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Clinicopathologic and Immunohistochemical Analysis of Parapharyngeal Ganglioneuroma: A Case Study and review

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Abstract

Ganglioneuromas is usually arising in the posterior mediastinum and the retroperitoneum, but parapharyngeal ganglioneuromas are so rare that only 11 cases have been reported in the literature. We report a case of a 26-year-old woman with a parapharyngeal ganglioneuroma. who presented with a history of a indolent right cervical mass for 24 years. Computed tomography scan suggested that the mass was located between the carotid sheath and cervical vertebrae. The mass was completely resected under general anesthesia. It was a well-circumscribed, grayish-white and fish-shaped mass, 3.9 × 1.3 × 5.2 cm in size. Histological examination gave the diagnosis of ganglioneuroma, which was also confirmed by immunohistochemical stainings for Neuron-specific enolase and S-100, which presented intensive positive expressions. Dysphagia and Horner's symptoms improved after surgery. There was no recurrence or metastases after 12 months.

Keywords: Ganglioneuromas, Parapharyngeal, Clinicopathologic, Immunohistochemical, Dysphagia, Horner's symptoms

1. INTRODUCTION

Ganglioneuromas (GNs) are rare, benign tumors of primordial neural crest tissue that, originate from the sympathetic chain. GNs are most frequently diagnosed in patients between the ages of 10 and 29 years and are most commonly located in the posterior mediastinum (41%), followed by the retroperitoneum (37%), adrenal gland (21%), and neck (8%)(Cavanaugh DA, et al. 2010). GNs are rarely located in the parapharyngeal space, and complete surgical resection is considered curative. The authors present a case of retropharyngeal GN; the clinical presentation, radiographic findings, treatment and postoperative complications are discussed.

2. CASE PRESENTATION

The patient, a 26-year-old female, presented to an out-patient clinic in August 2018with chief complaints of indolent swelling on the right side of the necks, difficulty swallowing, and difficulty breathing while

lying down. This swelling had developed 24 years prior to admission. The swelling was first noted when the patient was 2 years-old, following a traumatic injury to her neck, and thereafter gradually increased in size. There was no other significant clinical history. On clinical examination, a mass was present in the upper right cervical region; it was firm, non-tender, and measured 6.0 × 7.0 cm in size. The overlying skin that was elastic in consistency showed stretched-out, prominent veins. General physical examination revealed normal vital signs and an essentially normal systemic examination. Magnetic resonance (MR) imaging of the neck detected a densely enhancing soft tissue mass between the carotid sheath and cervical vertebrae. The mass measured 3.9 × 1.3 × 5.2 cm and was located outside of the hyoid, which was being pressed by the mass. The carotid sheath, which was under pressure from the mass, was displaced to the front and outward, adjacent to lateral wall of the pharynx. The mass had medium signal intensity on T1-weighted images (Figures 1A, 1B), heterogeneous, high signal intensity on T2-weighted images and fat saturation (Figure 2A, 2B). A complete resection of the lesion was performed under general anesthesia. The lesion consisted of a rubbery nodule; the cut section of the nodule was grayish-white, soft, and fish-shaped (Figure 3). Microscopically, hematoxylin and eosin stains showed mature spindle Schwann cells and scattered ganglion cells in myxoid stroma (Figures 4A, 4B). No immature elements were noted. Immunostaining showed that the spindled Schwann cells were strongly reactive towards S-100 (Figure 5A, 5B) and that the ganglion cells were strongly reactive towards neuron-specific enolase (Figures 6A, 6B), which confirmed the tumor neurogenic origin. The histology confirmed the diagnosis of ganglioneuroma. After surgery, the patient presented with right palpebral ptosis and anisocoria with homolateral mydriasis typical of Horner's syndrome. The surgical incision healed well. There was no recurrence or metastases 12 months after surgery. Dysphagia and Horner's symptoms improved.

