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QUIZ CASES

Ganglioneuroblastoma in children

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Abstract

Introduction Neuroblastoma ranks third among pediatric malignancies.

Case report The case of a 3-year-old child is presented, who suddenly had frequent, unproductive, emetic cough; fever; and weight loss. Lung X-ray showed an opacity situated in the posterior superior mediastinum. Thoracic ultrasound revealed a slightly inhomogeneous, hypoechoic mass located in the posterior superior mediastinum. Computed tomography evidenced a tumor mass with homogeneous appearance in the costo-vertebral groove. Histological examination confirmed the diagnosis of ganglioneuroblastoma.

Conclusion Although history and clinical examination provided few elements, diagnosis was made based on imaging and histopathological examination.

Keywords Neuroblastoma · Ganglioneuroblastoma · Child neuroblastoma

Introduction

Ganglioneuroblastoma (GNB) is a rare peripheral neuroblastic tumor. GNB represents 20% of all neuroblastomas and has pronounced cell polymorphism with ganglionic cells with different degrees of maturation and calcification areas [1, 2]. GNB is slightly predominant in the male sex and is more frequently found in the white race [3]. The malignant potential of GNB is in between that of neuroblastomas and ganglioneuromas. Prognosis depends on the disease stage, the degree of differentiation of neuroblastoma, the location of the primary tumor, and nutritional status [4–6].

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Case report

Patient A.S., male, aged 3 years, was admitted to the Clinic of Pediatrics III with fever and unproductive, emetic cough. His personal physiological history showed that he was the second child, from a pregnancy with physiological evolution, eutocic birth at term, with a weight of 4000 g, and normal somato-psychic development. His family and personal pathological history was insignificant. The clinically manifest onset of the disease occurred 3 weeks before admission, through unproductive cough which became persistent, associated with fever and weight loss of about 1 kg over the past 6 months. At admission, objective examination revealed a patient with a weight of 13.8 kg (25th percentile), with good general status, moderate fever, with reduced appetite, frequent emetic cough, physiological vesicular murmur, respiratory rate 24/min, heart rate 90/min; without peripheral adenopathy or organomegaly, spontaneous micturition, without neurological focal signs. Paraclinical investigations did not detect anemia or thrombocytopenia, and the vanylmandelic acid value was normal (2.34 mg/24 h).

Thoracic radiographs, thoracic ultrasound, and thoracic tomography computer were performed from the imaging investigations.

Chest X-ray was performed, which detected an opacity situated in the posterior superior mediastinum (Fig. 1).

Chest ultrasound revealed a slightly inhomogeneous, hypoechoic mass of parenchymatous nature, with more hyperechoic areas and microcalcifications, 75 mm/52 mm in

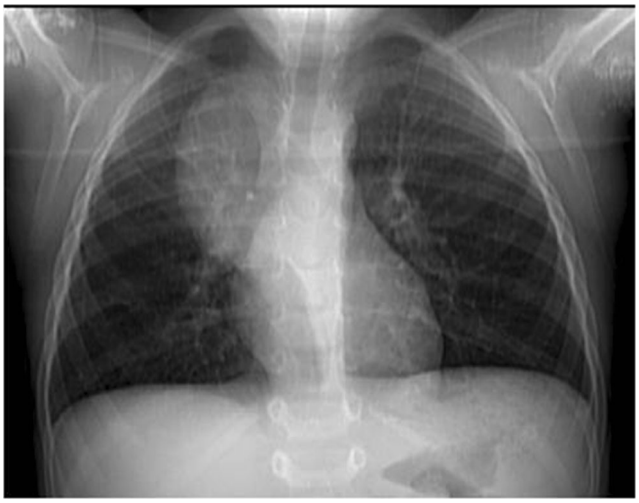

Fig. 1 AP chest X-ray

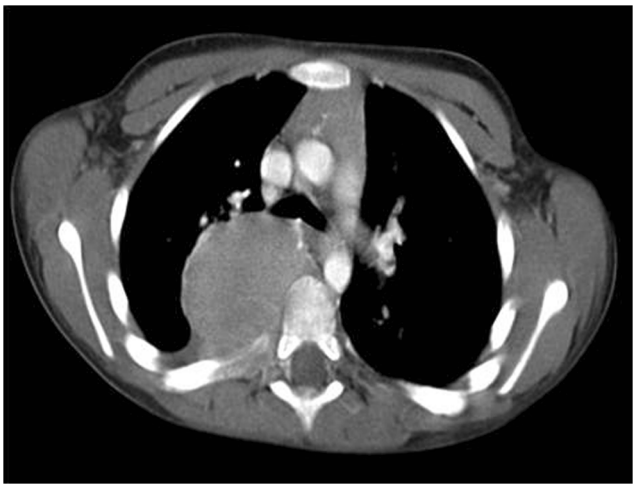

Fig. 3 Chest computed tomography

size, poorly vascularized, located in the posterior superior mediastinum, and to the right. Superficial to this mass, a hypoanechoic ovoid mass 15 mm/12 mm in size was also detected in the intercostal space 5–6, in the right paravertebral area, which was apparently well delineated from the mediastinal mass (Fig. 2).

