features with emphasis on the histologic features that are most important and reliable for diagnosis. This study will also propose immunohistochemistry profiles such as neural markers and how they may be helpful for diagnosis.

Material and Methods

Data from the surgical files of the Pathological Department, Faculty of Medicine, Chulalongkorn University collected between January 1989 and December 1998 was searched and five cases of ganglioneuroma were selected and analyzed for clinical and pathological features. The clinical features consisted of sex, age, location, presenting and associated symptoms such as diarrhea, treatment and follow-up time. The pathological features were the gross and microscopic examinations, including the immunohistochemistry profiles. Regarding the gross examinations, the size and number of masses were evaluated. The examination also inspected the capsule and cut surfaces. The light microscopic examination, analyzed all compositions composed of ganglion cells, spindle

cells, blood vessels and stroma. The four-micron sections used for light microscopic study were cut from paraffin-embedded material and stained with haematoxyline and eosin. Additionally, immunohistochemistry staining was performed on formalin-fixed tissue using the avidine-biotin complex method. Commercially available polyclonal antibodies against S-100 protein (dilution 1:10,000, DAKO), and monoclonal antibodies against neurofilament (dilution 1:400, DAKO) were used. Fontana-masson stain was used to identify the melanin pigment.

Results

Clinical findings

The clinical data for the five ganglioneuroma patients is summarized in Table 1. At the time of tumor presentation, the age of patients ranged from 14 to 51 years (mean 32.5, median 35 years). Three of the five patients were female thus the ratio of females to males was 3:2. The lesions were usually asymptomatic and three cases (60%) were detected from accidental findings from check-ups such as X-ray. There were two cases (40%) related to enlarging mass. Tumors were localized at the posterior mediastinum (40%), retroperitoneum (40%), and neck (20%). All masses were resected and all specimens received. After follow-up for 3 to 77 months, all patients were alive and free of disease.

Pathological findings

Gross examination of all ganglioneuroma lesions revealed well-circumscribed masses with fibrous capsules. No nerve association was noted. Two (40%) had solid, grey white and whorl-like cut surfaces (Fig. 1). Three cases (60%) showed soft,

Table 1. Ganglioneuroma : Clinical data.

Case No.	Age / Sex (years)	Location	Presenting symptom	Associated symptom	Therapy	Follow-up (months)
1.	35 / F	Posterior mediastinum	Accidental finding	No	Surg	A&W, 77
2.	27 / M	Neck	Mass	No	Surg	A&w, 74
3.	14 / F	Posterior mediastinum	Accidental finding	Delay secondary sex characteristic	Surg	A&W, 11
4.	36 / F	Retroperitoneum (extraadrenal)	Mass	No	Surg	A&W, 4
5.	51 / M	Retroperitoneum (extraadrenal)	Accidental finding	No	Surg	A&W, 3

Surg = surgery, A&W = Alive and well



Figure 1. The tumor mass showed fibrous encapsulation with greyish white and whorl-like cut surface.

greyish white and slimy cut surfaces. There was no evidence of diffuse hemorrhage, necrosis or calcification. The majority of cases (80%) presented as single masses ranging from 1.5 to 13.0 cm in greatest dimension (mean 6.7, median 7.0 cm.) (Table 2).

Summarization of microscopic findings is shown in Table 3. The tumors showed as well-encapsulated masses composed of cellular or compact features made of spindle-shaped cells that were relatively uniform in size and shape. They

Table 2. Gross examination of ganglioneuroma.

Case No.	Number of mass (greatest dimension, cm)	Size	Capsule	Cut surface	Association with nerve
1.	3	4.5, 7.0, 13.0	Encapsulation	Grey, soft and slimy	No
2	1	8.2	Encapsulation	Grey, soft, slimy with small foci of hemorrhage	No
3	1	7.0	Encapsulation	Grey, lobulated and slimy with small cystic spaces	No
4	1	6.0	Encapsulation	Greyish white ,solid and whorl-like	No
5	1	1.5	Encapsulation	Greyish white, solid	No

Table 3. Demonstrate the microscopic findings of ganglioneuroma.

