

Case Report

Ganglio neuroma With Mononuclear Cell Infiltration – A Diagnostic Dilemma

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Abstract: Ganglio neuromas are childhood Peripheral Neuroblastic tumors (pNTs) derived from precursor cells of the sympathetic nervous system. The differential diagnosis includes Ganglio neuroblastoma. A definite diagnosis & typing is necessary as prognosis depends on it. Here we report a case of Ganglio neuroma in a nine year old child presenting as solitary mediastinal mass. Our study specially shows the importance of immunohistochemistry in this regard.

Keywords: Ganglio neuroma; Peripheral Neuroblastic tumors (pNTs); LCA.

INTRODUCTION:

Ganglio neuroma is a rare slow growing benign neoplasm belongs to Peripheral neuroblastic tumour (pNTs), cells of which are of sympathoadrenal lineage migrating from neural crest [1]. PNTs represent a spectrum ranging from most mature Ganglio neuroma to Neuroblastoma (most primitive form) depending on cellular & extracellular maturation [2]. Ganglio neuroblastoma stands in between them & come in main differential diagnosis of Ganglio neuroma. Presence of mature ganglion cell differentiates it from neuroblastoma & ganglio neuroblastoma [3]. A definite diagnosis & typing is necessary as prognosis depends on it. Here we report a case of Ganglio neuroma in a nine year old child presenting as solitary mediastinal mass. Our study specially shows the importance of immunohistochemistry in this regard.

CASE REPORT:

A nine years old male child presented in Pediatric OPD with gradual onset of chest discomfort since one year. He had also complained of easy fatigability during playing or climbing upstairs. Physical examination was normal. On routine chest X-ray, an oval shaped radio-opaque mass was found in posterior mediastinum. CT scan also confirmed the presence of solid well defined 8x6x6 cm mass without significant contrast enhancement. Preoperative diagnosis based on radiological & clinical finding was neurogenic tumour or sarcoma. He was operated in this tertiary care hospital & and the specimen was sent to the department of Pathology for histopathological examination.

On gross examination, it was gray to tan colored firm lobulated soft tissue mass measuring 8x7x5 cm. It was firm in consistency. Cut section has a whorl appearance. No hemorrhagic or calcified area found.

On microscopical examination H & E stained sections showed the lesion was composed of spindle shaped cells with wavy nucleus in a matrix of fibrous elements. There were isolated collections of mature ganglion cells. Some areas showed collections of small mononuclear cells in small groups in the fibrous stroma (Fig.1).

The provisional differential diagnosis were –

1. Ganglio neuroma (mature type with lymphocytic infiltration).
2. Ganglio neuroma (maturing type).
3. Ganglio neuroblastoma (stroma rich intermixed type).

Immunohistochemical study was done using monoclonal antibody against leukocyte common antigen (LCA) and neuron specific enolase (NSE). It showed that the small mononuclear cells in small groups were LCA positive (Fig.2) and NSE negative confirming their lymphocytic nature. So the final diagnosis was ganglio neuroma (mature Type) with lymphocytic infiltration.

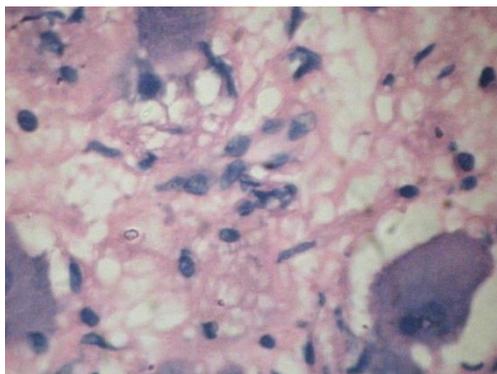


Fig 1: Photomicrograph showing fibrous stroma, small mononuclear cells and mature ganglion cells (H&E X 400).

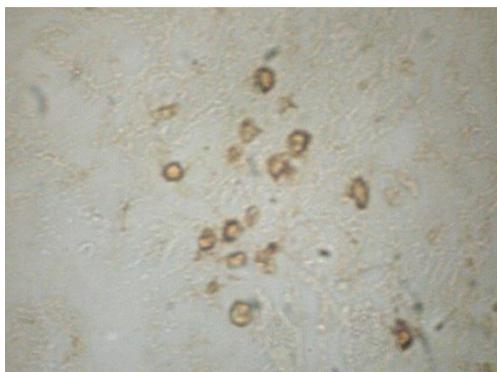


Fig 2: Photomicrograph showing LCA positivity of the small mononuclear cells (immuno staining by monoclonal antibody against LCA X 400).

DISCUSSION:

Ganglioneuromas are arising most frequently in the mediastinum and retroperitoneum in children & young adult [4]. Other possible locations are adrenal gland, cervical & parapharyngeal area, genitourinary tract, pancreas, skin, orbit and appendix [1]. A predilection for woman has been noted, particularly in maxillary sinus, liver, adrenal & mediastinum [1]. Incidence of Ganglio neuroma is reported as one per million populations [2]. It can be a primary tumour or arising from neuroblastoma or ganglio neuroblastoma either spontaneously or therapy induced [5]. Though it is usually sporadic but cases have been found in association with Neurofibromatosis type I [1] and also with Neurofibromatosis type II, Multiple Endocrine Neoplasia type II.[5] Copresentation with Pheochromocytoma also reported [3]. Prognosis of Ganglio neuroma is good with estimated 5 year survival rate >90% [6].

Macroscopically, they are large encapsulated masses of firm consistency & a tan-white color. Hemorrhage & calcification are not common. Microscopically, it is a mass of neuritis and originating ganglion cells. There are two subtypes – maturing & mature as per INPC scheme [1]. The “mature” ganglio

neuroma is composed of fully mature ganglion cells surrounded by satellite cells, embedded in Schwannian stroma. The “maturing” subtype shows presence of differentiating neuroblasts and immature cells along with fully mature ganglion cells [7].

Immunohistochemistry shows positive neuron specific enolase (NSE) & other neuronal markers e.g. Synaptophysin, neuro filament protein, etc. It is recommended that in the immunohistological diagnosis of neuroblastic tumors, positive staining for neuronal markers combined with negative staining for markers of other small round cells should be considered [8]. In our study, as the small round cells were NSE negative, possibility of their neuronal origin was excluded. LCA positivity confirmed their lymphocytic nature. Lauder *et al* showed the significance of lymphocytic infiltration in neuroblastoma [9].

A diagnostic dilemma arises in subtyping the tumor when the neuroblasts of maturing subtype are confused with infiltrating lymphocyte in mature subtype, especially in H & E stain. Moreover it may also be confused with the intermixed neuroblasts of stroma rich ganglio neuroblastoma. In the present study, these small mononuclear cells were found to be leukocytic origin as they were LCA positive and NSE negative in immunohistochemical study. As the prognosis depends on degree of maturation, this immunohistological comparison is of immense importance. Pauchmaur *et al.*; showed that histopathological classification has prognostic impact in predicting overall and event free survival in peripheral neuroblastic tumors [10].

Hsiao *et al.*; showed expression of delta-like gene and protein in mature neuro matous stroma & gangliocytes of ganglio neuroma, but not in neuroblasts of neuroblastoma and ganglio neuroblastoma, neither in gangliocytes of ganglio neuroblastoma [11].

CONCLUSION:

Ganglio neuroma is a benign slow growing tumour with excellent prognosis after surgical resection. Preoperative diagnosis is difficult as there are no characteristic imaging finding. Diagnosis is based on histopathological examination after surgical excision and immunohistochemical study is helpful for proper classification of neuroblastic tumors which is essential for assessment of prognosis.

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