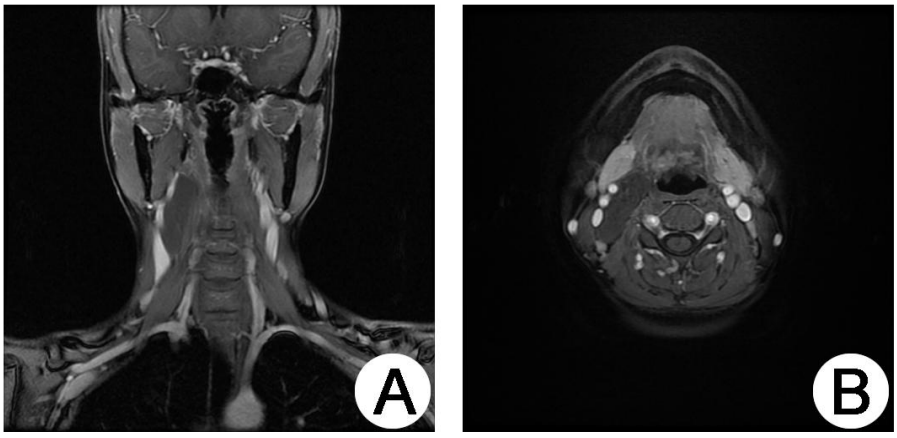

Fig. 1. Magnetic resonance imaging showing the isodense lesion which is uniformly enhancing with the surrounding vessels in the parapharyngeal on T1-WI. (A) coronal view; (B) axial view.

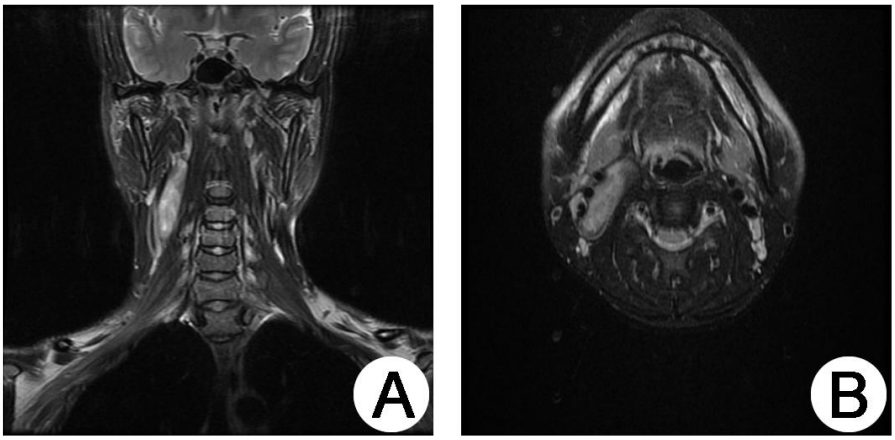

Fig. 2. Magnetic resonance imaging showing a hyperdense lesion in the right parapharyngeal as compared to the surrounding muscle with a variable signal and distinct margins on T2-WIFS. (A)coronal view; (B) axial view.

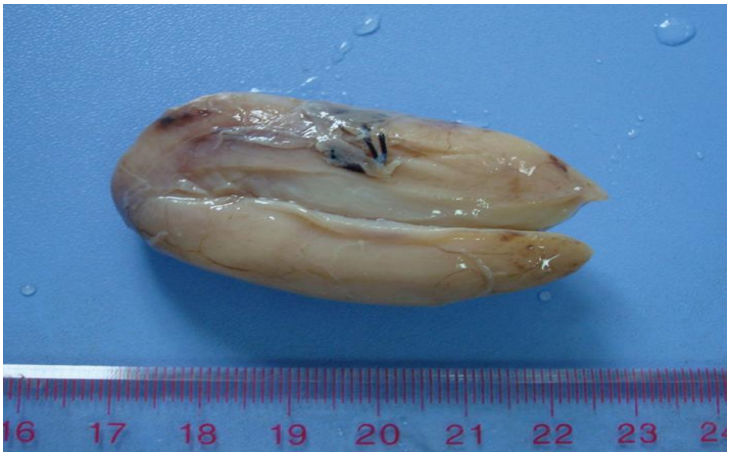

Fig. 3. Tumor mass exposed after longitudinal section.