Case No	Pattern	Lymphocytic presentation	Expression of ganglion cell	Number of ganglion nuclei	Calcification	Pigment
1	Compact	paucicellular	Scarce	1	No	No
2	Compact	diffuse distribution	Scarce	1-2	No	No
3	Edematous	diffuse distribution	Numerous	1-3	yes	yes
4	Compact	infiltrate surrounding blood vessel	Numerous	1	No	No
5	Compact	diffuse distribution	Numerous	1-2	No	Yes

crisscrossed each other in an irregular fashion. The ganglion cells were round and had large amounts of cytoplasm. They presented as isolated cells and as a few clusters. The intervening collagen bundles were in general distribution. None of the cases showed thick bands of collagen. This compact feature was demonstrated in four cases (80%) (Fig 2 A). The remaining case (20%) disclosed edematous features. The hypocellular foci were composed of

loosening stroma which mainly consisted of myxomatous components with diffuse distribution admixed with islands of cells(Fig 3 A, B) but it did not have the clear distinct pattern of schwannoma. The number of ganglion cells ranged from one to three nuclei but predominantly at one (Fig 4A). There was no evidence of atypia. The expression of ganglion cells, when compared with stroma, was scarcely seen and which is identical to neurofibroma (40%) (Fig 4B).

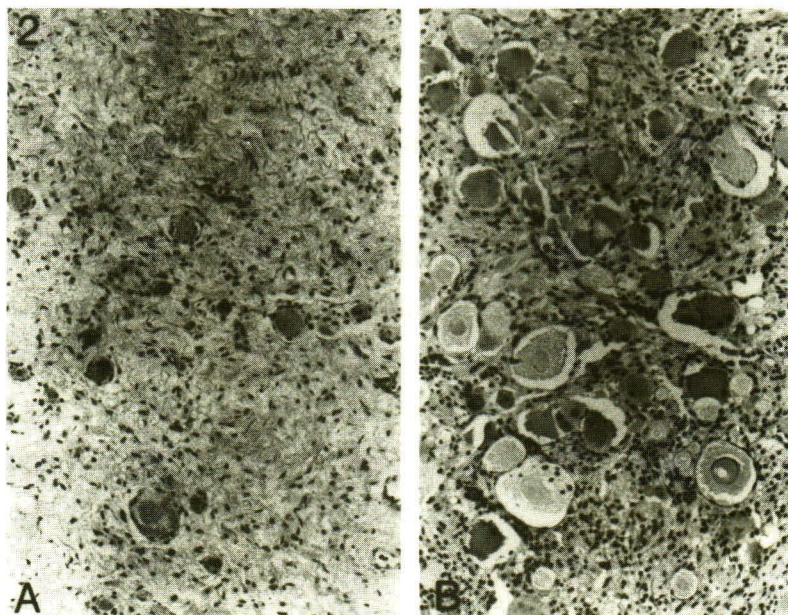


Figure 2 A. The compact feature revealed hypercellularity of mature schwann cells with scattered ganglion cells cluster. (x 200)
B. The cluster of ganglion cells disclose numerous large and voluminous pink cytoplasm. (x 400)

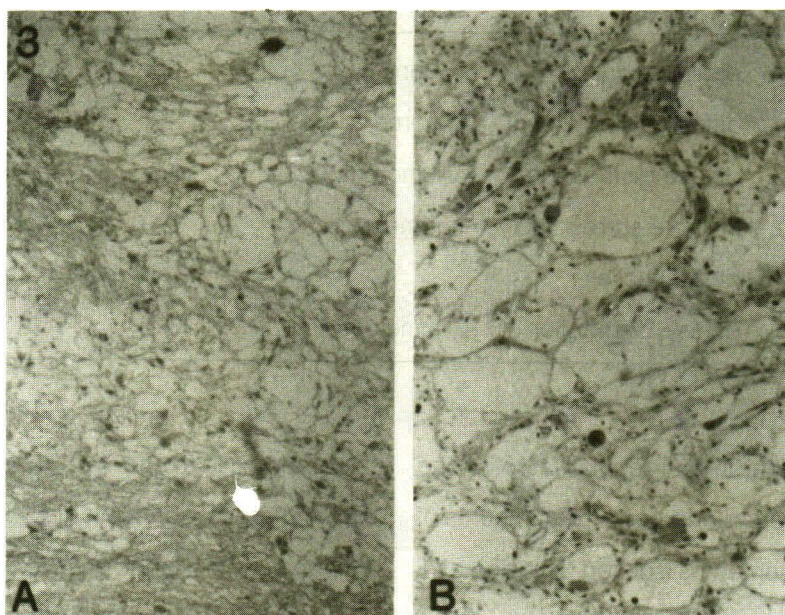


Figure 3 A. The edematous feature, loosening stroma (x 100)
B. The high power field of loosening myxomatous stroma with scattered ganglion cells (x 200)

