CYSTIC & NEUROECTODERMAL LESIONS OF THE MEDIASTINUM

Mark R. Wick, MD

Division of Surgical Pathology
University of Virginia Health System
Charlottesville, VA, USA
mrwick1@usa.net

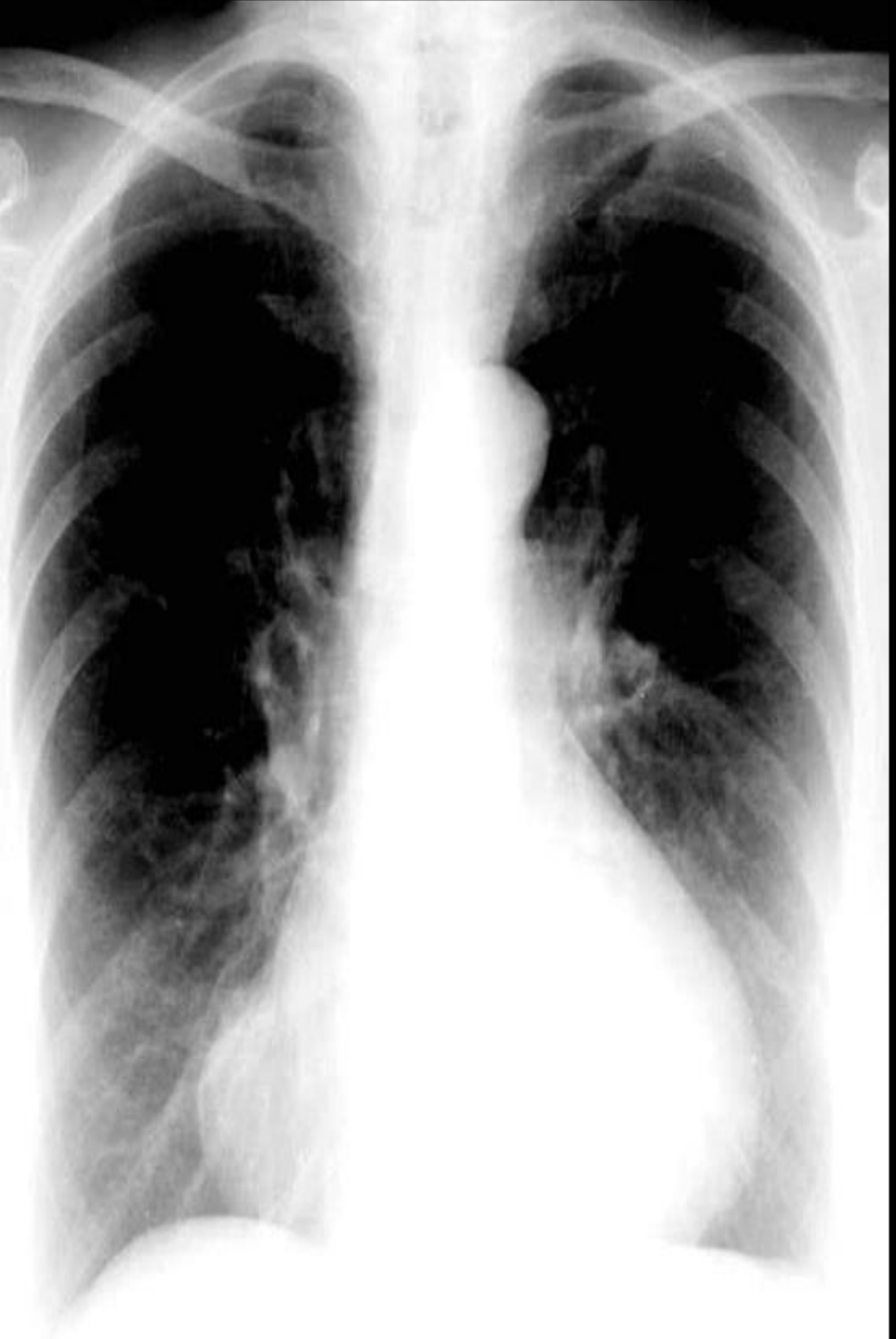
Cystic Mediastinal Lesions

