

Solid Tumour Section

Mini Review

Lung: Pleuropulmonary blastoma

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Identity

Note

Pleuropulmonary blastoma is a rare aggressive malignant tumor of infancy and early childhood. The tumor arises in the lung and pleura and is regarded as a pulmonary dysontogenetic or embryonic neoplasm. It is the pulmonary analog of other tumors of childhood including Wilms' tumor, neuroblastoma, hepatoblastoma, pancreatoblastoma, and retinoblastoma.

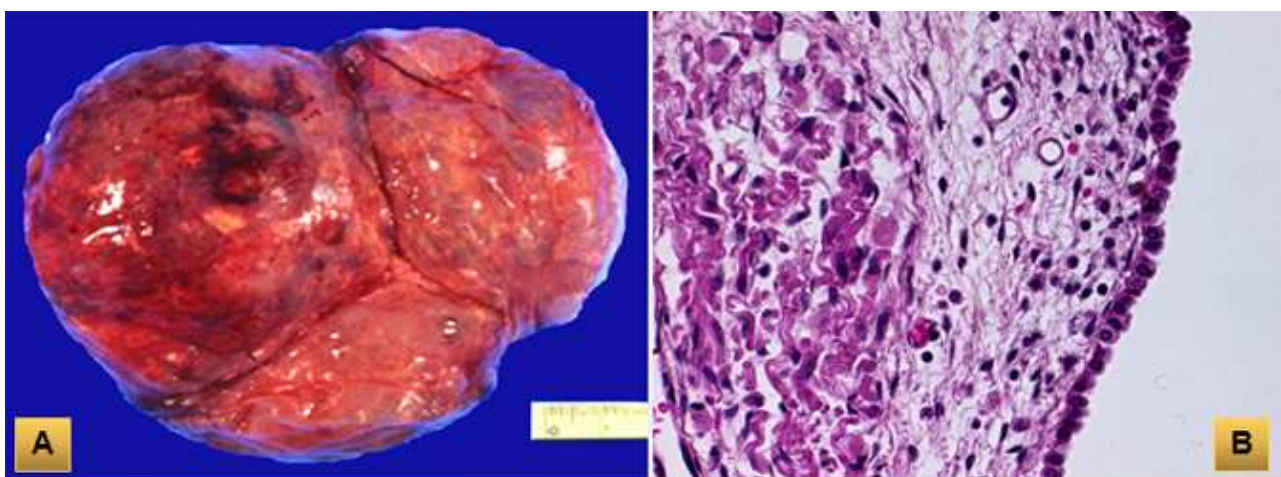
Synonyms include embryonal rhabdomyosarcoma arising in congenital bronchogenic cyst, rhabdomyosarcoma arising in congenital cystic adenomatoid malformation, pulmonary sarcoma

arising in mesenchymal cystic hamartoma, pulmonary blastoma associated with cystic lung disease of childhood.

