Cervical ganglioneuroma
A case report and review of the literature
Tianni Xu, PhD, Wei Zhu, MD∗, Ping Wang, MD

Abstract
Rationale: Ganglioneuromas are benign neoplasm of neuroblastic origin which arise from central or peripheral parts of the autonomic nervous system. They are normally found at posterior mediastinum, retroperitoneum, and the adrenal gland but ganglioneuromas are rarely found in the cervical region.

Patient concerns: A 12-year-old boy was admitted with a left-lateral neck mass slow growing over a 7-days duration. The tumor was painless and was not associated with any systemic or compression-related symptoms. No symptoms of Horner’s syndrome, including ptosis, myosis, ipsilateral facial anhidrosis, and flushing, were observed. Laboratory routine tests were within normal limits, and magnetic resonance imaging demonstrated a solid and well-circumscribed mass in the carotid space.

Diagnosis: Due to the patient’s symptoms, laboratory test results together with radiographic investigation findings, the 12 years old boy was diagnosed with cervical ganglioneuroma combined with tetralogy of Fallot.

Interventions: Surgical excision.

Outcomes: The postoperative period was uneventful with the exception of Horner’s syndrome on the left side in short period, and it was finally resolved after 8 months recovery. The patient is now in stable condition after operation, with improvement in symptoms during follow-up recovery.

Lessons: Ganglioneuromas should be accounted as the differential diagnosis of pediatric soft tissue tumors of the head and neck. The diagnosis for ganglioneuromas in cervical region can only be ascertained with postoperative pathologic examination, and excision is considered as the only effective treatment modality known so far which may cause Horner’s syndrome at times. However, patients have a favorable prognosis without recurrence overall.

Abbreviations: CT = computed tomography, GN = ganglioneuromas, HE = hematoxylin and eosin, MRI = magnetic resonance imaging.

Keywords: ganglioneuroma, Horner’s syndrome, peripheral neuroblastic tumors, surgical complications, tetralogy of Fallot

1. Introduction
Ganglioneuromas (GN) are benign, neoplasm of neuroblastic origin which arise from central or peripheral parts of the autonomic nervous system.[1] Besides, common sites such as posterior mediastinum, retroperitoneum, and the adrenal gland, GN are rarely demonstrated in the cervical region.[2] As reported in literatures, only 1% to 5% of the patients present with neck masses.[3] Nowadays, surgical excision is considered as a suitable treatment for this benign tumor, given that it is challenging and risky at times. Here, we reported a cervical ganglioneuroma case of a 12-year-old boy combined with tetralogy of Fallot which presented as a slow growing mass with no apparent symptoms, and this case has not been reported from reviewed cases of cervical ganglioneuroma that have been published. Additionally, we elucidated the Horner’s syndrome as it was related to the primary location of the tumor and the completeness of surgical excision. The patient’s guardians consented to the publication of the study. This case report was approved by the ethics committee of First Hospital of Jilin University (2018-344), Changchun, China, and the informed consent form was signed by patient’s parent.

2. Case report
A 12-year-old boy was admitted with a left-lateral neck mass slow growing over a 7-days duration. The child with tetralogy of Fallot underwent cardiac surgery at 1 year old. Postoperatively, he had no complications. The tumor was painless and was not associated with any systemic or compression-related symptoms. No symptoms of Horner’s syndrome, including ptosis, myosis, ipsilateral facial anhidrosis, and flushing, were observed. In palpation, the mass was firm, solid, non-tender, nonfluctuant. Moreover, it was not moving with deglution or protrusion of the tongue. The GN was measured 4.0 × 2.0 cm in size, and the
overlying skin was normal. Routine laboratory tests were within normal limits. Ultrasonography showed a mass located near left lobe of the thyroid gland which displayed solid, hypoechoic, and well-encapsulated characteristic. The magnetic resonance imaging (MRI) identified 1 ovoid mass located in the left carotid space region from C4 to C6 level and measured 4.6 × 1.7 × 1.6 cm (Fig. 1). MRI showed low-signal intensity on T1WI. T2WI showed higher signal intensity. Enhanced T1WI showed inhomogeneous predominantly marked enhancement.

After preliminary investigations, the child accepted operation. Complete surgical excision of the mass was performed under general anesthesia through a transcervical approach. In terms of gross examination, a single, ovoid and well-circumscribed tumor was found beneath the sternocleidomastoid muscle in the left-lateral neck. The internal jugular vein and the common carotid artery were observed to be displaced laterally due to the mass. With careful sharp and blunt dissection, the anterior, posterior, and medial margins of the mass were dissected from the contents of the neck. Due to technique limitation for separation of its attached nerve, the completeness of surgical excision could not be avoided. The operation is success, and the postoperative period was uneventful with the exception of immediate observed Horner’s syndrome on the left side in short period, and it was finally resolved after 8 months recovery. No signs of recurrence were noticed during an 8-months follow-up observation.