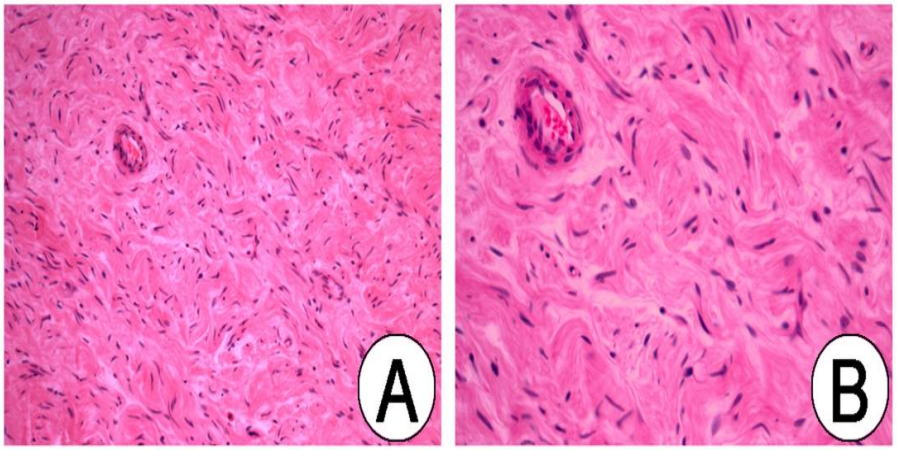

Fig. 4. Mature spindle Schwann cells with scattered ganglion cells in myxoid stroma. (A) haematoxylin and eosin, original magnification × 40. (B) haematoxylin and eosin, original magnification × 100.

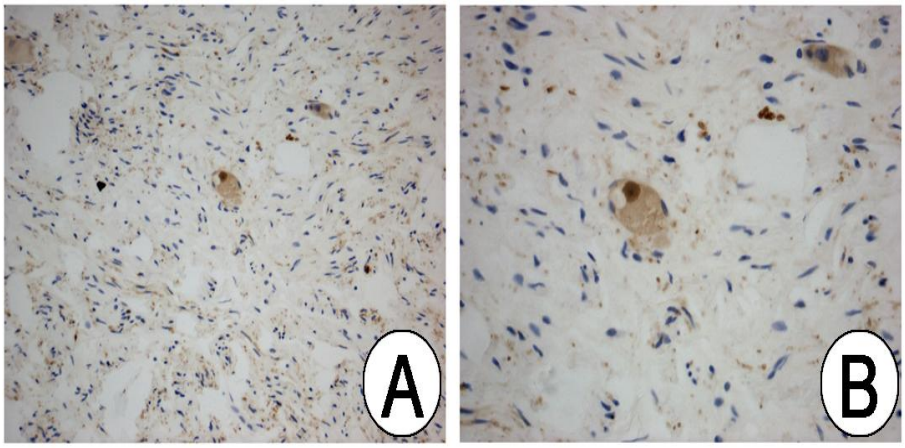

Fig. 5. S-100 positivity in both spindl cells and ganglion cells. (A) S-100, original magnification × 100. (B) S-100, original magnification × 200.

