Cervical Neuroblastoma

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Abstract

Cervical neuroblastoma is relatively uncommon. It presents, most often as a firm mass in the lateral neck. Primary neuroblastomas of the neck usually arise in the cervical sympathetic ganglia. They are the sixth most common head and neck extracranial neoplasms. Neuroblastoma is the most common malignancy in children under 1 year of age. No known cause of Neuroblastoma has been reported.

Introduction

Neuroblastoma is the most common extracranial solid malignancy in children, arising from undifferentiated precursor cells of the sympathetic nervous system. A cervical location is relatively uncommon [1] (3–5%) as compared with other reported sites such as the abdomen (65 %) posterior mediastinum (15%), pelvis (5%), and miscellaneous (12%). Cervical neuroblastomas present, most often as a firm mass in the lateral neck. 70% of neuroblastomas that are discovered in the head and neck region are metastatic lesions [1]. Primary neuroblastomas of the neck usually arise in the cervical sympathetic ganglia.

Neuroblastoma is more common in whites, and it is slightly more prevalent in boys than in girls. The male-to-female ratio is 1.3:1. The average age at diagnosis is two years. 97% are diagnosed by age 10 years.

Keywords Cervical neuroblastoma · Cervical sympathetic ganglia · Neuroblastoma

A case of primary cervical neuroblastoma in a 13 years old girl is presented here.

Case History

A 13-year-old female child was admitted in ENT Deptt. with complaints of swelling neck (left) for three months. It was progressive and within 3 months had reached massive size. It was associated with pain (Fig. 1). Family/Personal History was non contributory. Routine blood investigations were normal. CT scan demonstrated soft tissue density mass with calcification, from infratemporal region to level of thyroid gland, extending up to left parapharyngeal space & oropharynx (Fig. 1). There was no bony erosion. There were multiple LN masses at level I & III on Lt side. Her USG-Doppler Neck revealed high vascularity of mass with specks of calcification. As mass was very big no comment on vessels was possible. Her incisional biopsy revealed Neuroblastoma (Fig. 2). She was further investigated to R/O intrabdominal or metastatic involvement. Then she was put on chemotherapy: Vincristine, Adriamycin and Cyclophosphamide. Four cycles were given. Except few nodes and a small mass near the great vessels in the neck, rest of Tumour disappeared with chemotherapy (Fig 2). Surgical management of remaining lesion was not possible because of its propensity to great vessels.

Discussion

Virchow first described neuroblastoma in 1864, and, at that time, it was referred to as a glioma. In 1891, Marchand histologically linked neuroblastoma to sympathetic ganglia. In 1957, Mason published a report of a child with neuroblastoma whose urine contained pressor amines.

During the fifth week of embryogenesis, primitive sympathetic neuroblasts migrate from the neural crest to the site where the adrenal anlage eventuates into the developing embryo [2]. These neuroblasts migrate along the entire sympathetic chain; therefore, neuroblastoma can

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Fig. 1 Photograph and CT scan at presentation

Fig. 2 HPE slide of lesion and post chemotherapy appearance

arise anywhere along the sympathetic nervous system. The name neuroblastoma is derived from the fact that the cells resemble primitive neuroblasts.

Multiple primaries can occur and may reflect an inherited predisposition. This embryonic neoplasm often encases major blood vessels and, unlike most solid cancers, usually presents with substantial metastatic disease [3]. About 60% of patients have metastases in cortical bone, bone marrow, lymph nodes, and liver, but spread to lung or brain is rare despite hematogenous dissemination.

Neuroblastoma has been called the great mimicker because of its myriad clinical presentations related to the site of the primary tumor, metastatic disease, and its metabolic tumor by-products.

According to Knudson and Stong [4] (1972), 20% of neuroblastomas are inherited through an autosomal dominant pattern. A variety of karyotypic abnormalities can occur, but deletion of the short arm of chromosome 1 is found in 70–80% of all patients with neuroblastomas or amplification of the *N-myc* oncogene. Recent studies, however, favor chromosome 16p12–13 as a more likely predisposition locus.

Neuroblastoma is the most common malignancy in children under 1 year of age [5]. More than a third of cases

(36%) are diagnosed in children younger than 1 year. The average age at diagnosis is two years. 79% diagnosed children are younger than 4 years, and 97% are diagnosed by age 10 years. There is also a second peak of tumor incidence that affects older children. It is extremely difficult to diagnose in small children, and once diagnosed, its progression is often rapid, and very painful. Although neuroblastoma accounts for only 8% of all cancers, it is responsible for over 15% of the deaths.