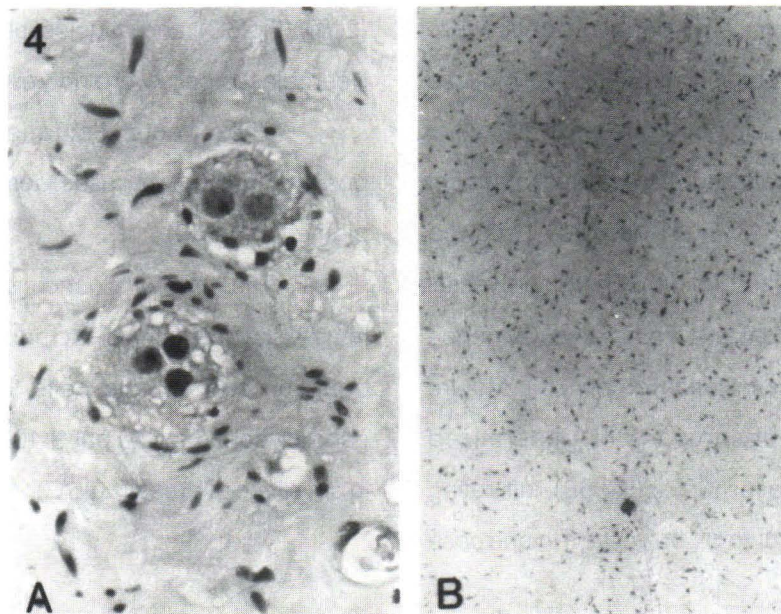


Figure 4 A. The three nuclei within one ganglion cell (x 400)
B. The hypocellular area with rare ganglion cells,
mimic neurofibroma (x 100)

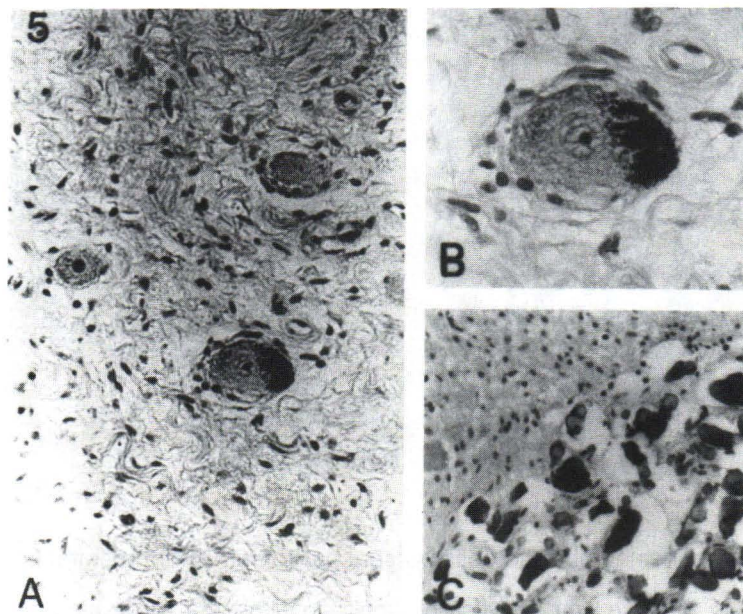


Figure 5 A. The brown-black pigment within the cytoplasm of ganglion cells. (x 2000)
B. The Fontana masson stain yeild fine granular black pigment within cytoplasm. (x 400)
C. Foci of calcification. (x 200)

Numerous presentations of ganglion cells were demonstrated in three patients (60%) (Fig 2B). Mitotic figures were not increasing. Two cases (40%) were discovered to have scattered brown black pigment in the cytoplasm (Fig 5A). One case (20%) showed microscopic calcification (Fig 5C). The blood vessel pattern was not prominent and there was no evidence of proliferation or hyalinization of the wall. Mature lymphocytes were observed with generalized distributions in three cases (60%) (Fig 6B), infiltrating predominantly surrounding blood vessels in one case

(20%) (Fig 6C), and paucicellular in one case (20%).

