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Case Report

Cervical Ganglioneuroma with Lymph Node Metastasis

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ABSTRACT

Ganglioneuroma (GN) is an uncommon, most mature variant of neuroblastic tumors of neural crest origin. Though benign, metastasis is rarely encountered in lymph node, liver, bone, spleen and soft tissues. A six year old female child presented with swelling in the right side of the neck of four and half years duration. Computed Tomography (CT) scan showed mass in the neck extending from base of the skull to the level of C7 vertebral body with multiple enlarged level II lymph nodes bilaterally. The excised mass showed features of GN (Schwannian stroma- dominant) mature type with metastasis in adjacent lymph node. It is important to recognize this entity as the prognosis is excellent following complete excision of primary tumor and the metastatic focus.

Key Words: Ganglioneuroma, lymph node, metastasis

INTRODUCTION

Ganglioneuroma (GN) is a rare, most differentiated variant of neuroblastic tumors of neural crest origin, arising from sympathetic ganglia and adrenal medulla. [1] The clinical behaviour of these tumors is invariably benign. [2] Most of them develop de novo rather than by way of maturation of previous neuroblastoma(NB) or ganglio-neuroblastoma (GNB). [3] Rarely they may show metastasis in lymph node, liver, bone, spleen and soft tissues. [1,3-6]

CASE REPORT

A female child aged six years was admitted with history of swelling in the right side of the neck of four and half years duration. Biopsy done four years back showed features of GN. Partial excision was done one year later and since then the swelling was of the same size. The child was not put on any chemotherapeutic drugs or radiation. There were no other complaints. On examination the swelling measured 5X4 cms, non-tender, freely mobile with a scar mark on the overlying skin. The blood pressure was normal. All the laboratory investigations including urine levels of catecholamines and their metabolites were within normal limits. Ultrasonography of the neck showed soft tissue density on the right side measuring 6X5 cms displacing vessels. Computed tomography (CT) scan showed minimally enhancing mass on the right side of the neck measuring 7.5X5.3X5 cms extending from base of the skull to the level of C7 vertebral body. There was no extension to intervertebral foramina (Figure

1a). There were multiple enlarged level II lymph nodes bilaterally. CT scan of thorax and abdomen were unremarkable. Intra-operatively multiple nodules were seen on the right side of the neck displacing carotid artery and its bifurcation laterally and jugular vein posteriorly. The three nodules were excised.

The larger nodule measured 5X4X3 cmsand each smaller nodules measured 1X1X0.5 cms. They were solid, yellowish gray with trabeculations (Figure 1b).Microscopy of the larger and one of the smaller nodules showed tumor composed of spindle cells resembling Schwann cells and collagen bundles arranged in fascicles separated by myxoid stroma. They were admixed with ganglion cells. Few of them were in clusters. There were no neuroblasts or areas of haemorrhage or necrosis or mitotic activity(Figure2a).Sections from the other nodule showed structure of lymph node with tumor deposits morphologically similar to other nodules (Figure 2b). There were foci of calcification.

On immunohistochemistry the spindle cells were diffusely positive for S-100 protein (Figure 3a). Immunostains for chromogranin and synaptophysin were negative (Figure3b). The lymphocytes at the periphery were positive for LCA. Based on these findings a diagnosis of GN (Schwannian stroma-dominant) mature type with lymph node metastasis was made.

The patient is doing well without any recurrence or new lesions four years after the operation. No additional therapy was administered.

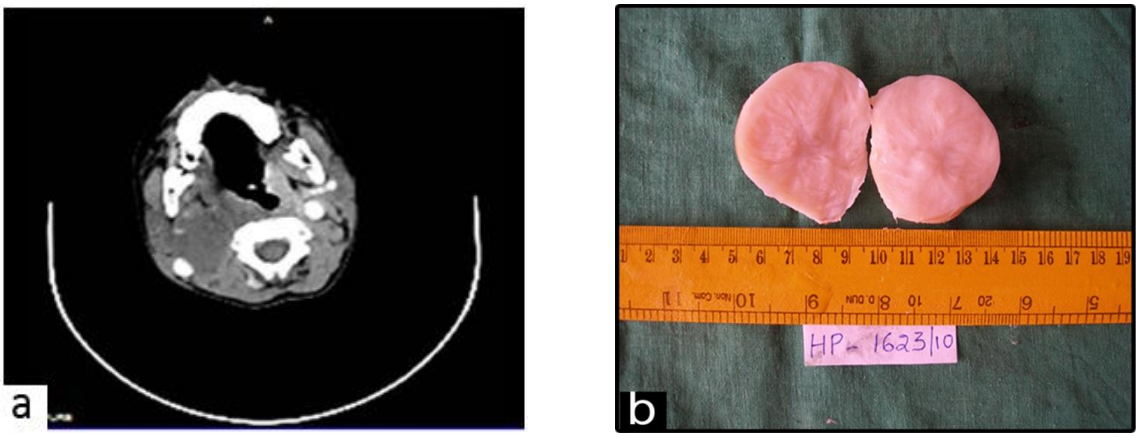

Figure 1. a) CT (Contrast enhanced axial view) scan showing minimally enhancing mass in the neck region. b) Gross photograph of primary tumor with solid yellowish cut surface.