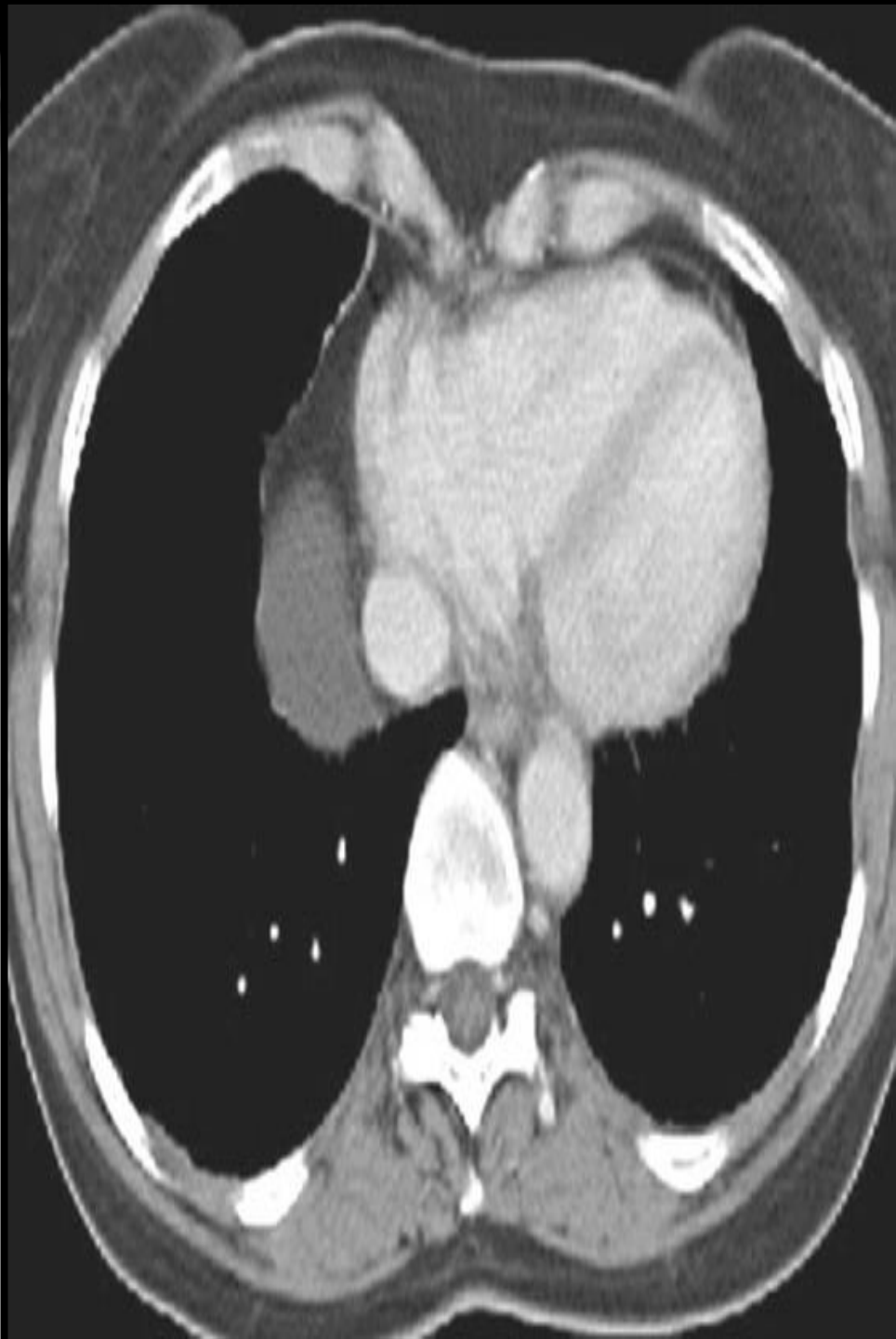
- Account for 10-15% of intrathoracic masses found by radiographic imaging
- Several tissue types are represented, including pericardial, thymic, enteric, and bronchogenic elements
- Represent a mixture of developmental and acquired lesions

