Primary thoracic neuroblastoma in an adult
A rare case report
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Abstract
Rationale: Neuroblastoma is one of the most common malignant tumors in childhood, which mainly occurs in adrenal glands and peripheral sympathetic nerve system. Neuroblastoma occurring in adulthood is rare, and adults with neuroblastoma arising from thorax are exceedingly rare. A case of neuroblastoma that originated from thorax was reported, and was treated by resection operation.

Patient concerns: A 46-year-old woman was admitted to our hospital with left side chest pain for 5 days. Laboratory examinations were all normal. Chest computerized tomogram (CT) showed a lesion with clear boundary that was located at the left dorsal pleura. The nature of the mass was heterogeneous, showing slight heterogeneous enhancement after contrast and there was no obvious necrosis.

Diagnoses: Based on the morphologic and immunohistochimical features, the tumor diagnosis was favorable for neuroblastoma.

Interventions: A resection operation was carried out.

Outcomes: Three years postoperative, no sign of recurrence or metastasis has been observed.

Lessons: Primary neuroblastoma in adulthood is rare and has poor prognosis. Resection can be an important treatment option, and combining with other methods like chemotherapy, stem cell transplantation, the survival rate may be improved.

Abbreviations: CT = computerized tomogram, HIV = human immuno deficiency virus, Hu = Hounsfield Unit, INRG = International Neuroblastoma Risk Group.

Keywords: neuroblastoma, surgery, thorax

1. Introduction
Neuroblastoma is one of the most common malignant tumors in childhood, which mainly occurs in adrenal glands and sympathetic nerve chain in the neck, chest, abdomen, or pelvis.(1) The overall incidence for neuroblastoma is approximately 1 case per 100,100 children in the United States.(2) However, neuroblastoma occurring in adulthood is rare, counting for only 1 case per 10 million diagnosis per year.(3–4) There are only a few case reports about adulthood neuroblastoma.(5–7) While adult neuroblastoma that originated from thorax is exceedingly rare. Here we report a case of this kind with surgery treatment. We have obtained the informed consent from the patient for publication of this case.

2. Case report
A 46-year-old woman was admitted to our hospital with left side chest pain for 5 days. The pain was dull and was relieved after resting. There were no cough or sputum, no hemoptysis, no shortness of breath, no fever or night sweating, and no limb numbness or fatigue. She denied smoking, drinking, nor a history of human immunodeficiency virus (HIV) or exposure to hepatitis B. There was no occupational or recreational exposure to toxins either. The physical examination found no other symptom or physical abnormalities.

Laboratory examinations were all normal, including blood routine test, coagulation function test, liver and kidney function tests, urinalysis, test for tumor markers.

Chest computerized tomogram (CT) showed the lesion with a clear boundary located under the left dorsal pleura with dimension 43 mm × 36 mm × 39 mm. The mass appeared to be heterogeneous, with a CT value about 17 HU. After contrast, the mass showed a mild heterogeneous enhancement with no obvious necrosis, and the CT value was about 32 HU (Fig. 1).

As there was no evidence of local or distant metastasis, a resection operation was carried out. During the operation, the mass was found to be located at the left dorsal pleura, about 4 cm in length, hypervascular, and with a firm texture. The tumor did not invade adjacent ribs and was completely resected. The intraoperative pathological examination showed that the small...
cells were in chrysanthemum shape encompassing a neuropil. Immunohistochemical investigations revealed that the tumor cells expressing CD56, S-100, Syn. Based on its morphologic and immunohistochemical features, the tumor was finally diagnosed as neuroblastoma (Fig. 2). Unfortunately, patient refused to have further genetic testings, and we were unable to properly assess her staging based on the International Neuroblastoma Risk Group (INRG) Task Force. According to the International Neuro-

Figure 1. The CT scan shows a large heterogeneous mass locating at the left dorsal pleura. A: It shows low density before contrast, and the boundary is clear. B and C: After contrast, the mass shows slight heterogeneous enhancement with no obvious necrosis. D: Coronal position of chest CT shows the mass under the left dorsal pleura. CT = computerized tomogram.

Figure 2. Microscopic appearance of the tumor. Hematoxylin-eosin stain (×400) shows small cells are in chrysanthemum shape encompassing a neuropil.
blastosma Staging System (INSS) criteria, the patient had stage 1 neuroblastoma.[9] According to the INSS criteria, the treatment for patients with stage 1 neuroblastoma is surgical resection alone.[9] The patient had not received any chemotherapy or radiotherapy after surgery. Prognosis was promising so far, as there was no signs of recurrence or metastasis 3 years postoperatively.

3. Discussion

Neuroblastoma is an embryonal origin tumor of the sympathetic nervous system, arising either from primitive sympathetic neural cells in the adrenal medulla or the paraspinal sympathetic ganglia.[11] Although neuroblastoma is classified as the most common form of solid extracranial malignancy in childhood and the most common malignancy in infancy, neuroblastoma in adult arising from thorax is exceedingly rare. The studies done by Conter et al.[10] reported 118 adult with neuroblastoma, only 5 patients have disease origin in the thorax.

