Clinical Case Report

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Cervical ganglioneuroma

A case report and review of the literature

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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, nontender, nonfluctuant. Moreover, it was not moving with deglutition or protrusion of the tongue. The GN was measured 4.0×2.0 cm in size, and the

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Written consent was obtained from the patient's parents for publication of this study.

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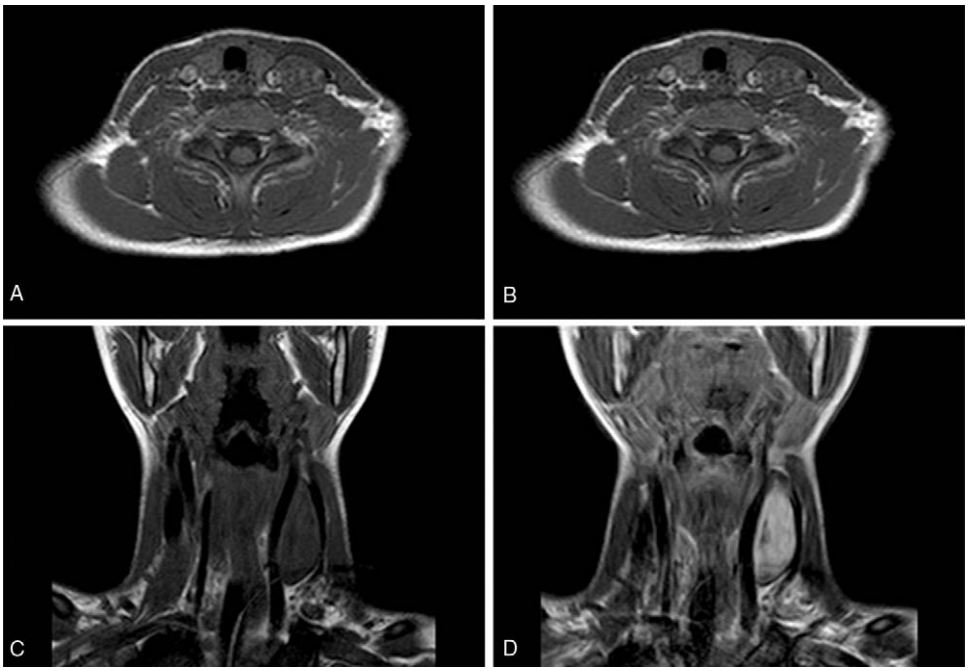

Figure 1. Contrast-enhanced MRI scans, (A) T1WI shows low-signal intensity less than muscle. (B) T2WI shows higher signal intensity than that of cerebrospinal fluid. (C) T1WI shows low-signal intensity less than muscle. (D) Enhanced T1WI shows inhomogeneous marked enhancement. MRI = magnetic resonance imaging.

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 $4.6 \times 1.7 \times 1.6$ 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.

Figure 2. Macroscopic appearance of the tumor.

Gross examination revealed an oval, encapsulated $4.0 \times 2.0 \times 1.5$ 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.[4] 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%).[5,6] Other less common locations

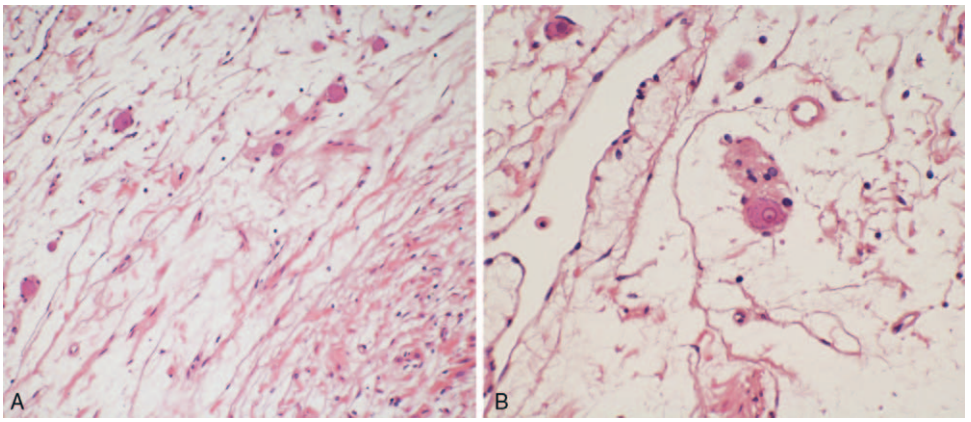

Figure 3. Hisopathology of ganglioneuroma. HE stain showing mature ganglion cells and schwannian stroma. (A) Original magnification ×200. (B) Original magnification ×400. HE=hematoxylin and eosin.