Neuroblastic cells were not revealed in any case.

The special Fontana-Masson stain was positive in the two cases demonstrating the black pigment (Fig 5B).

The immunohistochemistry staining for neural markers was positive for neurofilaments in both ganglion and spindle cells. It appeared in some ganglion cells (Fig 7A) but S-100 protein was positive in spindle cell areas (Fig 7B).

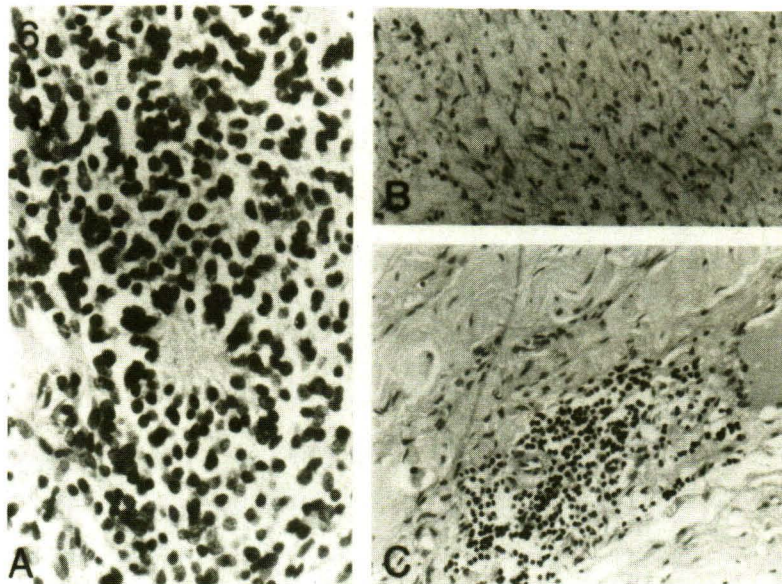


Figure 6 A. The neuroblastic cells present as Homer-Wright rosette. (x 400)
 B. Diffuse lymphocytic cells infiltrate within the schwannian cells and delicate collagen fibers. (x 100)
 C. The lymphocytes infiltrate surrounding blood vessel. (x 200)

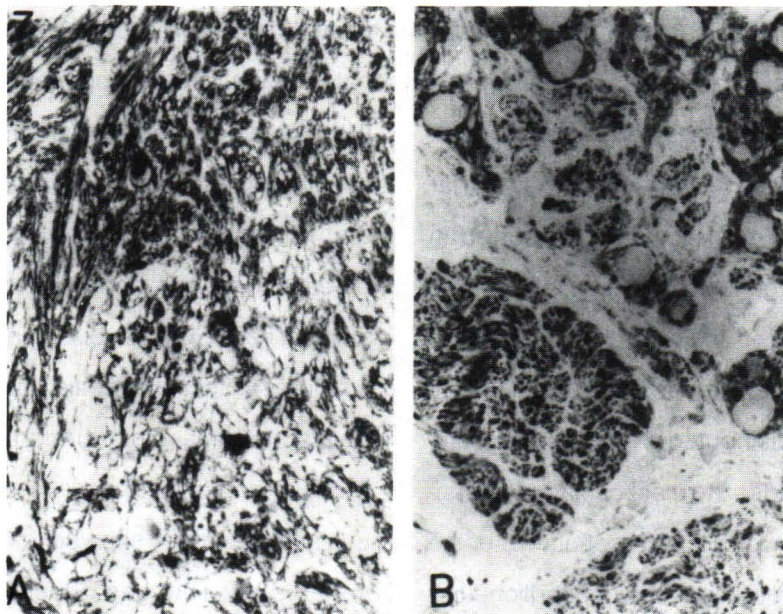


Figure 7 A. The neurofilament stain reveals diffuse and strongly positive staining with the schwannian cells and some ganglion cells. (x 200)
B. The S-100 protein shows reactive within the schwann cells. (x 200)

