Large mediastinal nodular ganglioneuroblastoma in a child from Africa

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Ganglioneuroblastoma, nodular (GNBn) is a subtype of neuroblastic tumors. This is a rare malignancy typically affecting young children. Few cases are reported in adolescents and adults. The prognosis is related to the surgical excision radicality.
Hereby we present a case of a young male patient age 13 from the Horn of Africa presenting with vague symptoms of fatigue and weight loss. Chest X-ray showed a large radiopaque mass occupying the right thorax. The chest Computed Tomograpy confirmed the presence of an 18-cm large mass originating from the posterior mediastinum and invading most of the right hemi-thorax.
Surgical excision and histopathology study of the lesion clarified its rare nature: ganglioneuroblastoma nodular with a particular coexistence of a fibrous benign surface encapsulating a necrotic malignant core.
In this case of large GNBn in a young adolescent, the surgical resection alone played a curative treatment role.

KEY WORDS: Adolescent, Ganglioneuroblastoma nodular, Radical surgical excision

Introduction

Neuroblastic tumours (NT) are defined as embryonal tumours of the sympathetic nervous system, derived from the neural crest and arising in the adrenal medulla, paravertebral sympathetic ganglia, and sympathetic paraganglia [1]. NTs are divided into three categories by differentiation: neuroblastoma, ganglioneuroblastoma and ganglioneuroma. Neuroblastoma is a high-grade malignancy, while ganglioneuroma is a well-differentiated benign neoplasm. Ganglioneuroblastoma is an intermediate malignant composite tumour containing both primitive neuroblasts and mature ganglion cells, less aggressive than neuroblastoma [2].
NTs are the most common extracranial solid tumours of childhood, accounting for 8% to 10% of paediatric malignancies and are responsible for approximately 15% of all childhood cancer deaths. The incidence is ten per million in white children and eight per million in black children in the United States [3].

Case report

We report a case of an African boy aged 13 who presented to our department complaining of a one-year history of persistent dry cough and weight loss.
A chest x-ray showed a large radiopaque mass occupying most of the posterior mediastinum and right thorax (Fig. 1).

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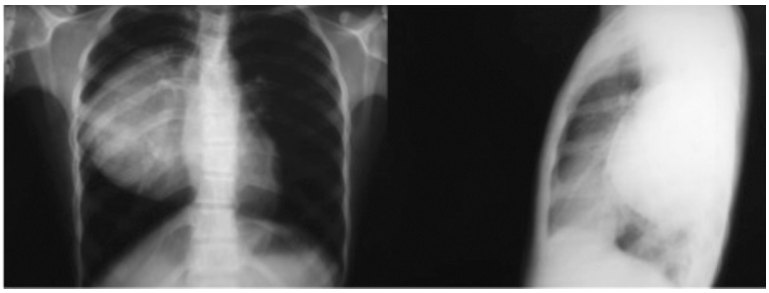

Fig. 1: Chest Xray showing the large mediastinal radiopaque mass. Anteroposterior (Left), Lateral (Right). The right paraspinal density appears well-defined and retrocardiac.

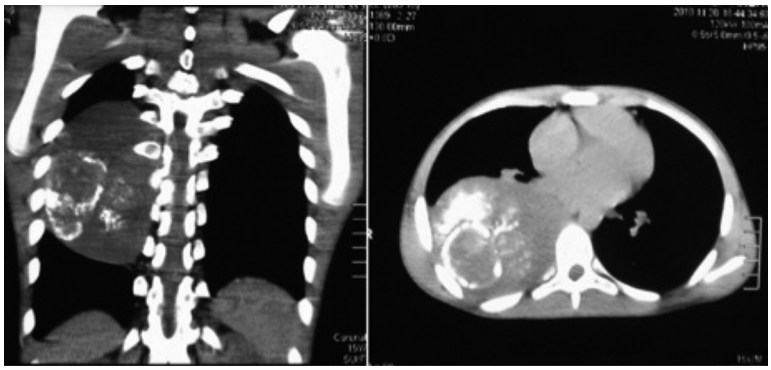

Fig. 2: Computed Tomography showing coronal (left) and axial (right) views of the mediastinal mass occupying most of the right hemi-thorax. Gross calcifications are seen within the lesion. The mass appears adjacent to T4-T5 and T5-T6 intervertebral foramina without clear signs of extension into them.

