

NEUROGENIC TUMORS OF THE MEDIASTINUM

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Mediastinal lesions are uncommon and usually neurogenic in origin, located almost in the posterior mediastinum. Their special location is generally paravertebral sulci. Thymomas (27.8%), benign mediastinal cysts (20.0%), and lymphomas (16.1%) were most common. The distribution of lesions varied among mediastinal compartments; thymomas (38.3%), benign cysts (16.8%), and neurogenic tumors (53.9%) were the most common lesions in the prevascular, visceral, and paravertebral mediastinum. The relative incidence of the various cell types and their corresponding risk of malignancy are strongly correlated with age. Children and young are having more tumors of the autonomic ganglia, two thirds of which are malignant. In adults, tumors arising from nerve sheath show vast majority and are with benign nature. These lesions differed by continent or country, with benign cysts being the most common mediastinal lesions in the People's Republic of China, thymomas in Europe, and lymphomas in North America and Israel. Benign cysts, thymic carcinomas, and metastases were more often seen in larger hospitals, whereas lymphomas and thymic hyperplasia occurred more often in smaller hospitals (1).

For malignant mediastinal masses of children, lymphoma was most common diagnosis (66.0%) following neuroblastoma (10.7%), germ-cell tumour (5.4%) and T-cell acute lymphoblas-

tic leukaemia (17.9%). Intensive care unit (ICU) admission ratio may be 37.5%. Factors that are significantly associated with ICU admission are stridor, pericardial effusion and need for pleural drainage. Almost all patients (98.2%) were symptomatic on presentation, of which lymphadenopathy was the most common (69.6%) (2-3). Within the mediastinal masses, neurogenic tumors have a relatively high number. Distribution of diagnosis was neurogenic tumour 52%; thymic tumour 20%; teratoma 14% and lymphoma 14%. For cystic group 66% bronchogenic cyst; 17% pericardial cyst and 7% hydatid cyst^{1,2,3,4}.

Neurogenic tumors may arise from neural elements anywhere within the thorax including nerve sheath, autonomic ganglia and paraganglionic tissues. All of which trace their embryologic heritage to the neurologic crest. These tumors may exhibit a variety of cytologic products and immunohistochemically markers that aid in pathologic diagnosis⁵. Intraspinal extension of tumor via the spinal foramen occurs in approximately 10% of cases. They may be asymptomatic and discovered incidentally. Significant correlation has been found without a capsule, low degree of atypia, a low mitotic index, and low cellularity for the potential for malignancy. Surgical resection was the main treatment and the mean survival was estimated to be 51.3 months. Significant difference in survival was detected according to

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differentiate the masses from neurogenic tumors and other posterior mediastinal diseases⁷⁰.