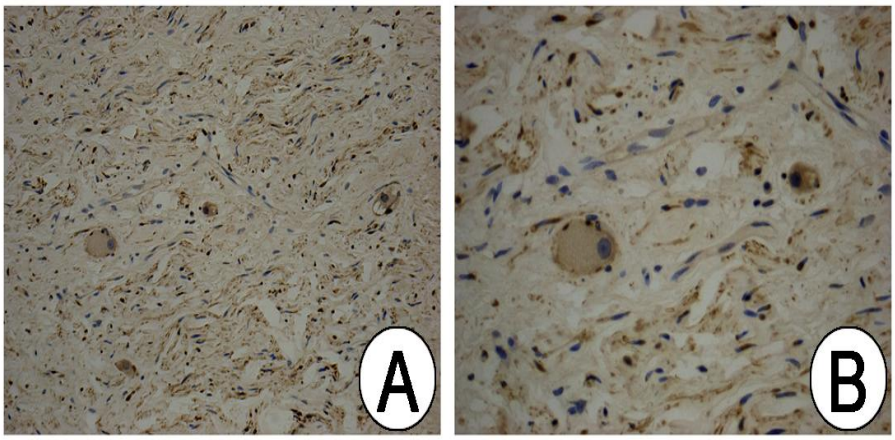

Fig. 6. Ganglion cells showing strong reactivity for neurone specific enolase. (A) NSE, original magnification × 100. (B) NSE, original magnification × 200.

3. DISCUSSION

Neuroblastoma, ganglioneuroblastoma, and GNs are tumors of the sympathetic nervous system that arise from neural crest cells. They arise wherever sympathetic tissue exists and can be found in the neck, posterior mediastinum, adrenal gland, retroperitoneum, and pelvis. The three tumors are considered different stages of cellular and extracellular maturation: for example, a sympathetic neuroblastoma may be the precursor of a ganglioneuroma (Cushing and Wolbach, 1927). GN is the most mature form of neuroblastoma. GN is composed of gangliocytes and mature stroma. Primitive neuroblasts with malignant potential were not observed in our patient. Some authors have reported malignant neuroblastomas transform into benign GNs spontaneously or after radiotherapy (Cushing and Wolbach, 1927; Shimada, et al. 1999).

GNs of parapharyngeal lesions are rare that only 8 cases have been reported in the literature (Albonico, etal. 2001;Danosos, et al. 1980;DIBRINO and GRIGI, 1964;Hazarika, et al. 1993;Kaufman, et al. 2001;PAROLARI, 1961;Pop, et al. 1976;Sinha, et al. 2011), compared with the appearance of salivary gland tumors (40%-

50%), which are the most common, with neurogenic tumors (17%-25%) and paragangliomas (10%-15%) following closely behind(Ralli, et al. 2018). GNs arising in the parapharyngeal space usually occur within the first months of life and can stay clinically latent for a long period. The signs and symptoms often present as swelling without other symptomology, but are usually related to the mass's effect. Geoerger reported that patients with a primary GN were significantly older than patients with a neuroblastoma. The median age at GN diagnosis was 79 months. The relatively late age at diagnosis in children is attributed to the tumors remaining asymptomatic. As in the reported case, the patient complained that this mass had developed 24 years prior to admission and presented with dysphagia and, positional dyspnea.

Pre-operative diagnosis of tumors is based on radiological detection of a lateral neck mass in the age-appropriate population. A parapharyngeal neurogenic tumor is diagnosed by the imaging appearance of the lesion, including its position, shape and internal architecture. It is difficult to differentiate between benign and malignant neurogenic tumors unless distant metastases are obesrved. However, most neurogenic tumors in adults are benign. CT and MR imaging characteristics of ganglioneuromas can lead to a specific diagnosis or contribute to further specifying the differential diagnosis. CT imaging shows a relatively hyperdense area, and punctate calcifications are observed. In MR imaging, GNs show a low signal on T1-weighted images and a high intensity signal on T2-weighted images. Several studies in the literature report that high, heterogeneous intensity on T2-weighted images correlates with GN(Majbar, et al. 2014). In our case, MR imaging demonstrated displacement of surrounding cervical structures with a high intensity signal on T2- weighted images and fat saturation and, a medium intensity signal on T1-weighted images.