A chest Computed Tomography (CT) scan confirmed the presence of an 18-cm large mass within the posterior mediastinum compressing the organs of the right hemithorax (Fig. 2).

On the CT the lesion appeared heterogenous and containing coarse calcification. The mass appeared closely adjacent to the intervertebral foramina between T4-T5 and T5-T6. On the CT there was no evidence of intervertebral foramina invasion. To better assess the extension of the lesion through the foramina, a Magnetic Resonance would have been helpful. This was not performed for lack of resources.

In the differential diagnosis other conditions had been taken in consideration: rhabdomyosarcoma, Wilms tumour, germ cell tumours, and lymphoma.

Rhabdomyosarcoma is the most common soft tissue sarcoma in children. To evaluate the mass further and obtain more specific preoperative information, a core biopsy of the lesion could have been advised.

Considering the invasiveness of the bioptic procedure and the lack of highly developed medical facilities in this geographic area, no further pre-operative diagnostic tests were performed. Moreover, whichever other information a core biopsy could have added, we couldn't have offered any other options apart from surgery to the patient. In other circumstances, a complete staging would have been advisable including abdomen CT and skeletal scintigraphy.

The young patient underwent surgical excision of the lesion via a right posterolateral thoracotomy. The huge mass was carefully detached from the other mediastinal structures, not infiltrating nor adhering to any of the surronding organs. Some of the feeding vessels were found to originate from intercostal vessels with others branching directly from the aorta. The mass was confirmed not invading the intervertebral foramina. A right sided chest drain was left *in situ*. The post-operative course was uneventful. The patient was discharged back home on day five post-operatively. No short- nor mid-term complications were reported.

At the one-year follow up appointment the patient was in good health; the examination and chest X-ray did not reveal any signs of local or systemic recurrence.

Macroscopically the mass was 11.5 x 8 x 9-cm. The outer surface was smooth and appeared encapsulated. Once sectioned, the mass presented a deeper well-defined 6-cm area that appeared straw-coloured with smaller reddish areas. In consistency it was softer than the surrounding tissues and partially necrotic with calcification.

Histology revealed a ganglioneuroblastoma nodular: the bulk of the lesion showed the appearance of ganglioneuroma but an abrupt transition was noted towards a smaller nodule composed of cytologically uniform neuroblasts (synaptophysin positive). The cytologically malignant component had a low mitosis-karyorrhexis index. The immunoistochemestry helped in the diagnosis showing strong positivity to PS100 antibody in the stromas sections.