The manifestation of neuroblastoma varies in different patients, tumor cells can behave from spontaneous regression to maturation, or to an aggressive form.[11] In 1993, the INSS published a surgicopathologic staging system.[9] However this criteria have some limitations, especially for patients who are yet to have surgery. Then the scholars found that the neuroblastomas’ clinical behavior is affected by many factors. Some of the most important biologic and molecular factors are age, disease stage, the status of MYCN, histopathologic classification, chromosome 11q status, and DNA ploidy.[8] Now, these factors are incorporated into the international neuroblastoma risk assessment system performed by the INRG Task Force (Table 1).[8] Because of the rarity of adult neuroblastoma, staging systems and risk assessment tools have been developed using pediatric data primarily.[12]

There are no well-established treatment guidelines for adults with neuroblastoma. In general, the treatment principle is decided by the risk assessment system. If the tumor falls in low risk category, surgery may have a good prognosis. For patients in intermediate or high-risk group, survival may be improved by local surgical control with postoperative intensive induction chemotherapy. Some commonly used chemotherapy agents include cisplatin, etoposide, vincristine, cyclophosphamide, and doxorubicin.[13] Chemotherapy-caused myelosuppression can be treated by stem cell transplantation, while the remaining small lesion could be managed by targeted therapy.[14] For patients with metastatic neuroblastoma, radiation therapy can be an effective treatment in local control but it may hinder attempts at total resection of the tumor.[15] According to the INSS criteria, the patient we reported with stage 1 (low-risk) disease, could receive surgery treatment without adjuvant chemotherapy or radiotherapy, but regular follow-up checks are required.[8] Until now, there was no sign of recurrence or metastasis.

Studies done by Podda et al.[16] reported the 5 years survival rate for stage I and II neuroblastoma was 83% and for stage III and IV disease was 28%. The overall survival of all stages was 40% at 5 years and 20% at 10 years. Another study conducted by Conter et al.[10] reported the overall prognosis for adult patients with stage L1 was 18.1 year, and 9.8 years for stage L2, and 1.6 years for stage M. Different literatures all demonstrate that younger children, and especially infants <1 year old have significantly better disease-free survival outcomes compared with older children, for that all stages of neuroblastoma beyond stage 1, where the tumor is still in the localized state. Some suggested that the reason why adult patients usually have poorer prognosis can be due to unfavorable histological features and less MYCN amplification.[17–19] However, other results show that there are no differences in prognosis between patients younger than 18 and those in adulthood 18.[10] The INRG risk assessment system is recommended for high risk patients of any age, to allow proper staging.[10]

4. Conclusion

Primary neuroblastoma in adulthood is rare. Compared with infant or pediatric patients with neuroblastoma, the overall

| INRG stage | AGE (mo) | Histologic category | Grade of tumor differentiation | MYCN Aberration | 11q | Pretreatment risk group |
|-----------|---------|---------------------|-------------------------------|----------------|-----|------------------------|
| L1/L2     |         | GN maturing; GNB intermixed | Differentiating | NA | Amp | A very low |
| L1        |         | Any, except GN maturing or GNB intermixed | NA | No | Yes | B very low |
| L2 <18    |         | Any, except GN maturing or GNB intermixed | NA | No | Yes | D low |
| ≥18       |         | GNB nodular; neuroblastoma | Poorly differentiated or undifferentiated | NA | Amp | E very low |
| M <18     |         | Any, except GN maturing or GNB intermixed | NA | No | Yes | G intermediate |
| <12       |         | Hyperdiploid | GNB nodular; neuroblastoma | Amp | Yes | H intermediate |
| 12 to <18 |         | Diploid | GNB nodular; neuroblastoma | NA | Yes | I intermediate |
| <18       |         | Diploid | GNB nodular; neuroblastoma | NA | Yes | J intermediate |
| ≥18       |         | Amp | GNB nodular; neuroblastoma | Amp | Yes | K high |
| MS <18    |         | NA | GNB nodular; neuroblastoma | NA | Yes | L high |

GN = ganglioneuroma, GNB = ganglioneuroblastoma.
survival rate of adult is low. Surgery can be an important intervention, combined with intensive induction chemotherapy, stem cell transplantation and radiotherapy, the survival rate can helpfully be improved.

Author contributions
Data curation: Jin-Fan Li, Wen-Shan Li.
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References
[1] Brodeur GM. Neuroblastoma: biological insights into a clinical enigma. Nat Rev Cancer 2003;3:203–16.
[2] Siegel R, Naishadham D, Jemal A. Cancer statistics, 2012. CA Cancer J Clin 2012;62:10–29.
[3] Esiashvili N, Goodman M, Ward K, et al. Neuroblastoma in adults: incidence and survival analysis based on SEER data. Pediatr Blood Cancer 2007;49:41–6.
[4] Hsieh MH, Meng MV, Walsh TJ, et al. Increasing incidence of neuroblastoma and potentially higher associated mortality of children from nonmetropolitan areas: analysis of the surveillance, epidemiology, and end results database. J Pediatr Hematol Oncol 2009;31:942–6.
[5] Wu XL, Dai YJ, Sun GY, et al. Adult neuroblastoma in the retroperitoneum: a case report. Medicine (Baltimore) 2018;97:e0345.
[6] Podda MG, Luksch R, Polastri D, et al. Neuroblastoma in patients over 12 years old: a 20 year experience at the Instituto Nazionale Tumori of Milan. Tumouri 2010;96:684–9.
[7] Conte M, Parodi S, De Bernardi B, et al. Neuroblastoma in adolescents: the Italian experience. Cancer 2006;106:1409–17.