Clinical Case Report

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Primary cervical ganglioneuroblastoma

A case report

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Abstract

Rationale: Ganglioneuroblastoma is usually located in the adrenal gland, retroperitoneal ganglia, or posterior mediastinum, but rarely occurs in the parapharyngeal space.

Patient concerns: A 4-year-old girl presented with complaint of progressive inspiratory dyspnea and dysphagia, accompanying left-side Horner's syndrome.

Diagnose: Computed tomography (CT) scan revealed a giant mass with irregular low density in left oropharyngeal and posterior pharyngeal wall. The left carotid artery sheath was pushed to the right. After enhancement, the central part of the mass was strengthened, and the surrounding bones structures appeard normal. Magnetic resonance imaging(MRI) showed a solid mass in the left parapharyngeal space displacing the left carotid sheath posteriorly and laterally. A ganglioneuroblastoma was diagnosed.

Intervations: The girl was treated by surgery.

Outcomes: The postoperative course was uneventful. There was no recurrence was observed during the 1-year follow-up.

Lessons: The primary cervical ganglioneuroblastoma is rare, we recommended the ganglioneuroblastoma should be considered in the differential diagnosis of a child presenting with a parapharyngeal space mass.

Abbreviations: CD15 = cluster of differentiation 15, CD30 = cluster of differentiation 30, CgA = chromogranin A, CT = computed tomography, MRI = magnetic resonance imaging, NSE = neuron-specific enolaseb, S-100 = soluble protein-100, Syn = synaptophysin.

Keywords: cervical mass, ganglioneuroblastoma, neuroblastoma, parapharyngeal space, pediatric

1. Introduction

Ganglioneuroblastoma is most commonly located in the adrenal gland (35%) and the retroperitoneal ganglia (30%), followed by the posterior mediastinum (20%) and pelvis (2–3%),[1] but is also rarely located in the cervical region. To our knowledge, there have been only 8 cervical ganglioneuroblastoma cases reported in the literature among Western countries.[2] In China to date, there has been no report of ganglioneuroblastoma arising from the cervical region. In this report, we present the case of a 4-year-old girl with cervical ganglioneuroblastoma.

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DL and JL contribute equally to this article.

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2. Case report

2.1. Clinical characteristics

A 4-year-old girl was admitted to our department with complaints of progressive inspiratory dyspnea and dysphagia. About 1 year prior, her symptoms were snoring and mouth-breathing during sleep. Nine months prior, ptosis of the left eye was found, and her left eye pupil was smaller compared with the right. She was diagnosed at that time with myasthenia gravis in the neurology department and neostigmine bromide was prescribed. However, after administering neostigmine bromide for more than 6 months, her symptoms did not remit. Six months prior to being seen in our clinic, the patient experienced progressive inspiratory dyspnea which aggravated by exercises and dysphagia. When she was admitted to our clinic on December 2016, she had a grade 1 laryngeal obstruction. Physical examination revealed that the pharyngeal cavity narrowing was caused by a giant mass located in the submucosa of the pharynx, which pushed the left wall of the oropharynx across the midline. Left Horner's syndrome was also detected at that time. No positive lymph node was found during neck palpation. A computed tomography (CT) scan revealed a giant mass of irregular low density located in the left oropharyngeal and posterior pharyngeal walls, and the left carotid artery sheath was pushed to the right. The size of the mass was about 4.0 cm × 2.4 cm × 5.0 cm. With enhancement, the central part of the mass was strengthened while the surrounding bone structures appeared normal (Fig. 1A–C). The lesion was also seen on a magnetic resonance imaging (MRI) scan (Fig. 1D–F), with imaging results showing no neck lymph node involvement. In view of the mass growth modality, its appearance, and the imaging characteristics, an initial diagnosis of parapharyngeal