Discussion

Ganglioneuroblastomas (GN) are rare tumours of the sympathetic nervous system originating from the neural crest; they are a particular subtype of Neurogenic Tumours.
Neurogenic tumours are the most common mediastinal tumours encountered in children [4]. About 20% of these tumours are malignant, and neuroblastic tumours are the most common malignant neurogenic tumour type in children [5,6]. The clinical course of NT is very variable, raging from extremely benign cases with spontaneous regression to more aggressive conditions with liver and bone metastasis [7,8].
The benign type of NT is known as ganglioneuroma while the malignant one as neuroblastoma.
Ganglioneuroblastoma is considered as a transitional tumor that contains both malignant neuroblastomatous and benign ganglioneuromatous elements [4]. GNs have a less aggressive course compared to Neuroblastomas. About a half of ganglioneuroblastoma patients are asymptomatic and are discovered by routine chest X-ray examinations [9]. Adam and colleagues [9] reported an 88% 5-year actuarial survival rate for ganglioneuroblastoma and found that prognosis was related to histologic growth pattern, age, and disease extent at diagnosis. They also proved that the absence of a MYCN amplification in ganglioneuroblastoma was related to a better prognosis [9].
More than 90% of GN are reported in children younger than 5 years of age, with a spike at 18 months [10]. They occur with equal frequency in both the genders, their occurrence after 10 years of age being extremely rare [11].
Ganglioneuroblastoma, nodular (GNBn) is classified as a further rare subtype of ganglioneuroblastoma.
This particular histotype is characterized by the macroscopic coexistence, within the tumor mass, of hemorrhagic neuroblastic nodule(s) with ganglioneuroblastoma(s) or ganglioneuroma(s). The neuroblastic nodules are conceptually regarded as the consequence of evolution of one or multiple aggressive or malignant clones, either because of newly acquired genetic aberrations or the persistence of two or more genetically and biologically different clones [1]. Microscopically one usually finds the abrupt demarcation between the expansive and infiltrating type of growth of the neuroblastic nodules pushing against the outer stromal structures.
GN can potentially arise anywhere along the sympathetic nervous system. They occur most commonly in the adrenal medulla, extra-adrenal retroperitoneum, and posterior mediastinum, with the neck and pelvis being less common sites of occurrence [12].
The Magnetic Resonance (MR) and the Computed Tomography (CT) are the preferred method to investigate ganglioneuroblastoma [13-15]. The MR is of particular relevance to evaluate the extension of these tumours into the intervertebral foramina [16].
The clinical presentation mostly depends on the anatomical site of origin. Pain is one of the most common presenting complaints, this being caused either by the primary tumour or by metastatic localisations. Mediastinal tumours can present with shortness of breath and stridor secondary to tracheal deviation or narrowing [17]. Large thoracic tumours can cause mechanical obstruction resulting in superior vena cava syndrome. Nerve or nerve root compression by the mass can result in peripheral neurological signs [17]. Patients with cervical masses can present with Horner's syndrome. [18] In our case, the young patient did not complain the usual symptoms but only a non-specific fatigue and weight loss.
The type of treatment for NT is planned on the base of risk evaluation. Low-, intermediate-, and high-risk groups are defined according to patient age, INSS stage,
MYCN status, Shimada histology, and tumour cell ploidy [19]. In estimating the prognosis of ganglioneuroblastomas it is important also to take in consideration the amount of malignant component within the tumour mass and the mitosis-karyorrexis index in the malignant component.
In our case the preoperative risk assessment was hard to establish as biopsy was not performed and the staging was only limited to a chest CT with no information about possible metastasis.
Stage I and II patients with no MYCN amplification are considered low risk. In these patients, surgery alone as primary treatment has showed excellent survival rates [20]. Intermediate- and high-risk groups are treated using multimodality therapy, usually surgery followed by adjuvant chemotherapy. The role of surgery in stage IV metastasized tumours is still controversial. Kang et al [4] have observed encouraging results by combining surgical resection and adjuvant chemotherapy in stage IV advanced NT with good survival rate.

Conclusions

We presented a case of ganglioneuroblastoma nodular of the posterior mediastinum in a young adult male patient. The tumour mass was characterised by the presence of two well-defined and separate components. The presence of the outer benign, smooth and encapsulated neurofibromatous tissue, surrounding the inner necrotic and malignant component is linked to a better prognosis and increases the chances of performing a curative radical excision of the tumour compered to the purely malignant neuroblastomas. It is likely the large mass had been increasing in size over several years, allowing the other chest organs to accommodate its presence and leaving the patient relatively symptom-free. We believe, in this case, surgery has been a curative treatment.

Riassunto

Il ganglioneublastoma nodulare (GNBn) è un sottotipo di tumore neuroblastico. Questo rappresenta un tumore

maligno tipico dell'età infantile. Pochi casi sono stati riportati in età adolescenziale e adulta. La prognosi è strettamente correlata alla radicalità dell'escissione chirurgica.
Presentiamo un caso di un giovane adolescente di 13 anni che si presentava alla nostra osservazione con sintomi vaghi di affaticamento e perdita di peso. La radiografia del torace evidenziava una grossa massa radiopaca occupante l'emitorace destro. La TC confermava la presenza di una lesione di 18-cm che originava dal mediastino posteriore e che si estendeva in quasi tutto l'emitorace destro. La resezione chirurgica e il successivo esame istologico hanno rivelato la rara natura della lesione: ganglioneuroblastoma nodulare con la tipica coesistenza di una superficie fibrosa benigna racchiudente un nucleo necrotico maligno.
In questo caso di tumore neuroblastico, la chirurgia da sola ha giocato un ruolo di trattamento definitivo.

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