Discussion

Most commonly, ganglioneuroma arise from sympathetic chains that extend from the base of the skull to the neck, posterior mediastinum, and retroperitoneal regions, including adrenal glands.⁽¹⁾ Typically, it is a slow growing and benign tumor. It may remain clinically silent for a considerable time if favorably situated. Many large examples have been discovered incidentally on X-ray examination or in routine abdominal palpitation.⁽⁴⁾ Ganglioneuroma is most often encountered in patients older than ten years. The age distribution from collecting data of AFIP indicates 57% that of patients ranged between 10-39 years, and 14% were patients younger than ten years. There have been no reports of any sex predilection. The masses are usually localized at mediastinum (39%), retroperitoneum (30%), adrenal gland (22%), pelvic area (6%), cervical area (2%), and parapharyn-

geal (1%).⁽⁵⁾ Other sites have been reported in the gastrointestinal tract^(6,7,8), uterus, ovaries and skin⁽⁹⁾. It can arise as multiple masses and/or associated with other independent types of neurogenous neoplasm such as pheochromocytoma.⁽¹⁰⁾ Many instances of associated symptoms have been documented such as watery diarrhea, sweating, hypertension, and rarely virilization and myasthenia gravis. The diarrhea symptoms have been related to the presence of vasoactive intestinal peptide.⁽¹¹⁾

Regarding our own data, the five patients had a female to male ratio of 3:2. The median age was 32.5 years. All were older than 10 years. The majority (60%) were asymptomatic and the majority of the tumors occurred at the posterior mediastinum (66%). The remaining cases (40%) presented as large masses at the neck and retroperitoneum. No patient had any associated symptoms such as diarrhea, but

one patient (number 3) who was 14 years developed a delayed secondary sex characteristics. Our patients were followed up to 77 months and remained well. The age group of ganglioneuroblastoma was similar to neuroblastoma and most commonly occurred in children less than 10 years old, and it affected males and females equally. The majority of ganglioneuroblastoma were located at the retroperitoneum (65%). The remaining were distributed in the mediastinum, neck, and adrenal glands. The most common presenting symptoms often involved the local effects of the mass. The 5 year overall survival rate of ganglioneuroblastoma was up to 88%. However, the nodular subtype behaved more aggressively when compared with the diffuse type. The nodular subtype metastasized 75% versus only 4 % for the diffuse type.⁽²⁾ The series reported by Stout showed the benign behavior of ganglioneuroma with no evidence of metastasis.⁽¹²⁾ However, the rare reports of metastatic focus of ganglioneuroma in lymph nodes adjacent to the main tumor or distant site was discussed. It was assumed that it represented the metastasis of neuroblastoma as well as primary tumor maturation.⁽¹³⁾

The majority of masses were presented as solitary (80%) and were equally located at posterior mediastinum and retroperitoneum (extra-adrenal) sites (40%). The less common site was the neck (20%). Our study resulted in a mean size of 6.7 cm and the median was 7.0 cm. All masses were resected and there was no association with nerves that normally encountered in neurofibroma.⁽¹⁴⁾ Grossly, they appeared as fibrous capsules, solid, grey and with a whorl-like cut surface in two cases (40%). The majority of cases (60%) showed a greyish, soft and slimy cut surface. However, all did not demonstrate

multiple or large foci of hemorrhage, necrosis or calcification. The homogeneous gross appearance with the whorl-like cut surface could demonstrate within leiomyoma. However, the different location and microscopic examination can separate out this disease. The soft and slimy cut surface is usually found in neurofibroma but generally without encapsulation. Another differential diagnosis was ganglioneuroblastoma. This formerly had two subtypes (nodular and diffuse) and when examined by us the cut surface often showed encapsulation but had variable cut surfaces depending in part upon the extent of the differentiated elements. The more differentiated tumors may resemble ganglioneuroma with a glistening, pink-tan and fibrous encapsulation while the less differentiated showed the soft, focally hemorrhagic areas that might express as nodules or diffusely admixed.⁽²⁾ Additionally, areas of calcification are found frequently but occurs in only one third of ganglioneuroma.^(2,5) Thus careful gross inspection and thorough sampling are very important.