Neuroblastoma is unique in several different ways. It has a documented spontaneous rate of resolution. Sometimes the cells die without any cause and the tumor disappears. This is part of a normal process known as programmed cell death (*apoptosis*), the normal process that occurs when cells die. This tumor disappearance is much more common in very young infants than in older children.

Another behavior that is unusual for childhood tumors is that the cells sometimes mature spontaneously to normal ganglion cells and stop dividing. This causes the tumor to become a ganglioneuroma, which is benign (non-cancerous).

It also is one of the few tumors in which the surgical capsule can be violated, leaving residual tumor, and a good outcome still might be achieved. It also releases hormones that

can cause strange changes in the body, such as constant diarrhea. It can also cause changes in some functions of the brain giving rise to *opsoclonus* (rotary movements of the eyes) and *myoclonus* (spastic jerks of the muscles). For unknown reasons, neuroblastoma tumors that produce this syndrome are less life threatening than other forms of the disease.

Tumors located in the head and neck may present as a smooth, solid, rubbery, painless mass in the neck. The child may have Horner's syndrome, ophthalmoplegia, conjunctival or eyelid edema or papilledema [6]. An associated finding of heterochromia irides is also possible. In addition, children whose disease has spread to the bones around the eye socket may have dark circles around the eyes. This is often referred to as "raccoon eyes."

Intracranial extension of a cervical neuroblastoma via the jugular foramen or carotid canal with potential involvement of cranial nerves IX, XI, XII has been noted. Blue or purple patches, resembling small bruises, may indicate spread to the skin. Sometimes there is bruising around the eyes.

If the bone marrow (the tissue that makes blood cells) is affected, the child may not have enough red blood cells, white blood cells, or blood platelets. These shortages of blood cells can result in weakness, frequent infections, and excessive bleeding from small cuts or scrapes.

The two most important factors in the prognosis for a child with neuroblastoma are the stage of the disease and the age of the child at the time of diagnosis. For all stages, infants less than one year old have a much better chance for remission and survival than older children. This age group has the best prognosis, with cure rates as high as 90%. Early diagnosis is one of our best weapons in the war against neuroblastoma.

The criteria necessary to make a diagnosis of neuroblastoma as established by the International Neuroblastoma Staging System includes:

- a definitive histologic diagnosis on light microscopy +/- immunohistochemistry, electron microscopy
- presence of elevated vanillylmandelic acid (VMA), or homovanillic acid (HVA), in their urine. A low VMA-to-HVA ratio is consistent with a poorly differentiated tumor and indicative of a poor prognosis.
- a bone marrow biopsy demonstrating unequivocal tumor cells

The metastatic work up for neuroblastoma is similar to that for other pediatric malignancies and includes chest x-ray, bilateral iliac crest bone marrow biopsy, bone scan, CT or MRI of the neck and abdomen. Abramson et al [6] in a report of cervical neuroblastoma in eleven infants have observed that MRI has been the method of choice for delineating the extent of disease. MRI has better soft-tissue resolution and also demonstrates well the relationship of the tumor to vascular structures.

Adverse clinical prognostic factors include osseous metastases, substantial involvement of bone marrow in infants, and any degree of distant bone marrow invasion in older patients. Genetic features associated with a poorer prognosis

include deletions of chromosome 1p, *N-myc* amplification and diploid or normal DNA content⁷.

A variety of staging systems for neuroblastoma exist that take into account tumor burden, surgical resectability and metastatic disease.

The TNM criteria:

Stage I:	Primary tumor <5cm with no regional or distant disease.
Stage II:	Tumors >5cm but <10cm with no regional or distant disease.
Stage III:	Tumors up to 10cm plus regional disease or tumors over 10cm +/- regional disease but without distant disease.
Stage IV:	Single primary tumor +/- regional disease and presence of distant disease.
Stage V:	Ulticentric primary tumors +/- regional or distant disease.

Treatments are available for children with all stages of neuroblastoma. More than one of these treatments may be used, depending on the stage of the disease. The four types of treatment used are:

Surgery
Radiation therapy
Chemotherapy
Bone marrow transplantation

Surgery is used whenever possible, to remove as much of the tumour as possible, and can generally cure the disease if there is no spread of disease. Adjacent lymph node chains, if involved with tumor, should also be removed. Chemotherapy (adjuvant chemotherapy) may also be used after surgery.

Before surgery, chemotherapy may be used to shrink the tumor so that it can be more easily removed during surgery (neoadjuvant chemotherapy).

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