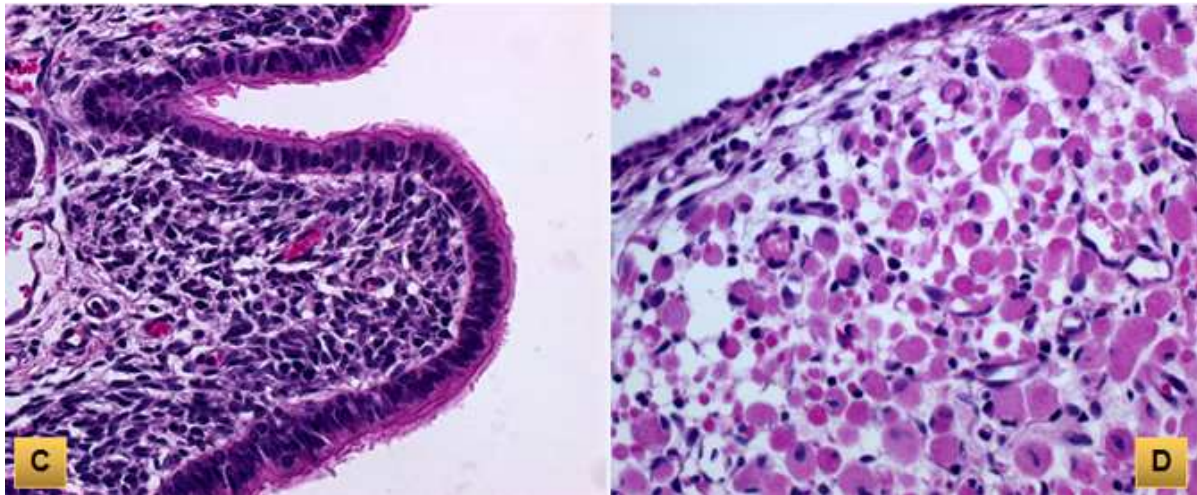
Clinics and pathology

Epidemiology

There are over 120 cases registered with The Pleuropulmonary Blastoma Registry (www.ppbregistry.org). The tumor affects mainly in children with age ranges from 1 month to 12 years. Most cases are diagnosed before 4 years of age. It can be found prenatally or present in older children and young adults. Males and females are equally affected.



(A) Type I pleuropulmonary blastoma consists of multiloculated cyst filled with scanty clear serous fluid. (B) The cysts are lined by cuboidal epithelium resting on loose mesenchymal tissue.



(C) There are areas of proliferating primitive cells with overlying stratified ciliated columnar epithelium. (D) Foci of rhabdomyoblasts with abundant eosinophilic cytoplasm and cross striations are noted.

Clinics

Approximately 25% of cases are associated with a heritable tumor syndrome. Additional tumors including cystic nephromas and other nephroblastic lesions, ovarian teratomas, multiple intestinal polyps, thyroid malignancies, medulloblastomas, and second pleuropulmonary blastomas have been observed in affected children. Clinical manifestations vary and depend on age and pathologic type of tumors. Most patients are presented with respiratory symptoms including dyspnea, chest pain, cough, and respiratory distress with or without pneumothorax. Asymptomatic lesions may be detected incidentally during investigation of unrelated clinical problems.

Pathology

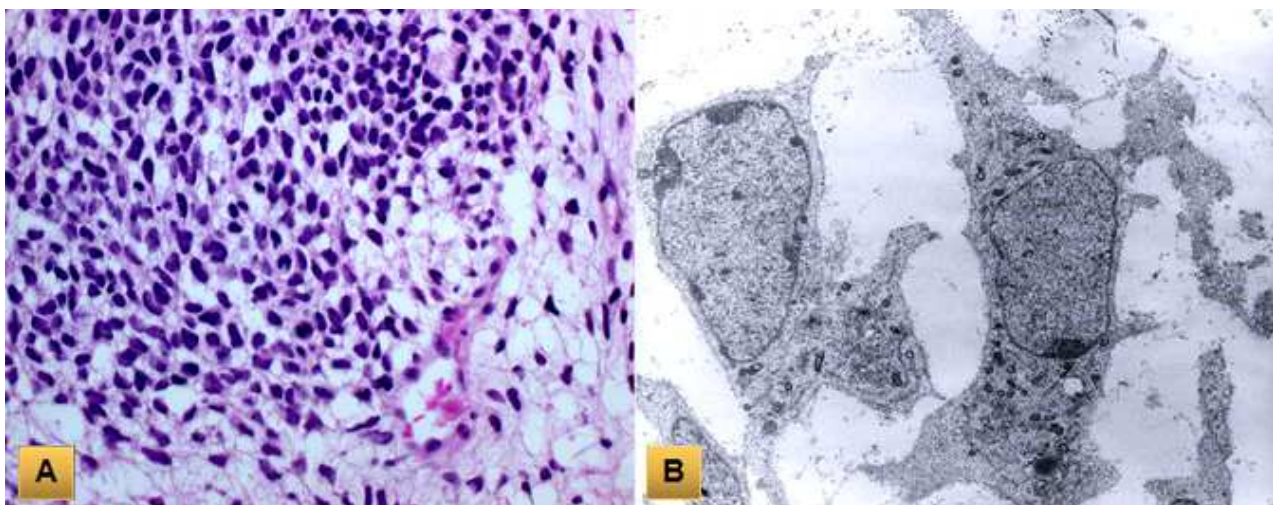
There are 3 pathologic types of pleuropulmonary blastoma with distinct macroscopic and microscopic features.