REFERENCES

- Roden AC, Fang W, Shen Y, Carter BW et al. Distribution of mediastinal lesions across multi-institutional, international, radiology databases. *J Thorac Oncol* 2020; 15:568-579.
- Lee SH, Oh BL, Kimpo M, Quah TC. Epidemiology of childhood malignant mediastinal masses and clinical factors associated with intensive care unit admission: A Singapore experience. *J Paediatr Child Health* 2020 Mar 12. doi:10.1111/jpc.14808 Epub.
- Scusi E, Vaporciyan A. Benign and malignant neurogenic tumors of the mediastinum in children and adults. *LoCicero, J. Shields' General Thoracic Surgery*, 8th Edition. Ch 170; pp 2194-2225
- Ayan E, Balci AE, Özalp K, Duran M, Vuraloğlu S, Çekirdekçi A. *Turkish J Thorac Cardiovasc Surg* 2005;13:127-130.
- Bousamra M, Wrightson W. Neurogenic tumors of the mediastinum. In *Patterson GA, Pearson's Thoracic and Esophageal Surgery*. 3th edition, 2008: Ch 134; 1634-40.
- Mlika M, Marghli A, Ines Souilem, Abdennadher M et al. A single-institution experience of neurogenic tumors of the mediastinum. *Asian Cardiovasc Thorac Ann* 2019;27:661-669
- Whooley BP, UrschelJD, AntkowiakJG, et al: Primary tumors of the mediastinum. *J Surg Oncol* 70:95-99, 1999
- Ovrum E, Birkeland S. Mediastinal tumours and cysts. A review of 91 cases. *Scand J Thorac Cardiovasc Surg* 1979;13:161-168.
- Czyzewski K, Gawrychowski J, Starossolski B, Dzedzic M et al. Surgical treatment of primary neurogenic mediastinal tumors (Polish). *Pneumonol Alergol Pol.* 1993;61:503-508.
- Loneragan GJ, Schwab CM, Suarez ES, Carlson CL. Neuroblastoma, ganglioneuroblastoma, and ganglioneuroma: Radiologic-Pathologic Correlation. *Radiographics* 2002; 22: 911-34
- Joshi VV, Cantor AB, Altshuler G et al. Age-linked prognostic categorization based on a new histologic grading system of neuroblastomas. A clinicopathologic study of 211 cases from the Pediatric Oncology Group. *Cancer* 1992; 69: 2197-2211.
- Peuchmaur M, d'Amore ES, Joshi VV, et al. Revision of the international Neuroblastoma Pathology Classification: confirmation of favorable and unfavorable prognostic subsets in ganglioneuroblastoma, nodular. *Cancer* 2003; 98: 2274-2281.
- Ebert W, Ryll R, Muley T, Hug G, Drings P. Do neuron-specific enolase levels discriminate between small-cell Lung cancer and mediastinal tumors? *Tumour Biol* 1996;17: 362-8
- Sandoval JA, Malkas LH, Hickey RJ. Clinical significance of serum biomarkers in pediatric solid mediastinal and abdominal tumors. *Int J Mol Sci* 2012; 13: 1126-1153.
- Chen C, Notkins AL, Lan MS. Insulinoma-associated-1: from neuroendocrine tumor marker to cancer therapeutics. *Mol Cacer Res* 2019; 17: 1597-1604.
- Rooper LM, Sharma R, Li QK, Illei PB, Westra WH. INSM1 Demonstrates Superior Performance to the Individual and Combined Use of Synaptophysin, Chromogranin and CD56 for Diagnosing Neuroendocrine Tumors of the Thoracic Cavity. *Am J Surg Pathol* 2017; 41: 1561-1569
- Scheibel E, Rechnitzer C, Fahrenkrug J, Hertz H. Vasoactive intestinal polypeptide (VIP) in children with neural crest tumours. *Acta Paediatr Scand* 1982; 71: 721-5.
- Zhang WQ, Liu JF, Zhao J, et al. Tumor with watery diarrhoea, hypokalaemia in a 3-year-old girl. *Eur J Pediatr* 2009;168(7):859-862.
- Newman EA, Abdessalam S, Aldrink JH, Austin M et al. Update on neuroblastoma. *J Pediatr Surg.* 2019;54:383-389
- Mueller S, Matthay KK. Neuroblastoma: biology and staging. *Curr Oncol Rep* 2009;11(6):431-438. (LoCicero, 20180619, p. 2223)
- Kaddour AA, Chaabouni s, Mlika M, Kilani T et al. Neuroblastoma of the posterior mediastinum in a 61 year-old woman. *Resp. Med extra* 2001; 3; 114-116
- Hasegawa T, Hirose T, Ayala AG, et al. Adult neuroblastoma of the retroperitoneum and abdomen: clinicopathologic distinction from primitive neuroectodermal tumor. *Am J Surg Pathol* 2001;25:918-924.
- Chalvatzoulis E, Wohlschlaeger J, Hager T, Chefou D, Eberhardt W et al. Resection of a giant neuroblastoma misdiagnosed as atypical mediastinal carcinoid. *J Thorac Oncology* 2014; 9:132
- Hoover EL, Hsu HK, Dressler C, et al. Neuroblastoma: a rare primary intrathoracic neurogenic tumor in adults. *Tex Heart Inst J* 1988;15(2):107-112. (LoCicero, 20180619, p. 2223).
- Taxy JB. Electron microscopy in the diagnosis of neuroblastoma. *Arch Pathol Lab Med* 1980;104(7):355-360.
- S Suita, T Tajiri, Y Sera, H Takamatsu, et al. The characteristics of mediastinal neuroblastoma. The characteristics of mediastinal neuroblastoma: *Eur J Pediatr Surg* 2000; 10: 353-9.
- Rudolf JA, Thapa M. Thoracic neuroblastoma. *Radiol Case Rep.* 2011; 6: 440.
- Brodeur GM, Pritchard J, Berthold F, et al. Revisions of the international criteria for neuroblastoma diagnosis staging and response to treatment. *J Clin Oncol* 1993;11:1466
- Kushner BH. Enigmatic entities: opsoclonus myoclonus ataxia syndrome linked to neuroblastoma. *Lancet Child & Adol Health* 2018; 2: 3-5
- Cotterill SJ, Pearson ADJ, Pritchard J, Foot ABM, Roald B et al. Clinical prognostic factors in 1277 patients with neuroblastoma: results of The European Neuroblastoma Study Group Survey 1982-1992. *Eur J Cancer* 2000; 36: 901-908.
- Tolbert VP, Matthay KK. Neuroblastoma: clinical and biological approach to risk stratification and treatment. *Cell Tissue Res* 2018; 372: 195-209.