Gross examination revealed an oval, encapsulated 4.0 × 2.0 × 1.5 cm in diameter mass with a yellowish-white cut surface (Fig. 2). Microscopically, the tumor was composed of proliferation of ganglion cells together with tipper end spindle cells in a fibrillary background with no mitosis. Additionally, several immature ganglion cells were found in part of the tumor (Fig. 3). Positive staining was observed with S-100, neurofilament, neuron-specific enolase in Fig. 4. A Ki-67 was expressed rarely. A pathological diagnosis of GN was established.

3. Discussion

GN are slow-growing, well-differentiated tumors of the autonomic nervous system, and they are normally asymptomatic. Clinical manifestations are local symptoms of obstruction but some patients may present diarrhea, hypertension, virilization, and myasthenia gravis. GN are typically sited in the thoracic cavity (60%–80%, posterior mediastinum), the abdominal cavity (10%–15%, adrenal gland, retroperitoneum, pelvic, sacral and coccygeal sympathetic ganglia, and the organ of Zuckerkandl), and the cervical region (5%). Other less common locations
are the middle ear, the parapharynx, the skin, the orbital space, and the gastrointestinal tract.\(^{7-9}\)

Cases of primary brain tumor associated with arteriovenous malformation have been reported. No previous case of tetralogy of Fallot together combined with ganglioneuroma has been published. Tetralogy of Fallot is normally associated with some other syndromes, such as Di George syndrome and velocardiofacial syndrome. More cases investigation and molecular confirmation will help us to determine whether tetralogy of Fallot associated with ganglioneuroma may be regarded as a family of diseases or not in the future. Additionally, we reviewed cases of cervical GN that were reported in references for the period from inception to February 2019. The criteria of included studies were categorized as follows:

1. papers that were associated with cervical GN.

The exclusion criteria of studies were:

1. GN located in the other site;
2. neurofibromatosis;
3. irrelevant to our topic;
4. duplicate data.

A total of 21 papers and 27 cases were included.\(^{10-30}\) The clinical data were summarized in Table 1. All of the tumors related reports were with no metabolically active. The tentative conclusion is that pediatric group was mainly affected based on data study, although they could be found in adults. Seven cases of Horner’s syndrome appear in these documents. One case of a mild left palpebral ptosis was observed. One child with postoperative myosis was indicated. One patient with left vocal cord palsy was noticed. Symptoms of Horner’s syndrome may ensue from the injury of the cervical sympathetic chain which is the most frequent structure of origin in the neck. Overall, patients with GN had a favorable prognosis based on the reported cases. The recurrence rate was 0 in the follow-ups observation.

Imageology is a great aid for preoperative surgical plan. Computed tomography (CT) and MRI provide valuable information on the size, location, composition of the mass, and its relationship to adjacent significant structures. We found that the characteristic CT and MR features of all demonstrated masses were:

1. a well-defined, oval mass;
2. low or intermediate CT attenuation;
3. markedly high intensity on T2WI, which were comparable to the other published studies.\(^{10-30}\)

Recent studies have shown that positron emission tomography could be meaningful for early diagnosis and helpful for surgical

---

**Figure 3.** Histopathology of ganglioneuroma. HE stain showing mature ganglion cells and schwannian stroma. (A) Original magnification x200. (B) Original magnification x400. HE = hematoxylin and eosin.

**Figure 4.** Immunohistochemical profiles of ganglioneuroma. Immunoperoxidase stains for S-100 protein and NSE. (A) Immunohistochemical staining is positive for S-100 protein. (B) Ganglion cells in ganglioneuroma show positive staining for NSE (original magnification x100). NSE = neuron-specific enolase.
strategy. Due to the sample scarcity of GN and the lack of specific signs and symptoms, it is often hard to confirm before pathological examination. Macroscopically, GN may frequently be circumscribed. Microscopically, tumors are composed of intersecting bundles of spindle cells, loose myxoid stroma, and dysplastic ganglion cells. Overall, the most common characteristic feature is the presence of mature ganglion cells. Ganglion cells are positive for S-100 protein in most cases. Immunohistochemistry can be used as reference in ascertaining the origin of the tumor and the differential diagnosis, but it is not essential.

For most cases, excision is regarded as the most effective treatment modality for GN. In rare cases, excision of the cervical GN could arise postoperative Horner’s syndrome. The syndrome results from disruption of the sympathetic innervation at different levels. The prognosis of Horner’s syndrome will depend on the mechanism of injury. If the lesion is indirect there will often be a spontaneous recovery. However, our review cases of complete section, the symptoms persist which is indirect there will often be a spontaneous recovery. However, our review cases of complete section, the symptoms persist which is indirect there will often be a spontaneous recovery. However, our review cases of complete section, the symptoms persist which is indirect there will often be a spontaneous recovery.