Type I pleuropulmonary blastoma is characterized by peripherally located, multicystic, and thin-walled

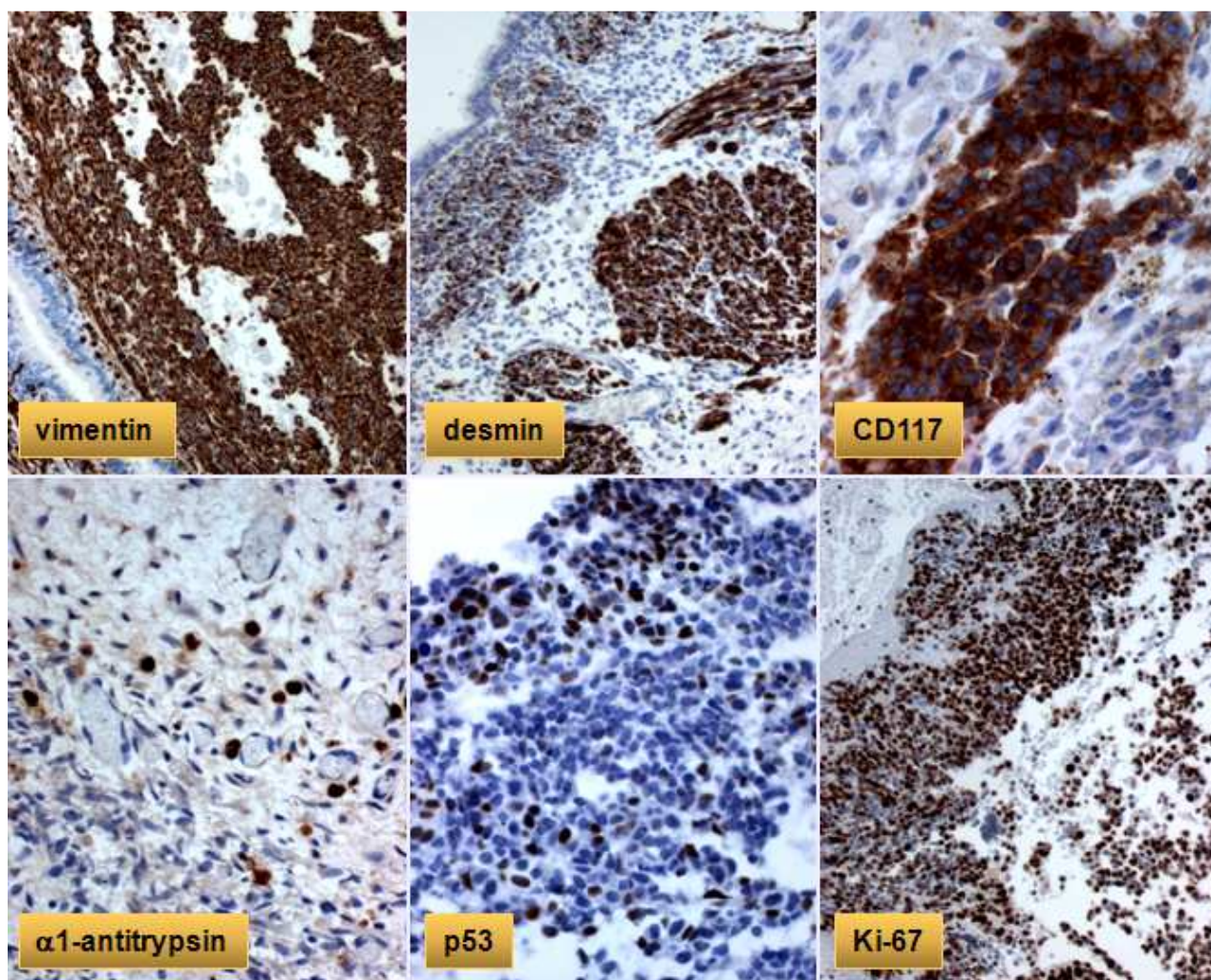
structure. No solid nodules are observed within the thin-walled septae and multicystic spaces. Neoplastic cells can be identified beneath a benign cyst lining surface epithelium. This "cambium layer-like" zone contains proliferating primitive cells with mixed small, rounded, or spindled hyperchromatic nuclei. Rhabdomyoblasts are seen occasionally. Some tumors have immature cartilage within their fibrous septae.