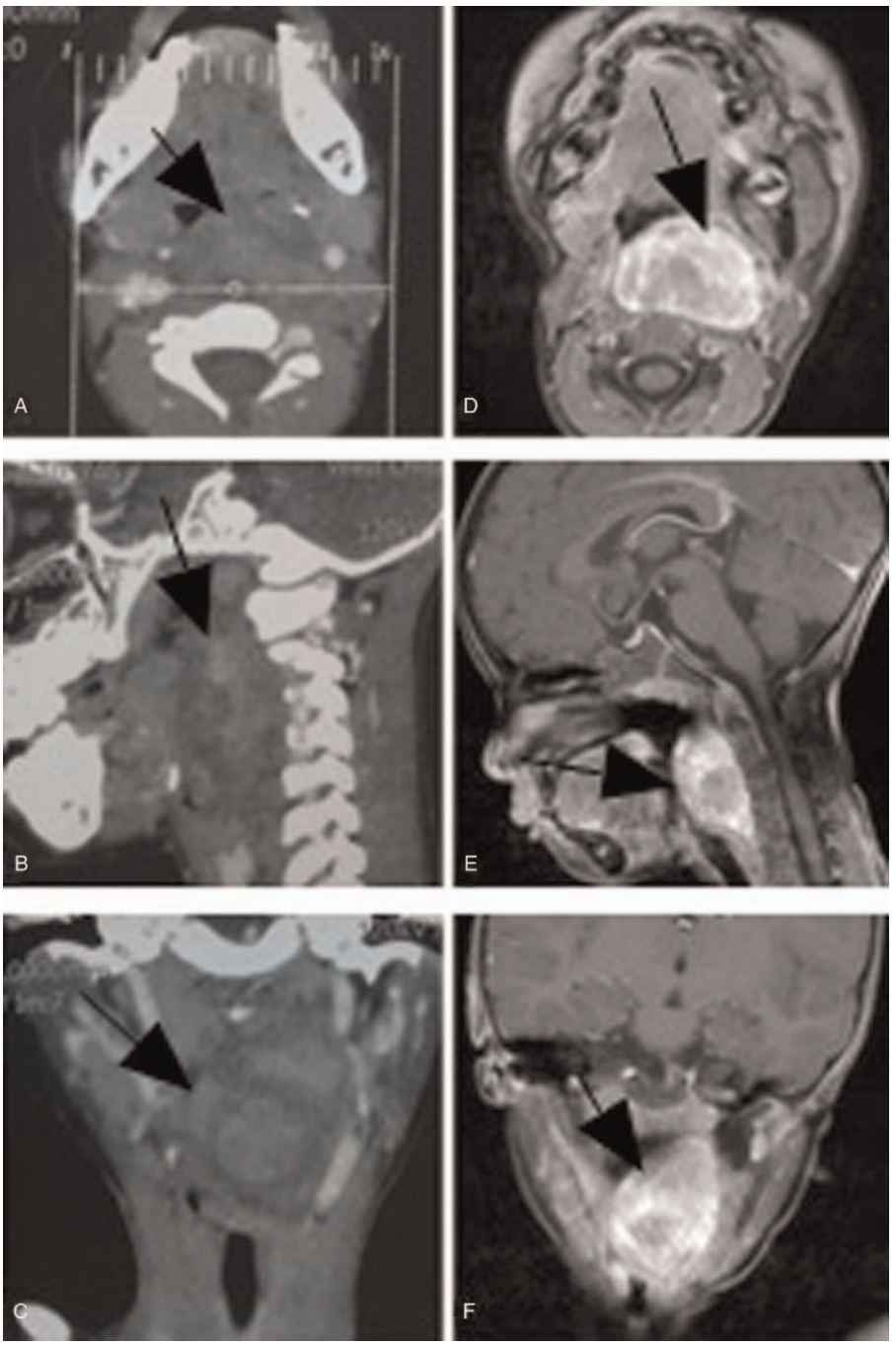

Figure 1. Preoperative computed tomographic (CT) and magnetic resonance imaging (MRI) images. (A–C) CT showed a giant mass with irregular low density in left oropharyngeal and posterior pharyngeal wall. The left carotid artery sheath was pushed to the right. After enhancement, the central part of the mass was strengthened, and the surrounding bones structures appeared normal. (D–F) MRI showed a solid mass in the left parapharyngeal space displacing the left carotid sheath posteriorly and laterally. CT = computed tomographic, MRI = magnetic resonance imaging.

