

CASE REPORT

Soft tissue swelling in children: case report, differential diagnosis, and diagnostic delay

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Introduction

A benign or malignant tumor can present as a soft tissue swelling. Often these tumors are visible with the eye, but still an important delay in the final diagnosis is common. Here, we present an asymptomatic young female with a subcutaneous mass, who was referred to our hospital almost 1 year after initial presentation to the doctor.

Case Presentation

A 4-year old-female was referred to our hospital because of a swelling between the left scapula and the spine. Her mother first noticed the swelling a year ago. She consulted her general practitioner, who suspected a lipoma and proposed a wait and see policy. After 2 months, she was reexamined and an ultrasound of the mass was requested. No action was undertaken by the family because the swelling was not painful and did not change in size. The parents were not concerned and thought that the mass was not growing. It took more than 10 months before the ultrasound was performed, after which she was

Key Clinical Message

A general practitioner faces regularly soft tissue swelling in otherwise healthy children. Delay in diagnosis of soft tissue malignancies is often due to asymptomatic nature and the unfamiliarity with the age-dependent differential diagnosis. Hence, an accurate knowledge is important to prevent important delay in diagnosis of potential malignancies.

Keywords

Diagnostic delay, ganglioneuroblastoma, soft tissue swelling.

referred to our hospital for further diagnostics and treatment.

The swelling had not grown since the first presentation at her general practitioner. It was not painful and did not cause any limitation of her left shoulder. No night sweats, weight loss, or fever was noticed. Her additional medical history was free of major events.

Physical examination showed a solid swelling of about 5 cm in size just medial to the left scapula. The mass is not mobile or painful and is covered with normal intact skin (Fig. 1). Further physical examination was normal.

An ultrasound of the shoulder region showed a highly vascular inhomogeneous mass of 50 × 21 × 26 mm fused with the scapula. MRI of thorax/thoracic spine revealed an extended multilobulated mass, originating from the left neuroforamen on T6 or T7 (Fig. 2). There was no destruction of the bones, but it had grown into the lung apex and the mediastinum as well as into the left paravertebral muscles. The spine was displaced to the right side. ¹²³I-MIBG scintigraphy did not show any tracer uptake in the area of the mass. Ultrasound of the abdomen was normal.



Figure 1. Swelling of about 5 cm in size just medial to the left scapula.



Figure 2. MRI T1 fat-weighted image of the thorax revealing an extended multilobulated mass.

Comprehensive blood tests, including lactate dehydrogenase, uric acid, creatinine kinase, kidney function, liver function, electrolytes, complete blood count, and inflammatory parameters were normal. A 24-h urine collection did not show increased amounts of catecholamines.

A Tru-cut biopsy revealed a ganglioneuroblastoma of the intermixed type. The genetic examination showed a normal array CGH (comparative genomic hybridization) analysis, and FISH (fluorescence in situ hybridization) was negative for 1p depletion and MYCN amplification. Bone marrow aspiration and biopsy were normal. In view of the complexity of the localization of the tumor, a multidisciplinary team consisting of a neurosurgeon, a thoracic, and a pediatric surgeon was assembled to perform the operation. They removed the tumor through a combined anterior and posterior approach. First, a multilevel laminectomy was performed in prone position to remove the spinal and subcutaneous part of the tumor. The intrathoracic part was removed through a left thoracotomy.

Three days after the operation, the MRI showed a complete resection. The pathology of the tumor confirmed the diagnosis of the biopsy; the margins were free of tumor. After a week, she was discharged in good condition. Follow-up MRI scans showed no recurrent tumor growth. At 3.5 years follow-up, she had only a minor thoracic scoliosis deformity which will be evaluated annually by a pediatric orthopedic surgeon.

Discussion

Our case stood out because of major doctor and patient delay in diagnosis of the tumor. Multiple studies have identified several risk factors for this delay. Brouns *et al.* [1] reviewed 100 patients referred with soft tissue sarcoma to determine doctor- and patient-related delay. The most frequent reason of doctor-related delay (median of 4 months) was a wrong diagnosis at presentation (on clinical basis or on ultrasound), while the main reason for patient-related delay was a painless mass that was ignored. If the first symptoms were presented at the emergency department, there was less doctors delay, compared with children who presented at the general practitioners office [2]. This can be explained by the fact that a general practitioner rarely sees a soft tissue malignancy, probably only once every 20 years [3]. Several studies examined the causes of the patients delay before presenting to a doctor with a significant swelling. Painless swelling, not causing any discomfort, was reported most often. Patients and/or their parents often assume that the swelling is harmless. Dang-Tan *et al.* [2] reviewed retrospectively the patient delay of 1360 children and adolescents in Canada diagnosed with leukemia or lymphoma and concluded that a lower age was associated with a higher patients delay. Abdelkhalek *et al.* [4] investigated 172 children with cancer in Egypt to determine the factors associated with delay in diagnosis. They concluded

that delay is related to the child's age, family's socioeconomic status and parental education, cancer type, and localization of the malignancy.