Fine needle aspiration cytology (FNAC) is a cytologic examination and a pre-operative method in the diagnosis of cervical masses. The typical cytologic features include a mixture of spindle Schwann cells and randomly distributed single or clustered mature ganglion cells embedded in the fibromyxoid matrix (Koshy, et al. 2019). However, because a single sample is inadequate and is not representative, an extensive sampling is needed, requiration aspirating from multiple tumor sites. As a result, performing this process is complicated and unrealistic in the parapharyngeal space. Therefore, a correct diagnosis of GN can't be established and made reliably based on cytology alone. It is difficult to diagnose a parapharyngeal space GN radiologically and cytologically; therefore, GN requires tissue investigation for diagnosis by completely resecting the lesion, and performing hematoxylin and eosin (HE) stains and immunohistochemical stains of histopathology sections. Ganglion cells and Schwann cells in a loose myxoid stroma can been seen using HE stains. A wide range of well-characterized monoclonal antibodies are available to serve as reliable immunohistochemical tumor markers, including neuron-specific enolase (NSE), S-100 protein and neurofilament. The most sensitive immunohistochemical neuroendocrine markers in neuroblastic tumors are NSE and S-100 protein. NSE-positive cells might be useful in discriminating the neurogenic origin of GN. These positive cells have been found in mature ganglion cells and well-differentiated tumors. Moreover, S-100 proteins may help to determine degree the grade of tumor cell maturation, which is an important indicator of prognosis. The cytoplasm and nucleus can be colored. A greater number of mature tumor cells is indicative of a better prognosis. This

observation is in accordance with the findings of several investigators (Iwanaga, et al. 1989). Immunohistochemical stains (performed with the following monoclonal antibodies: neuron-specific enolase, neurofilament, and S-100) confirm the ganglioneuroma diagnosis and rule out other parapharyngeal lesions such as, schwannoma, neurofibroma, or branchial cleft cyst. In our case, the diagnosis of ganglioneuroma was confirmed histologically after complete surgical excision of the mass. The lesion consisted of a rubbery nodule; the nodule section was grayish-white, soft, and fish-shaped. Hematoxylin and eosin stains of the histopathology section showed predominantly mature spindle Schwann cells with scattered ganglion cells in myxoid stroma. Immunostaining showed that the spindled Schwann cells were strongly reactive toward S-100, which confirmed benign nature of the tumor, and that the ganglion cells were strongly reactive toward neuron-specific enolase, which confirmed the tumor's neurogenic origin.

Although rare, ganglioneuromas should always be considered neuroblastomas. Neuroblastomas are highly malignant tumors and the most common extra-cranial solid tumor in childhood. It is difficult to differentiate between benign and malignant neurogenic tumors unless distant metastases are observed. The optimal treatment for neurogenic tumors in the parapharyngeal space is complete surgical removal when the tumors are localized with no evidence of distant metastasis in order to prevent further growth and compression of adjacent structures. However, some authors have reported no tumor progression or recurrence was discovered after a long follow-up period, even with incomplete surgical removal (Gary, et al. 2010).

Because this tumor originated from the sympathetic chain, surgical excision resulted in post-operative Horner's syndrome. The patient developed Horner's syndrome secondary to surgical excision of the cervical ganglioneuroma. Surgical excision can offer definitive therapy but may result in an iatrogenic Horner's syndrome for which the patients should be counseled prior to operative intervention (Albuquerque, et al. 2013). In this case, our patient's systemic symptoms were improving after twelve months. To conclude, irrespective of the site and age of the patient, a pre-operative diagnosis of GN should be based on cytology and radiological detection. The optimal treatment for parapharyngeal ganglioneuroma is complete surgical removal to prevent further growth and compression of adjacent structures. Tissue investigation for further diagnosis via lesion resection can determine whether chemotherapy is needed.

CONFLICTS OF INTEREST

No potential conflict of interest relevant to this article was reported.