space malignant tumor, highly suggestive of rhabdomyosarcoma was made. Based on this diagnosis, the treatment approach was surgical excision of the tumor. Preoperative evaluation revealed normal blood pressure, pulse, and blood biochemistry, chest radiography, and urinalysis results. To minimize damage, removing the mass via trans-oral surgery was attempted. However, since the oral approach resulted in poor exposure of the mass, the surgery was modified and the lateral cervical approach was used. An encapsulated, oval-shaped, solid mass was found below the left carotid sheath. The diameter of the mass was about 5.0 cm. The cut surface was yellowish-white in color and was separated easily from the surrounding tissues (Fig. 2). The upper and lower regions of the mass were innervated by a nerve that originated from the cervical sympathetic trunk. Postoperative histopathology showed that the mass contained neuroblasts, which were arranged in sheets and nests, and large mature hyperchromatic ganglion cells (Fig. 3A). Further immunohistochemical results revealed that the chromogranin A (CgA), soluble protein-100 (S-100), synaptophysin (Syn), neuron-specific enolase (NSE), and nestin were positive (Fig. 3B–

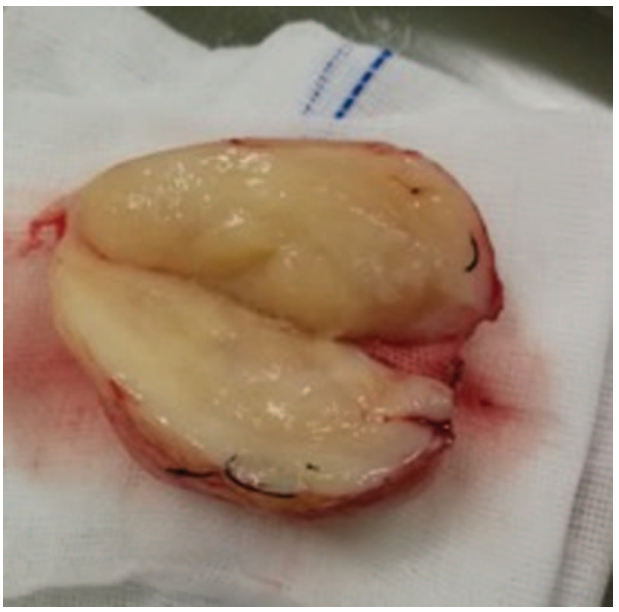

Figure 2. Gross examination of tumor.

F). After considering the histopathological and immunohistochemical results, the mass was diagnosed as ganglioneuroblastoma. There were no complications during or after surgery. The patient was discharged from the hospital on the seventh postoperative day. No adjuvant chemotherapy or radiotherapy were administered. She was followed for more than 1 year postoperatively. To date, she remains healthy and without evidence of recurrence and metastasis (Fig. 4A and B).

2.2. Informed consent

The patient's parents consented to our publishing this case report.

3. Discussion

Cervical masses are very common in the pediatric population and most are benign (e.g., lipoma, fibroma, hemangioma). Approximately 5% of neuroblastic tumors occur in the cervical region[2] and about 10% of these are malignant.[3] Ganglioneuroblastoma is a malignant tumor[4]; the mass is usually located in the adrenal gland, retroperitoneal ganglia, or posterior mediastinum. When it occurs in the neck, it is regarded as a subtype of neuroblastoma tumor that can arise anywhere along the sympathetic nervous system and are usually located in the lateral neck or are retropharyngeal masses.[2] It has been reported that ganglioneuroblastoma is seen most commonly during early childhood, especially in children under the age of 5 years with equal occurrence in males and females.[4,5]

An accurate diagnosis of cervical ganalioneuroblastoma involves not only observation of preoperative clinical symptoms, but also imaging, histopathologic examination, and immunohistochemical staining. The clinical symptoms of cervical ganglioneuroblastoma