In our case, there was a misinterpretation of the diagnosis of the mass at initial presentation. Although soft tissue masses in children are fairly common [5], they cover a heterogeneous group of lesions originating from extra skeletal nonepithelial tissues of the body, excluding the viscera, meninges, and lymphoreticular system. Also other tumors, not originating from the soft tissue, can present as a subcutaneous swelling. For that reason, when a child presents with a mass, the differential diagnosis is broad, consisting of malignant and benign tumors [6]. It may be clinically difficult to distinguish between the different diagnoses among other things, as a result of the (lack of) symptoms, the localization, and the age-related pathology.

Soft tissue tumors are general benign (approximately 100 times more common), especially when the swelling is superficial and less than 5 cm in diameter [7]. In adults, approximately one-third of all benign soft tissue swellings are lipomas, one-third are fibrous tumors, 10% are from vascular origin, and 5% are nerve sheath tumors [6]. In children, on the other hand, a benign subcutaneous swelling is more likely posttraumatic, a result of inflammation or a vascular or fibrous tumor [5]. A lipoma in childhood is quite rare and is only seen in about 4% of all soft tissue swellings [8]. Malignant soft tissue tumors account for less than 1% of the overall malignant tumors in adults [9]. In grown-ups, organ-specific tumors or metastasis are far more likely to cause subcutaneous masses [10]. In children, we have to consider lymphoma, rhabdomyosarcoma, and tumors of the sympathetic nervous system [11]. See Table 1 for an overview of the differential diagnosis of soft tissue tumors in children and adults.

Table 1. Differential diagnosis of soft tissue masses/subcutaneous swelling [5, 7, 11, 12].

	Children	Adults
Benign	Reactive swelling	Reactive swelling
	Inflammatory swelling	Inflammatory swelling
	Posttraumatic swelling	Posttraumatic swelling
	Hamartoma	Fibrous tumors
	Vascular tumors	Lipoma
	Myofibroma	Vascular tumors
Malignant	Lymphoma	Nerve sheath tumors
	Soft tissue sarcoma	Organ-specific tumors
	Rhabdomyosarcoma	Melanoma
	Ewing sarcoma	Non-Hodgkin lymphoma
	Synovial tumors	Metastasis
	Fibrosarcoma	Soft tissue sarcoma
	Sympathetic nervous system tumors	

Early referral of children suspected of soft tissue sarcomas, is believed to improve prognosis, although there are no studies to prove this. Due to the rarity of soft tissue sarcomas (about 7% of all childhood malignant tumors [12]), most general practitioners will never come across a soft tissue sarcoma during their professional career. Guidelines have been introduced to prevent important clinical delay [13]. Any child with a soft tissue mass increasing in size, with size larger than 5 cm or localized underneath the deep fascia, whether or not painful, should be referred to a tertiary center under suspicion of a soft tissue malignant tumor [14].

We report a female with a large ganglioneuroblastoma, an uncommon neuroblastic tumor arising from the sympathetic nervous system. Ganglioneuroblastomas occur most commonly in infants and young children. They are uncommon after the age of 10 years. Both genders are equally affected. Most of these tumors occur in the abdomen, mediastinum, neck, and pelvis [15]. The International Neuroblastoma Pathology Classification distinguishes four categories based on the balance between the undifferentiated neural-type cells and mature Schwann-type cells, reflecting the spectrum of maturity of the tumor [16]. The most benign tumor is the ganglioneuroma, which consist of mature Schwannian stroma. Ganglioneuroblastoma (intermixed or nodular), as present in our patient, is composed of both mature gangliocytes and immature neuroblasts. Neuroblastoma is the most malignant tumors and exist of immature, undifferentiated cells, or poorly differentiated and is Schwannian stroma-poor [17]. Most of the patients with a ganglioneuroblastoma present with a painful swelling due to local infiltration of the primary tumor. They can also present with metastatic disease (most often the bone or the liver) or other signs and symptoms due to the location of the tumor [18]. Our patient, however, was completely asymptomatic. Generally, ganglioneuroblastomas are regarded as less aggressive tumors than neuroblastomas [19]. They can produce catecholamines, which are important diagnostic markers. As in our patient with ganglioneuroblastoma of the intermixed type, surgery is the only necessary treatment. The prognosis is relatively good [19]. These tumors can sometimes even regress spontaneously or/and mature into benign ganglioneuromas [20].

Conclusion

We present a young female with a subcutaneous mass, who was diagnosed and treated after a long patient-related and doctor-related delay, due to the asymptomatic character of the lesion and the unfamiliarity of the health-care workers with the age-related differential diagnosis.

Conflict of Interest

The authors have no conflicts of interest to disclose.

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