Table 1
Clinicalopathologic features of cervical ganglioneuromas in the literature.

| Case          | Age/gender | Size, cm | Side and location       | Treatment          | Complication       | Follow-up, mo |
|---------------|------------|----------|-------------------------|--------------------|--------------------|---------------|
| Friedlander (2002) | 28/M       | 4.0 cm   | Carotid space/left      | Excision           | NA                 | NA            |
| Leonardis (2003) | 50/M       | 10.0 cm  | Carotid space/right     | Excision           | None               | NA            |
| González-Aguado (2012) | 41/F | 5.0 cm   | Upper neck/right        | Excision           | None               | NED (12)      |
| De Bernardi (2008) | 2/M        | 5.0 cm   | Neck/right              | Excision           | Homer’s syndrome   | NA            |
| Cavanaugh (2010) | 41/M       | 4.1 cm   | Paravertebral region/right | Excision           | Myosis in the right eye | NED (18) |
| Baisakhiya (2008) | 22/M       | 3.0 cm   | Neck/right              | Excision           | Homer’s syndrome   | NA            |
| Ramani (2013) | 25/F        | 4.7 cm   | Carotid space/right     | Excision           | Homer’s syndrome   | NA            |
| Cavanaugh (2010) | 41/M       | NA       | Carotid space/left      | Excision           | Homer’s syndrome   | NA            |
| Colte (2011)  | 8/F         | 5.0 cm   | Neck/left               | Excision           | NA                 | NA            |
| Mahajan (2011) | 7/M         | 7.0 cm   | Upper neck/left         | Excision           | NA                 | NA            |
| Ma (2012)     | 4/F         | 10.4 cm  | Prevertebral region/right | Excision           | None               | NED (96)      |
| González-Aguado (2012) | 41/F | NA       | Neck/right              | Excision           | Homer’s syndrome   | NA            |
| Ramani (2013) | 5/F         | 5.0 cm   | Below angle of mandible/left | Excision           | None               | NA            |
| Bhadare (2014) | 11/F        | 10.5 cm  | Sternomediastinal muscle/right | Excision           | None               | NA            |
| Jabbour (2015) | 53/M        | 3.2 cm   | Submandibular/left      | Excision           | None               | NED (10)      |
| Spinelli (2015) | 26/F       | NA       | Neck                    | Excision           | None               | NED (96)      |
| Dutta (2016)  | 1.5/M       | 3.0 cm   | Upper neck/left         | Excision           | None               | NED (84)      |
| Dalma (2016)  | 25/M        | 5.0 cm   | Carotid space/left      | Excision           | left vocal cord palsy | NA            |
| Paraskevopoulos (2017) | 17/F | 4.0 cm   | Paravertebral region/left | Excision           | Homer’s syndrome   | NA            |
| Kifu (2017)   | 7/F         | 5.0 cm   | Paravertebral region/left | Excision           | Homer’s syndrome   | NA            |
| Helal (2010)  | 10/F        | 15.0 cm  | Sternomediastinal muscle/right | Excision           | None               | NED (12)      |
| Our case      | 12/M        | 4.6 cm   | Carotid space/left      | Excision           | Homer’s syndrome   | NED (8)       |

F = female, M = male, NA = not application, NED = no evidence of disease.

Author contributions
Conceptualization: Tianni Xu.
Data curation: Tianni Xu, Wei Zhu.
Investigation: Wei Zhu, Ping Wang.
Methodology: Tianni Xu.
Resources: Tianni Xu.
Supervision: Wei Zhu, Ping Wang.
Writing – original draft: Tianni Xu.
Writing – review and editing: Wei Zhu, Ping Wang.