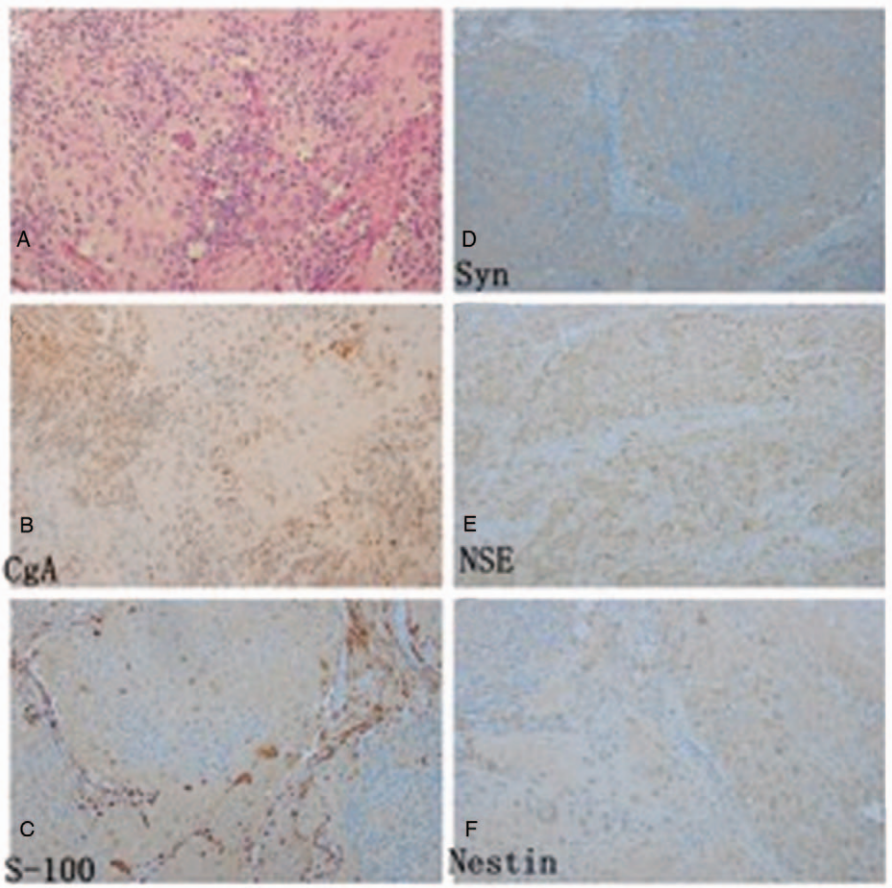

Figure 3. Histologic examination and immunohistochemistry of resected specimen. (A) The histopathological examination of the tumor showed neuroblasts arranged in nests and sheets, and large mature hyperchromatic ganglion cells (HE×200). (B) CgA was positive (×200). (C) S-100 was positive (×200). (D) Syn was positive (×200). (E) NSE was positive (×200). (F) Nestin was positive (×200). CgA =chromogranin A, NSE =neuron-specific enolaseb.

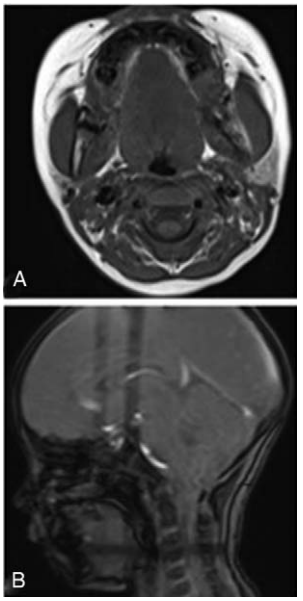

Figure 4. (A, B) Postoperative magnetic resonance imaging.

include compression of the cranial nerves or a giant undiscovered mass. Respiratory symptoms are frequently observed in patients with cervical ganglioneuroblastoma and severity of symptoms varies from snoring to severe respiratory distress. These patients may also show swallowing difficulties. Apart from these symptoms, Horner' s syndrome or iridis heterochromia are helpful for determining an accurate diagnosis.[6] Our case showed respiratory and swallowing symptoms, as well as Horner's syndrome. However, she was still misdiagnosed as myasthenia gravis because of the rarity of this disease. In fact, accurate preoperative diagnosis may be difficult without additional imaging or laboratory tests. Imaging studies play an important role in diagnosis because they can display not only the presence of the mass, but also its characteristics (e.g., the location, origin and size, internal structure, density, vascular encasement, and relationships between the tumor and peripheral organs).

CT can generally be used to reveal the mass, and Moukheiber et al[7] reported finding calcifications within the tumor in 50% of cases. CT may appear to have irregular low density with a central part that can be strengthened with enhancement.[8] However, descriptions based on CT scans are not specific enough for diagnosis. The MRI is considered superior to CT for checking invasion,[9] which is typically heterogenous and appears as high signal intensity in T1-weighted and low signal intensity in T2-weighted scans.[7] In our case, CT scan revealed a giant mass with an unclear border and irregular low density. After enhancement, the central part of the mass was greatly strengthened, without calcifications. However, MRI showed that the mass had a smooth border and high signal intensity on T1-weighted image. The case was initially identified as a rhabdomyosarcoma based on the MRI.