32. Mueller S, Matthay KK. Neuroblastoma: biology and staging. *Curr Oncol Rep* 2009;11(6):431-438.
33. Lee H, Han DK, Oh JW, Hong EK, Jeon SC. Occult mediastinal ganglioneuroblastoma presenting with myoclonic encephalopathy as paraneoplastic syndrome. *J Korean P Society* 1994; 37: 695-700.
34. Fatimi SH, Bawany SA, Ashfaq A. Ganglioneuroblastoma of the posterior mediastinum: a case report. *J Med Case Rep* 2011; 5: 322.
35. Kubote M, Suita S, tajiri T, Shono K, Fujii Y. Analysis of the prognostic factors relating to better clinical outcome in ganglioneuroblastoma. *J Pediatr Surg* 2000; 35: 92-5
36. Fraga JC, Aydogdu B, Auferi R, silva GVMS, Schopf L et al. Surgical treatment for pediatric mediastinal neurogenic tumors. *Ann Thorac Surg* 2010; 90: 413-418.
37. Husain K, Thomas E, Demerdash Z, Alexander S. Mediastinal ganglioneuroblastoma-secreting vasoactive intestinal peptide causing secretory diarrhea. *Arab J Gastroen* 2011; 12: 106-108.
38. Decarolis B, Simon T, Krug B, Leuschner I, Vokuhl C et al. Treatment and outcome of ganglioneuroma and ganglioneuroblastoma intermixed. *BMC Cancer* 2016; 16: 542.
39. Kirchweber P, Wundsam HW, Fischer I, Sophie C et al. Total resection of a giant retroperitoneal and mediastinal ganglioneuroma-case report and systematic review of the literature. *World J Surg Oncol* 2020; 18: 248
40. Okamatsu C, London WB, Naranjo A, Hogarty MD et al. Clinicopathological characteristics of Ganglioneuroma and Ganglioneuroblastoma: A Report from the CCG and COG. *Pediatr Blood Cancer* 2009; 53: 563-9.
41. Galganski AL, Hirose S, Saadai P. Resection of a thoracoabdominal ganglioneuroma via a retroperitoneal minimally invasive approach. *J Pediatr Surg Case R* 2019; 40: 47-49.
42. Jeon YJ, Son J, Cho JH. Harlequin Syndrome following resection of mediastinal ganglioneuroma. *Korean J Thorac Cardiovasc Surg* 2017; 50: 130-2
43. Benjamin Y, Walczyk K, Mohanty SK, Coren CV et al. Radiology-pathology conference: incidental posterior mediastinal ganglioneuroma. *Clin Imaging* 2009; 33: 390-394.
44. Boland JM, Colby TV, Folpe AL. Intrathoracic peripheral nerve sheath tumors-a clinicopathological study of 75 cases. *Human Pathology* 2015; 3: 419-425.
45. Koezuka S, Hata Y, Sato F, Otsuko H et al. Malignant peripheral nerve sheath tumor in the anterior mediastinum: A case report. *Mol Clin Oncol* 2014; 2: 987-990.
46. Wong WW, Hirose T, Scheithauer BW, Schild SE, Gunderson LL. Malignant peripheral nerve sheath tumor: analysis of treatment outcome. *Int J Radiat Oncol Biol Phys.* 1998;42:351-360.
47. Carli M, Ferrari A, Mattke A, et al. Pediatric malignant peripheral nerve sheath tumor: the Italian and German soft tissue sarcoma cooperative group. *J Clin Oncol.* 2005;23:8422-8430.
48. Ishibashi H, Takahashi K, Kumazawa S, Okubo K. Successful excision of a giant mediastinal vagal schwannoma causing severe tracheal stenosis through a median sternotomy. *Ann Thorac Surg* 2014; 98: 336-8.
49. Alexiev BA, Chou PM, Jennings LJ. Pathology of melanotic schwannoma. *Arch Path Lab Med* 2018; 142: 1517-1523.
50. Irmak İ, Kasapoğlu US, Güney PA, Günger S et al. Retrospective analysis of then cases of Schwannoma Localized in Mediastinum. *Okmeydanı Tıp Dergisi* 2016: 65-68.
51. Nagata M, İto H, Matsuzaki T, Furumoto H et al. Plexiform schwannoma involving trachea and recurrent laryngeal nerve: a case report. *Surg Case Rep* 2015; 67:
52. Lindholm K, Moran CA. Primary mediastinal melanotic schwannian tumors: a clinicopathological and immunohistochemical study of 5 cases. *Ann Diag Path* 2018; 37: 104-106.
53. Smahi M, Lakranbi M, Ounadnoui Y, Bouarhroum A et al. Intrathoracic phrenic nerve neurofibroma. *Ann Thorac Surg* 2011; 91: e57-e58.
54. Uchida K, Okada T, Honda S, Miyagi H et al. Giant mediastinal neurofibroma in a child with neurofibromatosis Type I. *Surg Science* 2012; 3: 564-567.
55. Pascoe HM, Antippa P, Irving L, Christie M and McCusker MW. Rare manifestation of neurofibromatosis type 1: A plexiform neurofibroma involving the mediastinum and lungs with endobronchial neurofibromata. *J Med Imag Rad Oncol* 2018; 63:
56. Friedrich RE, K. L., Funsterer C, Mautner VF: Malignant peripheral nerve sheath tumors (MPNST) in neurofibromatosis type 1 (NF1): diagnostic findings on magnetic resonance images and mutation analysis of the NF1 gene. 25, (3A)(May-Jun): 1699-702, 2005.
57. Segawa M, Kusajima Y, Senda K, Saito K. Mediastinal granular cell tumor arising from the left recurrent nerve, report of a case. *Kyobu Geka* 2007; 60: 595-8.
58. Askin FB, Rosai J, Sibley RK et-al. Malignant small cell tumor of the thoracopulmonary region in childhood: a distinctive clinicopathologic entity of uncertain histogenesis. *Cancer.* 1979; 43: 2438-51.
59. Zhang K, Lu R, Shen S, Li X. Askin tumor: 11 cases and a review of the literature. *Oncology Letters* 2015; 11: 253-6
60. Chen X, Ma Q, Wang S, Xhang H, Huang D. Surgical treatment of thoracic dumbbell tumors. *Eur J Surg Oncology* 2019; 45: 851-856.
61. Eden K. the dumb-bell tumor of the spine. *BSJ* 1941; 21; 549-70.
62. Akwari OE, Payne WS, Onofrio BM, et al. Dumbbell neurogenic tumors of the mediastinum. *Diagnosis and management.* *Mayo Clin Proc* 1978;53(6):353-358.
63. Takamura Y, Uede T, Igarashi K, Tatewaki K, Morimoto S. Thoracic dumbbell-shaped neurinoma treated by unilateral hemilaminectomy with partial costotransversectomy--case report. *Neurol Med Chir (Tokyo),* 1997, 37: 354-357.
64. Ando K, Imagama S, Wakao N, Hirano K, Tauchi R et al. Single-Stage of Thoracic Dumbbell Tumors from a posterior approach only with costotransversectomy. *Yonsei Med J.* 53: 611-617.
65. Rong H, Fan Y, Li S, Zhang Z et al. Management of dumbbell and paraspinal tumors of the thoracic spine using a single-stage posterolateral approach: case series. *Orthop Surg* 2018; 10: 343-9.

66. Maeda S, Takahashi S, Koike K, Sato M. Preferred surgical approach for Dumbbell Tumors in the Posterior Mediastinum. *Ann thorac Cardiovasc Surg* 2011; 17: 394-396.
67. Shadmehr MB, Gaissert HA, Wain JC, Monsure AC, Grillo HC et al. The surgical approach to “dumbbell tumors” of the mediastinum. *Ann Thorac Surg* 2003; 76: 1650-1654.
68. Yamaguchi M, Yoshino I, Kameyama T, Osoegawa A, et al. Thoracoscopic surgery combine with a supraclavicular approach for removing a cervico-mediastinal neurogenic tumor: a case report. *Ann Thorac Cardiovasc Surg* 2006 12:196-6.
69. Fraga JC, Rothenberg S, Kiely E, Pierro A. Video-assisted thoracic surgery resection for pediatric mediastinal neurogenic tumors. *J pediatr Surg* 2012; 47: 1349-53.
70. Matsumoto R, Yoshiyama K, Yokoyama S, Mitsuoka M et al. Surgical resection of extramedullary haematopoiesis in the posterior mediastinum. *Respirol Case Rep* 2018; 6