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

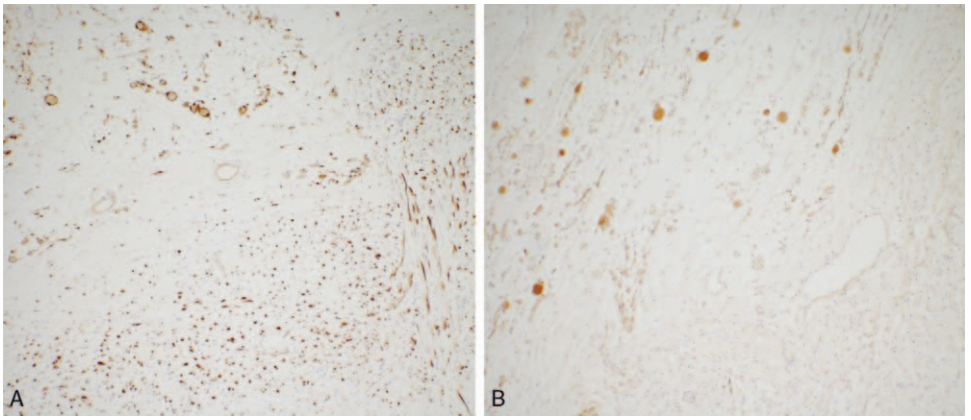

Figure 4. Immunohistochemical profiles of ganglioneuroma. Immunoperoxidase stains for S-100 protein and NSE. (A) Immunohistochemical staining is positive for S-100 protein. (B) Ganglion cells in ganglioneuroma show positive staining for NSE (original magnification ×100). NSE=neuron-specific enolase.

Table 1

Clinicopathologic features of cervical ganglioneuromas in the literature.

Case	Age/gender	Size, cm	Side and location	Treatment	Complication	Follow-up, mo
Friedlander (2002)[10]	28/M	4.0 × 2.0 × 4.3 cm	Carotid space/left	Excision	NA	NA
Leonardis (2003)[11]	50/M	10.0 × 6.8 × 4.0 cm.	Adjacent to the thyroid gland. /left	Excision	A mild left palpebral ptosis	NA
Cannady (2005)[12]	6/F	4.0 × 3.3 × 8.3 cm	Carotid space/right	Excision	None	NED (12)
	7	NA	Carotid space/right	Excision	None	NA
Zhang (2008)[13]	6/M	4.0 × 3.0 cm	Upper neck/left	Excision	None	NED
	62/F	8.0 × 4.0 cm	Upper neck/left	Excision	None	NED
	57/F	8.0 × 7.0 cm	Neck/right	Excision	None	NED
	9/M	4.0 × 2.0 cm	Neck/bilateral	Excision	None	NED
	53/F	4.0 × 4.0 cm	Upper neck/right	Excision	None	NED
Baisakhiya (2008)[14]	22/M	3.0 × 2.5 × 3.0 cm	Carotid space/left	Excision	Horner's syndrome	NA
De Bernardi (2008)[15]	2/M	NA	Neck	Excision	Horner's syndrome	NED (130)
Pucci (2009)[16]	25/F	4.7 × 2.2 × 2.2 cm	Carotid space/right	Excision	Horner's syndrome	NA
Cavanaugh (2010)[17]	41/M	NA	Carotid space/left	Excision	Horner's syndrome	NA
Kolte (2011)[18]	8/F	5.0 × 4.0 × 3.0 cm	Neck/left	Excision	NA	NA
Mahajan (2011)[19]	7/M	7.0 × 5.5 × 5.0 cm;	Upper neck/left	Excision	NA	NA
Ma (2012)[20]	4/F	10 × 6.4 × 5.7 cm	Prevertebral region/right	Excision	Myosis in the right eye	NED (18)
		4.1 × 2.6 × 5.0 cm	Paravertebral region/right			
González-Aguado (2012)[21]	41/F	NA	Neck/right	Excision	Horner's syndrome	NA
Ramani (2013)[22]	5/F	5.0 × 4.5 × 3.0 cm	Below angle of mandible/left	Excision	None	NA
Bhadarge (2014)[23]	11/F	10.0 × 5.5 × 4.0 cm	Sternocleidomastoid muscle region/left	Excision	None	NA
Jabbour (2015)[24]	53/M	3.2 × 2.5 × 2.2 cm	Submandibular/left	Excision	None	NED (10)
Spinelli (2015)[25]	26/F	NA	Neck	Excision	None	NED (96)
	37/F	NA	Neck	Excision	None	NED (84)
Dutta (2016)[26]	1.5/M	3.0 × 2.0 cm	Upper neck/left	Excision	NA	NA
Dalmia (2016)[27]	25/M	5.0 × 3.0 cm	Carotid space/left	Excision	left vocal cord palsy	NA
Paraskevopoulos (2017)[28]	17/F	4.0 × 2.5 × 1 cm	Carotid space/left	Excision	None	NA
Kiflu (2017)[29]	7/F	5.0 × 7.0 × 3.0 cm,	Paravertebral region/left	Excision	Horner's syndrome	NA
Helal (2018)[30]	10/F	15.0 × 6.0 × 5.0 cm	Sternocleidomastoid muscle region/right	Excision	None	NED (12)
Our case	12/M	4.6 × 1.7 × 1.6 cm	Carotid space/left	Excision	Horner's syndrome	NED (8)

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

strategy.[10–30] 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 useful 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.[10–30] In rare cases, excision of the cervical GN could arise postoperative Horner's syndrome.[14–17,21,29] 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 due to injury to cervical sympathetic ganglion.[21]

GN of the cervical region is an uncommon benign and neurogenic soft tissue tumor which often presents as a slow-growing neck mass. This tumor should be taken into special attention for children period in which may be shown asymptomatic, but present with long history of enlarging neck masses. Pathologic examination may be the only method to confirm the final diagnosis. Complete surgical excision is the most effective treatment, which may arise Horner's syndrome at times. In some cases, there will be a spontaneous recovery.

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.

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