Despite the disease characteristics described above, accurate preoperative diagnosis of this rare disease remains difficult due to a lack of standard clinical and imaging presentations characteristics. As such, it is unsurprising that misdiagnosis often occurs. Therefore, definitive diagnosis depends on histopathological examination and immunohistochemical staining. Histologically, ganglioneuroblastomas are composed of both mature and intermediate-form ganglion cells and neuroblasts. For immunohistochemical staining, neurofilament, Syn, CgA, S-100, cluster of differentiation 30 (CD30), and CD15 are generally positive in ganglioneuroblastoma.[10] In our case, the histopathological and immunohistochemical characteristics were in line with that of ganglioneuroblastoma. The tumor was classified as Stage 1 according to the International Neuroblastoma Staging System (i.e., a localized tumor with complete gross excision, with or without microscopic residual disease and representative lymph nodes negative for tumor microscopically[7]).

Treatments for ganglioneuroblastoma include surgery, chemotherapy, radiotherapy, and biological therapy. Treatments approach depends on tumor stage, patient age, and biological prognostic factors.[11] Surgical removal is the main treatment method. The principle of the surgery is to remove the tumor completely, while protecting important structures to avoid functional damage or loss. The excision approach is chosen based on the location of the mass, as well as its size and the neighboring structures. Risk assessment should be performed prior to surgery. Neck lymph node dissection is usually required even when there is negative detection by physical or imaging examination, and selective neck dissection is often preferred.[12] Postoperative complications include neural injury, severe bleeding, and airway and feeding compromise.[2] Irwin and Park[13] suggested that if the tumor is not completely removed and in metastatic stage, radiotherapy or chemotherapy should be performed. Akin et al[14] reported a case in which they used 1.8 Gray/30 fractions (54 Gray total) with conformal 3D radiotherapy, and 50% regression of the mass was detected after 3 months and the patient was considered cured after 1 year. Chemotherapy regimens utilized include adriamycin, cyclophosphamide vincristine, and combinations with platinum and etoposide.[15] In our case, since the patients were too young, neither radiotherapy nor chemotherapy was suggested. In addition, immunomodulators and retinoids may become good choices for treating neuroblastic tumors in the future.[8,9]

Ganglioneuroblastoma prognosis depends primarily on patient's age and disease stage. In generally, the prognosis for patients under 1 year of age is significantly better than for older children with the same tumor stage.[16] Lonergan et al[1,9] reported that the 3-year survival rate was more than 75% in children under 1 year old of age, whereas it was less than 50% in children older than 1 year or with a later stage tumor. Disease recurrence occurs mostly in the first 2 years following. About 1% of tumors will metastasize to bone, liver, lung, brain, skin, or bone marrow,[17] via the hematogenous or lymphatic system.[8] Therefore, the patients should be followed closely (i.e., every 3 months for the first and second years, then every 6 months thereafter). Since high levels of catecholamine are related to recurrence,[2] Bolzacchini et al[18] suggested that blood count, urinary catecholamine analysis, and imaging should be performed at every examination. Scintigraphy with ^{131}iodine-methyliodobenzylguanidine, which can help to detect bone metastasis, is recommended to perform every 6 months, which can help detect bone metastasis,[7,19]. In our case, the prognosis was favorable based on the complete mass resection. There was no recurrence or metastasis for 1 year after surgery. However, she will need longer term follow-up to ensure that there is no recurrence and metastasis.

4. Conclusion

Herein we have presented a case of a 4-year-old female with cervical ganglioneuroblastoma. This is the first such case reported from China. Our report suggests that clinicians should be alert to the pediatric patients with Horner's syndrome, respiratory

symptoms, and/or swallowing difficulties, which may indicate cervical ganglioneuroblastoma.

Author contributions

Data curation: Y. Chen.
Methodology: J. Liu.
Supervision: H. Yang.
Writing – original draft: D. Lu.
Writing – review & editing: F. Chen, H. Yang.

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