Computed tomography detected in the right costo-vertebral groove a tumor mass with an axial size of 4.5 cm × 3.5 cm, a cranio-caudal extension of 7 cm, and a homogeneous appearance, which was iodophilic, with uniform uptake, and without inducing bone lysis. The mass displaced the esophagus to the left and cranially in anterior direction (Fig. 3).

The patient was transferred to the service of Pediatric Surgery, where right thoracotomy under general anesthesia, with the complete excision of the tumor, was performed. The tumor was well delineated, encapsulated, in contact with the spine and the paravertebral ganglionic chain, with a size of 5/6/10 cm, and displaced the esophagus to the left. Post-surgery chest computed tomography did not evidence any residual mediastinal tumor masses.

Macroscopic examination described a large tumor mass 7/6.5/2.5 cm in size. On the section surface, whitish nodules with an apparently necrotic center, surrounded by a purple-gray framework, were found; one nodule was cystically transformed, and two small nodules 2 cm and 1.5 cm in diameter had a homogeneous appearance in the section. Microscopic examination indicated a relatively homogeneous appearance. Hematoxylin-eosin staining evidenced three categories of cells: lymphoid cells arranged focally in the form of follicles, neuroblastic cells with diffuse arrangement, and a third category with epithelioid appearance arranged in the form of

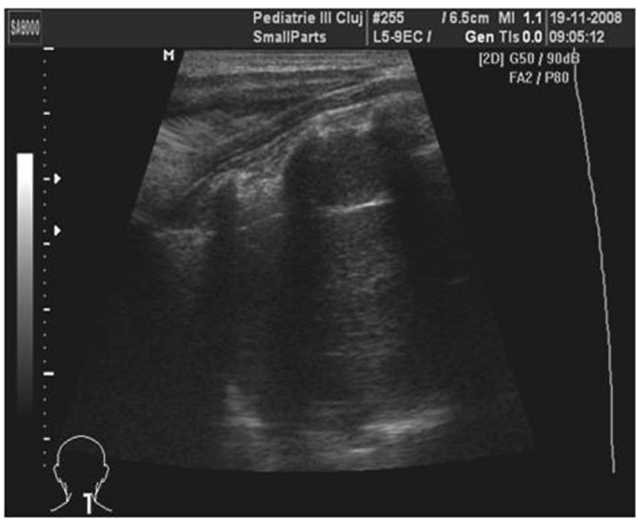

Fig. 2 Chest ultrasound

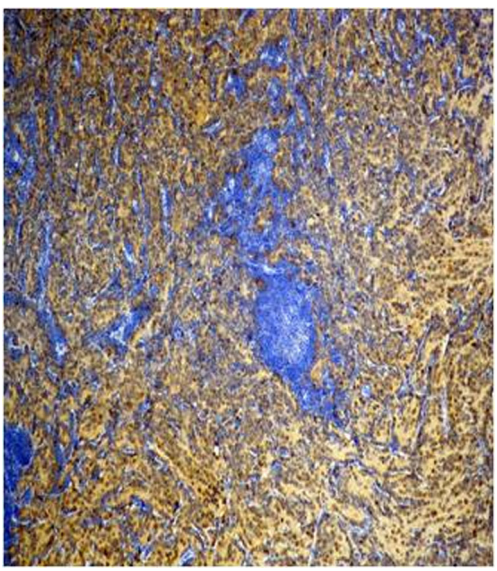

Fig. 4 Microscopic examination

trabeculae and rare ganglionic cells. Immunohistochemical staining showed that the neuroblastic component was positive for neuron-specific enolase, the epithelioid component was positive for protein S100, and the lymphocytic component was positive for CD 99 (Fig. 4).

The anatomopathological diagnosis was a poorly differentiated ganglioneuroblastoma. The patient was subsequently transferred to the service of Pediatric Oncology, where laboratory tests (hematologic, renal, hepatic, serum alkaline phosphatase, lactate dehydrogenase, serum ferritin, vanylmandelic acid, neuron-specific enolase) had values within normal limits, and chemotherapy was performed according to the protocol.