Basically, ganglioneuroblastoma and ganglioneuroma were designated for tumors with evidence of maturation. Ganglioneuroblastoma represented an intermediate stage between neuroblastoma and ganglioneuroma. Both contained the ganglion cells, Schwann cells and stroma. Thus the diagnosis of ganglioneuroma had to clarify and definitely not demonstrate the neuroblastic component. It was composed of small rounded cells and was often divided into small lobules. The cells were round to polygonal, with deeply staining nuclei, distinct nuclear borders and scanty amounts of cytoplasm. Some areas disclosed the attenuated cytoplasmic process which are polarized to the central point and form a

solid core (Homer-Wright rosette) (Fig 6A). In addition, the stroma contained neuropils.

The lymphocytes are often confused with primitive neuroblastic cells. Our study revealed the majority of cases (60%) presented as diffuse pattern that were occasionally confused with the diffuse pattern of ganglioneuroblastoma. The lymphocytes infiltrated surrounding blood vessels and could mimic perivascular pseudorosette. Even though, mature lymphocytes were presented throughout this tumor, the boundaries of neuroblast among these components were quite sharp in ganglioneuroblastoma^(15,16,17) Thus the exact and different histomorphology between lymphocytes and neuroblasts was most important and critical trait since the treatment of ganglioneuroblastoma is very aggressive.

Our study showed cellular or compact features in the majority of cases (80%). The cellular features were frequently misdiagnosed with neurofibroma when composed of relatively rare ganglion cells and myxomatous stroma. Our study also found scattered ganglion cells within stroma in 40% of the patients, hence we would like to suggest careful evaluation of ganglion cells in solid tumor masses that occur in asymptomatic patients and are located at the posterior mediastinum, retroperitoneum or neck. The number of nuclei ranged from one to three with no atypia. Actually, the definite number of nuclei has not been defined, thus we would like to propose the expectation of benign ganglion cells moreover. According to the blood vessel patterns, all cases did not show proliferation. Thus it represented the hypovascular tumor that corresponds with previous reports of general features from ultrasono-

graphic studies presented as hypoechoic lesions. Furthermore, the hyalinization of blood vessel walls that are often seen in schwannoma was definitely not demonstrated in our cases. The brown-black pigment demonstrated within cytoplasm had tinctorial properties of dermal melanin (Fontana-positive), however, the ultrastructural study could not exhibit the regular subunit of melanosome but consisted of lysosomal structure with myelinelike figures. It represented the catecholamine products that underwent auto-oxidation to a melanin-like substance (neuromelanin).^(19,20,21)

The neurofilament protein, the intermediate filament, has been identified within neuroblastoma, ganglioneuroma, and paraganglioma.^(22,23) The S-100 protein has been readily demonstrated in many cells, including Schwann cells. The neurofilament was reactive in neuronal cells which was able to identify the ganglionic differentiation.^(24,25) The S-100 protein is positive in portions of spindle cells that represent the Schwann cells⁽²⁶⁾

The malignant counterpart of this tumor has also been reported. Some occurred in de novo ganglioneuroma and others as a result of maturation. There is a recent report that ganglioneuroma developed malignant transformation about 10 years after surgery. This was explained as probably the dedifferentiating potential of ganglion cells, or the presence of a long-term quiescent form of neuroblastoma.⁽²⁹⁾ Reports of other examples of malignant peripheral nerve sheath tumors that arose in a de novo ganglioneuroma and developed from the maturation of neuroblastoma are now increasing.⁽²⁸⁻³²⁾

Conclusions

This study focused on ganglioneuroma that are normally curable. Even though it is relatively rare lesion and some clinicopathologic features have not been described, we would like to propose the full clinicopathologic features which focus on the histomorphology as being helpful when this tumor is encounter. This tumor, which arises from sympathetic chains, especially the posterior mediastinum and peritoneum in adults, should be recognized and given consideration. The differential diagnosis ranges from benign to malignant. Thus careful gross inspection and thorough sampling of the lesion is the most important tool to make a definite diagnosis. The immunohistochemistry study for neural markers was also employed. However, the positive result assists or supports the diagnosis since it is also reactive in the group of neural tumors of differential diagnosis.

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