References
[1] Lamichhane N, Dhakal HP. Ganglioneuroma of pelvis – an unique presentation in a young man. Nepal Med Coll J 2006;8:288–91.
[2] Weiss SW, Goldblum JR, Weiss SW, Goldblum JR. Weiss SW, Goldblum JR. Ewings sarcoma: PNET tumor family and related lesions. Enzinger and Weiss’s soft tissue tumors 5th ed. Philadelphia, USA: Mosby Elsevier; 2008;945–87.
[3] Leeson MC, Hite M. Ganglioneuroma of the sacrum. Clin Orthop Relat Res 1989;246:102–3.
[4] Kaufman MK, Reeve JS, Fiegelman LJ, et al. Ganglioneuroma of the parapharyngeal space in a pediatric patient. Otolaryngol Head Neck Surg 2001;124:702–4.
[5] Albionico G, Pellegrino G, Maisano M, et al. Ganglioneuroma of parapharyngeal region. Arch Pathol Lab Med 2001;125:1217–78.
[6] Calitano L, Zupi A, Mangone GM, et al. Cervical ganglioneuroma report of a case. Otolaryngol Head Neck Surg 2001;124:113–6.
[7] Cannon TC, Brown HH, Hughes BM, et al. Orbital ganglioneuroma in a patient with chronic progressive proptosis. Arch Ophthalmol 2004;122:1712–4.
[8] Ozluoglu LN, Yilmaz I, Cagici CA, et al. Ganglioneuroma of the internal auditory canal: a case report. Audiol Neurotol 2007;2:160–4.
[9] Wallace CA, Hallman JR, Sangueza OP. Primary cutaneous ganglioneuroma: a report of two cases and literature review. Am J Dermatopathol 2003;25:239-42.

[10] Friedlander PL, Hunt JP, Palacios E. Ganglioneuroma of the neck. Ear Nose Throat J 2002;81:435.

[11] Leonardi M, Sperb D, Alster C, et al. Ganglioneuroma of the neck, masquerading as a goiter. EJSO 2003;29:929-30.

[12] Cannady SB, Chung BJ, Hirose K, et al. Surgical management of cervical ganglioneuromas in children. Int J Pediatr Otorhinolaryngol 2005;70:287-94.

[13] Zebung Z, Jianwei S, Yan C, et al. Clinicopathological characteristics of neck ganglioneuroma. Oral Med Pathol 2008;12:131-4.

[14] Baisakhiya NK, Mukundan S. Ganglioneuroma of the neck. J Pak Med Assoc 2008;58:699-701.

[15] De Bernardi B, Gambini C, Haupt R, et al. Retrospective study of childhood ganglioneuroma. J Clin Oncol 2008;26:1710-6.

[16] Pucci A, Pucci E, Santini F, et al. A ganglioneuroma with features of a thyroid nodule: intense pain on fine needle biopsy as a diagnostic clue. Thyroid 2009;19:201-4.

[17] Cavanaugh DA, Jawahar A, Harper J, et al. Cervical ganglioneuroma in an adult man: case report and literature review of a rare occurrence. J La State Med Soc 2010;162:218-21.

[18] Kolte SS. Ganglioneuroma presenting as a neck mass diagnosed by fine needle aspiration cytology. Cytopathology 2011;22:203-6.

[19] Mahajan N, Aggarwal S, Khurana N, et al. Ganglioneuroma in the neck masquerading as a benign mesenchymal lesion on cytology: a morphological mimic. Cytopathology 2013;24:65-7.

[20] Ma J, Liang L, Liu H. Multiple cervical ganglioneuroma: a case report and review of the literature. Oncol Lett 2012;4:509-12.

[21] González-Aguado R, Morales-Angulo C, Obeso-Agüera S, et al. Horner’s syndrome after neck surgery. Acta Otorrinolaringol 2012;63:299-302.

[22] Ramani M, Radhika KOH, Ramesh RK, et al. An interesting case of differentiated neuroblasto-ganglioneuroma of the neck in a 5 year old female child. JEMS 2013;2:4298-301.

[23] Bhadarge PS, Poffet SV. Aspiration cytology in the preoperative diagnosis of ganglioneuroma presenting as a neck mass. J Cytol 2014;31:57-8.

[24] Jabbour MN, Zaatari GS, Salem Z, et al. Cervical ganglioneuroma in collision with a metastatic undifferentiated carcinoma. J Oral Maxillofac Pathol 2015;19:88-91.

[25] Spinelli C, Rossi L, Barretta A, et al. Incidental ganglioneuromas: a presentation of 14 surgical cases and literature review. J Endocrinol Invest 2015;38:347-54.

[26] Dutta HK. Cervical ganglioneuroma in a child. SM J Pediatr Surg 2016;2:1013-5.

[27] Dalmia D, Behera SK, Motiwala MA, et al. Cervical vagal nerve ganglioneuroma: a rare case report. Int J Otorhinolaryngol Head Neck Surg 2016;2:274-6.

[28] Paraskevopoulos K, Cheva A, Papaemmanuil S, et al. Synchronous ganglioneuroma and schwannoma mistaken for carotid body tumor. Case Rep Otolaryngol 2017;2017:7973034-5.

[29] Kifu W, Nigussie T. Ganglioneuroma presenting as a neck mass: a case report. Ethiop Med J 2017;55:69-71.

[30] Helal AA, Badawy R, Mahfouz M, et al. Adjacent cervical ganglioneuromas. J Pediatr Surg Case Rep 2018;34:7-9.