Type II pleuropulmonary blastoma is a mixed solid and cystic tumor characterized by varied amount of thickened or nodule-like areas composed of rhabdomyosarcomatous or blastematous components.

Type III pleuropulmonary blastoma is characterized by a well-circumscribed, mucoid, white-tan solid mass attached to the pleura and involves a lobe or entire lung. Necrosis and hemorrhage are sometimes present in the friable areas. Histopathologically, type III tumor is an apparently heterogeneous tumor composed of one or more of the following elements: primitive "blastema-like" small cells with hyperchromatic nuclei with high nuclear-to-cytoplasmic ratio and abundant mitoses;



(A) Pleuropulmonary blastoma is composed of compact zones with primitive blastematous cells embedded in a loose myxoid stroma. (B) Electron microscopy shows spindle primitive cells with high nuclear-to-cytoplasmic ratio and oval nuclei.



Immunohistochemical stains show strong positivity with vimentin, desmin, CD117, p53, and focal positivity with alpha-1-antitrypsin in the primitive tumor cells. The Ki-67 reveals high proliferative index of approximately 90%.

spindled and ovoid cells embedded in a myxoid stroma; spindle cell sarcoma; nodules of immature or malignant chondroid elements. Isolated or clusters of large anaplastic cells with pleomorphic nuclei, atypical mitotic figures, or eosinophilic hyaline bodies are present.

Immunohistochemically, the neoplastic cells are stained positive for vimentin. CD117 (c-kit) and alpha-1-antitrypsin are focally positive in tumor cells. CD99 is weakly positive. Other immunostains including EMA, myogenin, S100, GFAP, neuron specific enolase, TTF-1, alpha-fetoprotein, chromogranin, and synaptophysin are negative. The pneumocytes lining the cysts and small airspaces are highlighted by cytokeratin. Muscle specific actin and desmin are expressed in rhabdomyoblasts and primitive cells in the subepithelial regions of cystic lesions.

Cytogenetics

Gains of chromosome 8 detected by karyotyping and fluorescence in situ hybridization is the most consistent recurrent chromosomal aberration. Trisomy 2,

unbalanced translocation between chromosomes 1 and X, and p53 mutations/deletions have been reported. One case with brain metastasis reveals an abnormal karyotype of 44,XY,del(1)(p12),-14der(19)add(19)(q13.3),-20. Heterozygous germline mutations in DICER1 are found in pleuropulmonary blastoma families.

Treatment

The current treatment for type I pleuropulmonary blastoma is complete surgical excision followed by combination chemotherapy with vincristine, actinomycin-D, and cyclophosphamide. Complete excision and adjuvant multi-agent chemotherapy are also applied for type II and type III tumors. Tumor progression from type I to type III has been documented.

Prognosis

Type I pleuropulmonary blastoma has the most favorable prognosis with a 5-year survival rate of 83%, whereas type II and III have a worse outcome of less than 50%.

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