

Title: *DICER1*-Related Disorders *GeneReview* - Supplemental Material: Pathologic Findings, Part 1

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Pathologic Findings, Part 1

Pleuropulmonary blastoma (PPB)

When imaging studies show a multi-septated cyst suspicious for cystic PPB, lobectomy or wedge resection of one or multiple cysts is recommended. Complete open resection for tumors confined to one lobe provides the best material for diagnosis. While video-assisted thoracic surgery can be an effective and less invasive procedure than open thoracotomy, surgeons must ensure that the lung is not disrupted upon removal from the chest because disruption of the delicate multilocular cysts can significantly limit the ability to make a histologic diagnosis.

For tumors deemed unresectable, as many core biopsies as possible that represent several areas should be performed.

Pleural effusion cytology is rarely helpful in making a diagnosis.

Pathology. The four main pathologic types of PPB reflect the natural history of the disease. The clinical presentation and evaluation differ based on PPB type (see [Natural History](#)).

- Type I PPB is purely cystic
- Type IR (“regressed”) PPB, is cystic like type I PPB but lacks a primitive mesenchymal component beneath the surface epithelium
- Type II PPB, the malignant progression of a type I PPB, is cystic and solid
- Type III PPB, the most advanced type, is purely solid

Pathology of type I PPB. Type I PPB is completely cystic in nature. Grossly the cyst(s) can be unilocular, but is more often multilocular, and located in the periphery of the lung. Microscopically, type I PPB has a characteristic multilocular architecture with delicate septa at low magnification [Hill et al 2008]. A diagnostic population of small primitive mesenchymal cells is typically found in the cyst wall. These cells may be localized to a limited focus, several foci or in a diffuse band beneath the epithelium similar to that seen in botryoid type ERMS. The primitive small cells may display rhabdomyosarcomatous differentiation as seen in an ERMS. When there is rhabdomyoblastic differentiation, cells with prominent eosinophilic cytoplasm may be present. Small nodules of immature cartilage or mature spindle cells may be found in the septa and are not necessarily accompanied by the small primitive cells. Because the small primitive cells or nodules of cartilage are present only focally in some cases, it is necessary to submit an entire cyst specimen for microscopic examination.

Type IR PPB comprises cystic lesions that have the architecture of type I PPB without any primitive mesenchymal elements. Although it is thought that the biological potential of type IR PPB is limited, it is important to note that in children with multiple lung cysts, the absence of primitive mesenchyme in one cyst may not predict the histopathologic findings in other cysts (i.e., presence or absence of primitive small cells or rhabdomyoblasts).

Pathology of type II and type III PPB. Type II PPB differs from type I PPB in that the tumor cells within the cyst wall have proliferated creating a grossly visible thickening of the septa or formation of a solid mass. Type III PPB is purely solid.

Microscopically, the solid portions of a type II PPB and type III PPB show a multi-patterned sarcoma that typically includes ERMS areas with solid nests of undifferentiated cells (blastema), spindle cell sarcoma, and cartilage, often with immature or overtly sarcomatous features. One or more of these elements may predominate in any one tumor. Anaplasia, similar to anaplasia in Wilms tumor, occurs in 75% of type II and 85% of type III PPBs. Core biopsies typically show one or more sarcomatous patterns; rhabdomyosarcomatous pattern is the most common. A pathologic diagnosis of ERMS in the context of a primary lung mass in a child should alert the oncologist to the likelihood of PPB since the lung parenchyma is a rare site for a primary ERMS.

Pathology of metastatic PPB. The metastatic lesions of PPB generally are more monomorphic with high grade spindle cell sarcomatous or anaplastic sarcomatous patterns.

References

Hill DA, Jarzembowski JA, Priest JR, Williams G, Schoettler P, Dehner LP. Type I pleuropulmonary blastoma: pathology and biology study of 51 cases from the international pleuropulmonary blastoma registry. *Am J Surg Pathol.* 2008;32:282-95.