Discussion

Ganglioneuroblastoma (GNB) is a rare peripheral neuroblastic tumor, which derives from the development of neuronal cells of the sympathetic nervous system. The Shimada classification of neuroblastomas, based on the histopathological balance between neuronal cells (primitive, mature, and ganglionic) and mature Schwann cells, divides them into neuroblastoma, intermixed ganglioneuroblastoma, ganglioneuroma, and nodular ganglioneuroblastoma. Most of these tumors are sporadic, but in 1–2% of all cases, there is a family history of neuroblastic tumors characterized by autosomal dominant. Ganglioneuroblastomas are less mature forms [4–6].

The mean age for establishing diagnosis is 47.5 months. In 90% of cases, diagnosis is made under the age of 5 years and tumors diagnosed after the age of 10 years are extremely rare. [2, 7]. Etiology is unknown, but some studies suggest favoring factors such as prenatal exposure to diuretics, phenobarbital, and alcohol; exposure of fathers to electromagnetic fields; or random genetic mutations (rearrangement or deletion of the short arm of chromosome 1 and amplification of the *N*-myc protooncogene) [2, 8, 9].

The primary tumor can be located anywhere in the sympathetic nervous system: abdominal (65%), adrenal (25%), posterior mediastinal (20%), pelvic (4%), and cervical (1%) location [10–12]. In 60–70% of cases, metastases are present at diagnosis. Patients with mediastinal tumors may present stridor and respiratory difficulties secondary to tracheal compression. Large chest tumors may cause mechanical obstruction resulting in superior vena cava syndrome. The majority of these are unilateral, encapsulated, vascular, and do not cross the mid-abdominal line. They may evolve without being detected on time, because the tumor can increase in size without causing pain. Patients with GNB clinically present frequent pain caused by the primary tumor or metastases [13, 14].

Among clinical manifestations, the following are more frequent: fever, vomiting, weight loss, headache, palpitations, sweating, and regional and/or distant lymphadenopathy through lymph node metastasis. More rarely, the disease clinically manifests by chronic diarrhea through an increased production of vasoactive intestinal peptides, compression of adjacent structures (sphincter disorders through spinal cord compression), and intense bone pain [1, 2, 7, 8, 14, 15]. Although GNB has various signs and symptoms, the clinical manifestations present were few: moderate fever, weight loss, and respiratory manifestations.

CT scan is the imaging modality of choice for the assessment of neuroblastic tumors. There is sufficient evidence suggesting its superiority in the determination of the size of the tumor, including the organ of origin, tissue invasion, the vascular sheath, lymphadenopathy, and calcifications [11, 16, 17].

Histological confirmation is required for definitive certainty diagnosis. These tumors are considered histologically malignant because they contain primitive neuroblasts and mature ganglionic cells. GNB most frequently metastasize in the bone and liver, and under the age of 1 year, skin metastases develop [13].

Screening programs are available for the detection of child neuroblastomas by measuring urinary catecholamines, but they have not been associated with a difference in mortality [4, 18–20]. Thoracic CT was performed to establish the patient's diagnosis that revealed a right paravertebral tumor mass, and the histopathological examination confirmed the diagnosis of ganglioneuroblastoma. All laboratory examinations performed were normal. Our patient was diagnosed at the age of 3 years with mediastinal GNB with intermediate risk. No regional or remote metastasis was detected at the time of diagnosis. The treatment was complete resection of the tumor associated with chemotherapy according to the protocol [6].

Prognosis for patients with localized disease at younger ages is better. The younger the age of diagnosis, the better the survival rate [2, 4, 6, 8]. Mediastinal neuroblastomas have a better prognosis than abdominal neuroblastomas, because patients with mediastinal neuroblastoma seek medical help when the size of the tumor is small and its complete resection is possible. Complete surgical excision remains the main support of therapy for localized mediastinal neuroblastomas. Furthermore, reactive oxygen species generated by local hypoxia are vital for neuroblastoma development and other childhood diseases [15, 16], implying that targeting the production of reactive oxygen species by neuroblastoma cells can improve the therapeutic impact. Periodic check-ups require chest X-ray, and there are no data regarding the recommended duration of follow-up [21–24].

The prognosis of our patient was good, because the tumor had a mediastinal location, being completely resectable, and there were no metastases at the time of diagnosis. On post-surgery chest CT, no residual tumor was detected. The 2-year survival rate without events is 85–100%. Recurrences can be solved by subsequent surgery and chemotherapy [1, 2].

Conclusion

GNB is very rare in the pediatric population, and its clinical symptoms are extremely varied. Although history and clinical examination provided few elements, diagnosis was made based on imaging and histopathological examination. The prognosis is a good one, the tumor being fully resected with good survival rate.

Compliance with ethical standards

Conflict of interest The authors declare that they have no conflict of interest.

Ethical approval All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards.

Informed consent Informed consent was obtained from all individual participants included in the study.

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