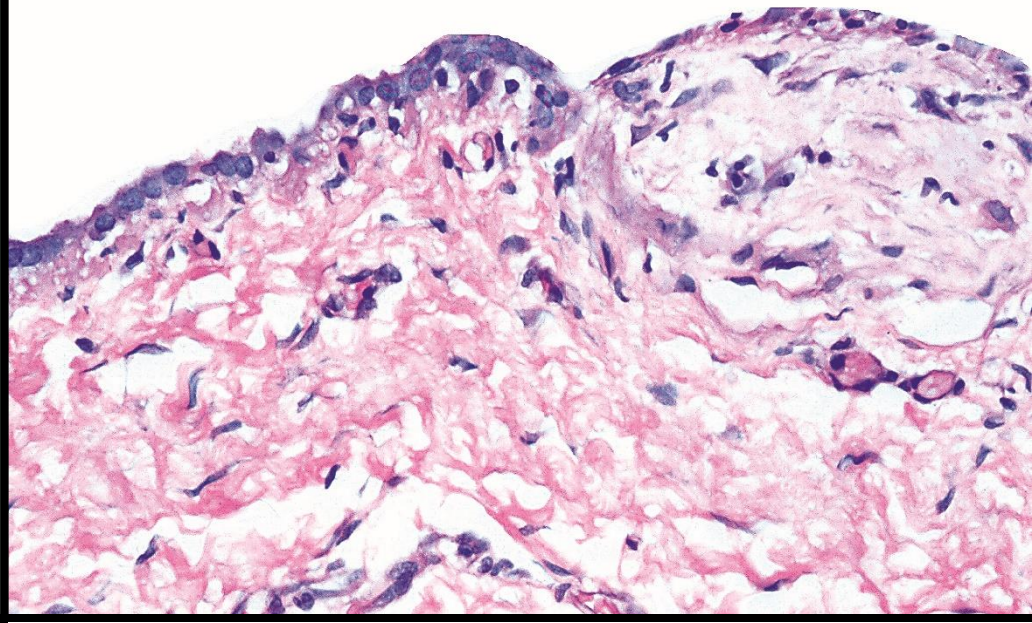
Developmental (Congenital) Mediastinal Cysts

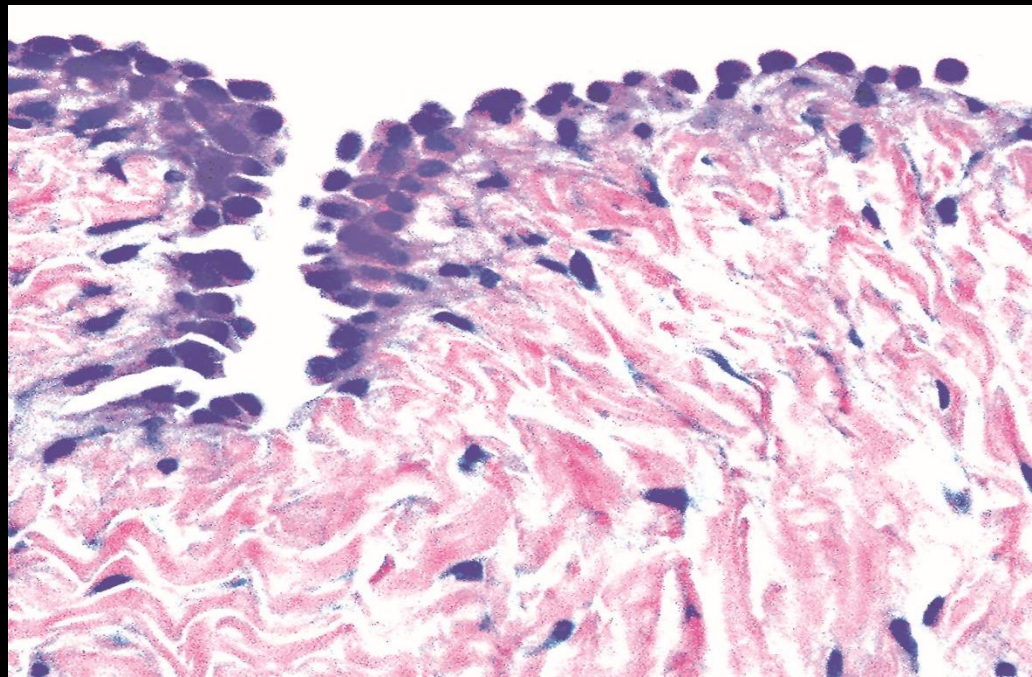
Pericardial Cysts

- Usually seen in the basal portion of the mediastinum, abutting the heart shadow, as a rounded mass of variable density on plain films
- CT scans demonstrate a fluid-filled, thin-walled cyst in continuity with the pericardium
- Microscopy shows a mesothelial-lined fibrous cyst– “the hernia sac of the mediastinum”









Pathol Int. 2011 May;61(5):319-21. doi: 10.1111/j.1440-1827.2011.02654.x. Epub 2011 Mar 8.