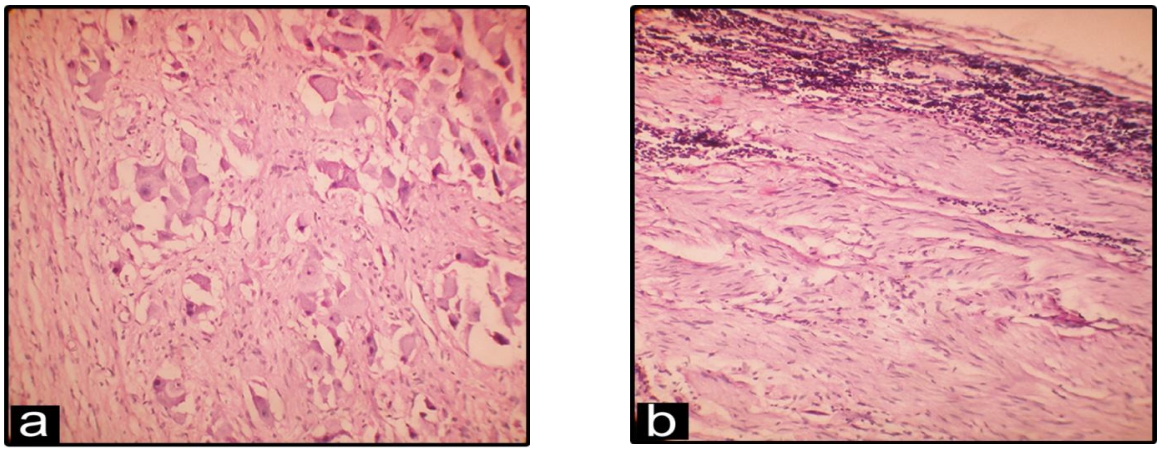

Figure 2. Microphotograph of a) primary tumor showing spindle cells and ganglion cells, b) lymphnode with metastatic deposit (H&E, X 400)

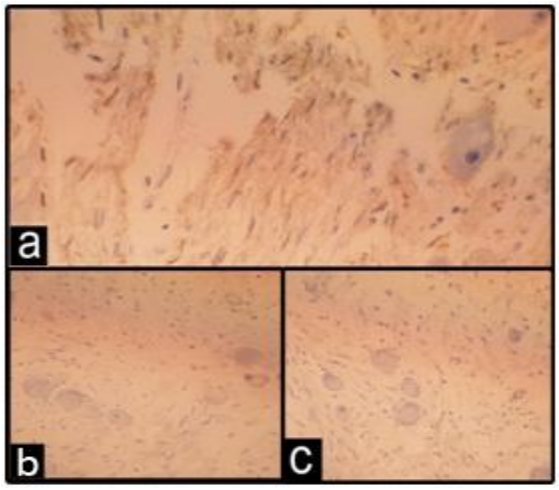

Figure 3. Immunohistochemistry showing a) reactivity of spindle cells for S-100 protein. Immunostain for b) chromogranin and c) synaptophysin were negative (IHC,X 400).

DISCUSSION

Ganglioneuromas are usually seen between 10-40 years. [3] The commonest sites are posterior mediastinum and retroperitoneum. [2] They are also reported in adrenal gland, heart, bone, intestine and parapharyngeal region. [4] In contrast, NB are seen in younger age group, [1] with adrenal medulla as the most common site. [5] Most of the cases of GN are asymptomatic. Rarely they may show hypertension, watery diarrhea, hypokalemia and masculinization. There are no clinical diagnostic features differentiating GN from NB. [3]

According to International Neuroblastoma Pathology Classification (INPC), the neuroblastic tumors are classified into NB, GNB and GN with varying maturation pattern. Ganglioneuroma is divided into mature and maturing subtypes. [3] Two unique features of NB are spontaneous regression and maturation. [7] Regression of NB most commonly occurs in stage IVS tumors. [5] Though spontaneous maturation is well known, its occurrence in metastatic sites is extremely rare. [6]

Studies have shown that NB cells exhibiting intact chromosome 1, near triploid DNA values and lack of N-myc overexpression mature into GN. [1] There is a tumor suppressor gene on chromosome arm 1p that is deleted in NB. [8] Hyperdiploid NB with normal chromosome arm 1p stimulates Schwannian proliferation within the tumor which promotes tumoral maturation. [8] It is postulated that increased levels of nerve growth factor (NGF) which is encoded by TrKA proto oncogene is responsible for spontaneous maturation. [3] This hormone is [essential for maintenance of sympathetic neurons acting primarily to accelerate differentiation. [6] In situ hybridization, flow cytometry or gene expression studies were not done in our case.

In a study done by Brook et al, favourable histological features in tumor differentiation of NB were tumors with stroma rich group and tumors with decreasing mitosis karyorrhexis index (MKI). [9] The presence and amount of immunohistochemical stains for S-100 protein, neuron specific enolase and protein gene product 9.5 tended to increase with tumor differentiation. [9] In peripheral neuroblastic tumors with genotype – phenotype discordance Suganuma et al have suggested that presence of prominent nucleoli which is critical for subsequent N-myc protein expression in NB cells is the key for predicting clinical behavior. [10] Some centers consider ratios of vanillylmandelic acid (VMA) to homovanillic acid (HVA) as an indicator of maturity. Ratios of VMA to HVA less than one are considered favorable and ratios greater than one suggest immature tumor. [8]

Ganglioneuromas often show incomplete maturation at the metastatic focus. [3] In our case the primary tumor and metastatic focus showed complete maturation. According to International Neuroblastoma Staging System (INSS), it would have been classified into stage II B. Studieshave shown that in metastatic GN, cytomaturation of NB is the only

satisfactory explanation and the concept of benign metastasizing GN is untenable, as the mature ganglion cells have little or no capacity for proliferation. [6]

The prognosis is excellent following complete excision. [1,3,5,10] Local recurrence and malignant transformation into peripheral nerve sheath tumor have been reported. [5] Hence long term follow up is necessary.

CONCLUSION

Fully differentiated metastasis of GN is a rarely documented phenomenon. We assume that, primary tumor and metastasis represent NB which probably matured into GN.

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