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REFERENCES

1. Albonico, G., Pellegrino, G., Maisano, M., Kardon, D.E., 2001. Ganglioneuroma of parapharyngeal region. Arch Pathol Lab Med. 125, 1217-1218
2. Albuquerque, B.S., Farias, T.P., Dias, F.L., Torman, D., 2013. Surgical management of parapharyngeal ganglioneuroma: case report and review of the literature. ORL J OtorhinolaryngolRelat Spec. 75, 240-244
3. Cavanaugh, D.A., Jawahar, A., Harper, J., McLaren, B.K., Wooten, T., Kerr, E.J., Nunley, P.D., 2010. Cervical ganglioneuroma in an adult

man: case report and literature review of a rare occurrence. J La State Med Soc. 162, 218-221

4. Cushing, H., Wolbach, S.B., 1927. The Transformation of a Malignant Paravertebral Sympathicoblastoma into a Benign Ganglioneuroma. Am J Pathol. 3, 203-216.7
5. Danosos, D.A., Santos, V.B., Ruffy, M.L., Polisar, I.A., Torno, R., 1980. Ganglioneuroma of the parapharyngeal space. Bull N Y Acad Med. 56, 616-622
6. DIBRINO, M., GRIGI, M., 1964. PARAPHARYNGEAL GANGLIONEUROMA. ANATOMO-CLINICAL CONSIDERATIONS ON A CASE OF RARE OBSERVATION. Boll Mal Orecch Gola Naso. 82, 401-411
7. Gary, C., Robertson, H., Ruiz, B., Zuzukin, V., Walvekar, R.R., 2010. Retropharyngeal ganglioneuroma presenting with neck stiffness: report of a case and review of the literature. Laryngoscope. 120 Suppl 4, S148
8. Hazarika, D., Naresh, K.N., Rao, C.R., Gowda, B.M., 1993. Parapharyngeal ganglioneuroma. Report of a case diagnosed by fine needle aspiration. Acta Cytol. 37, 552-554
9. Iwanaga, T., Takahashi, Y., Fujita, T., 1989. Immunohistochemistry of neuron-specific and glia-specific proteins. Arch HistolCytol. 52 Suppl, 13-24
10. Kaufman, M.R., Rhee, J.S., Fliegelman, L.J., Costantino, P.D., 2001. Ganglioneuroma of the parapharyngeal space in a pediatric patient. Otolaryngol Head Neck Surg. 124, 702-704
11. Koshy, A., Jain, R., Srinivasan, R., Bhatia, P., Kakkar, N., Rajwanshi, A., Gupta, N., Dey, P., Trehan, A., Bansal, D., 2019. Cytopathological spectrum of peripheral neuroblastictumours in fine needle aspiration cytology and categorisation as per International Neuroblastoma Pathology Classification. Cytopathology. 30, 634-643
12. Majbar, A.M., Elmouhadi, S., Elaloui, M., Raiss, M., Sabbah, F., Hrora, A., Ahallat, M., 2014. Imaging features of adrenal ganglioneuroma: a case report. BMC Res Notes. 7, 791
13. PAROLARI, P., 1961. Parapharyngeal ganglioneuroma (casuistic contribution and anatomo-clinical considerations). Arch Ital OtolRinolLaringol. 72, 238-251
14. Pop, V., Togănel, I., Draşoveanu, C., Schuller, L., 1976. Voluminous parapharyngeal tumor (ganglioneuroma). Rev Chir Oncol Radiol O R L OftalmolStomatolOtorinolaringol. 21, 211-216
15. Ralli, M., de Vincentiis M, Greco, A., 2018. Large parapharyngeal mass: a challenging differential diagnosis. Lancet Oncol. 19, e181
16. Shimada, H., Ambros, I.M., Dehner, L.P., Hata, J., Joshi, V.V., Roald, B., 1999. Terminology and morphologic criteria of neuroblastic tumors: recommendations by the International Neuroblastoma Pathology Committee. Cancer. 86, 349-363
17. Sinha, P., Sharma, S.C., Agarwal, S., Gupta, S.D., 2011. Parapharyngeal ganglioneuroma with neurofibromatosis: an unusual presentation. Ann OtolRhinolLaryngol. 120, 769-774