Multicystic mesothelioma of the pericardium.

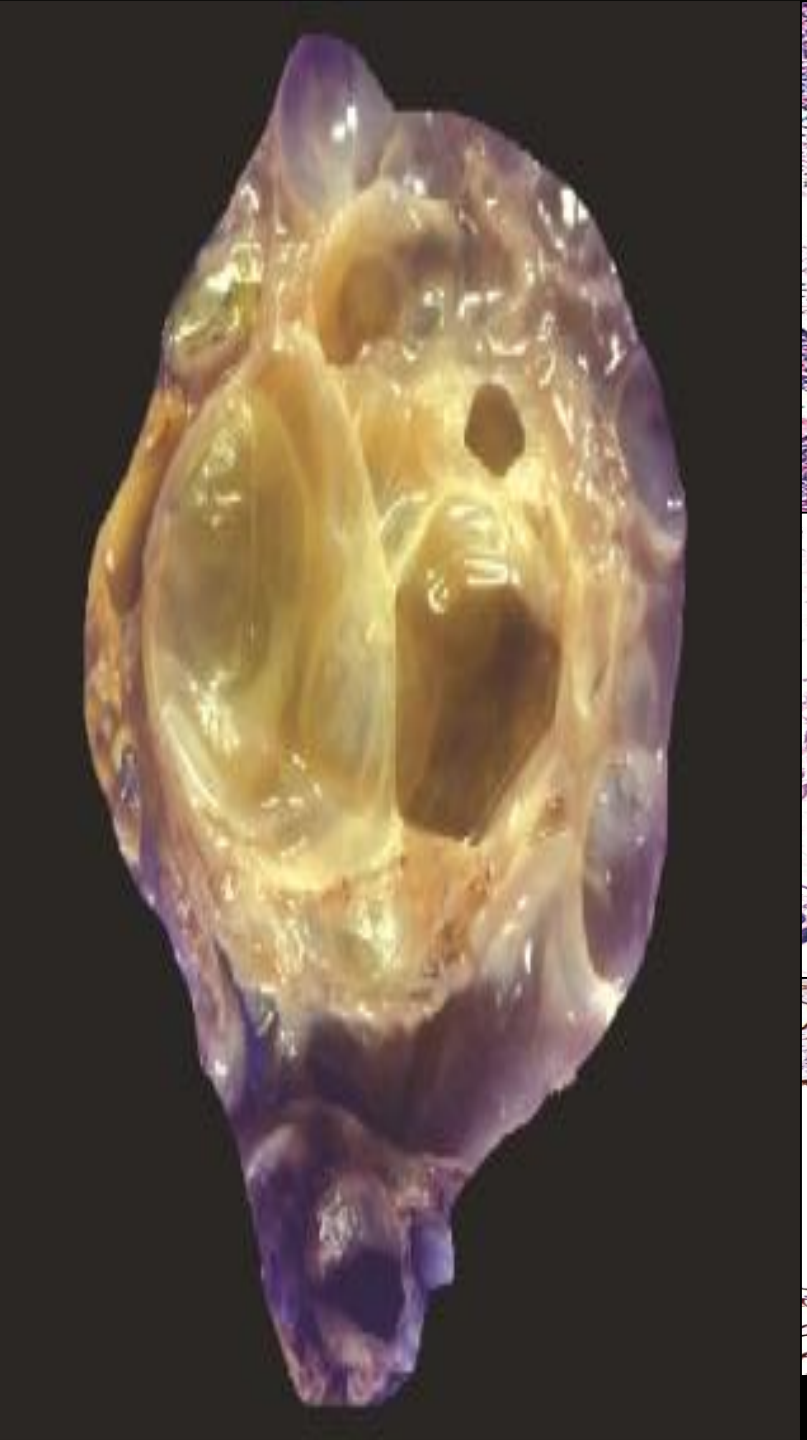
Morita S[1], Goto A, Sakatani T, Ota S, Murakawa T, Nakajima J, Maeda E, Fukayama M.

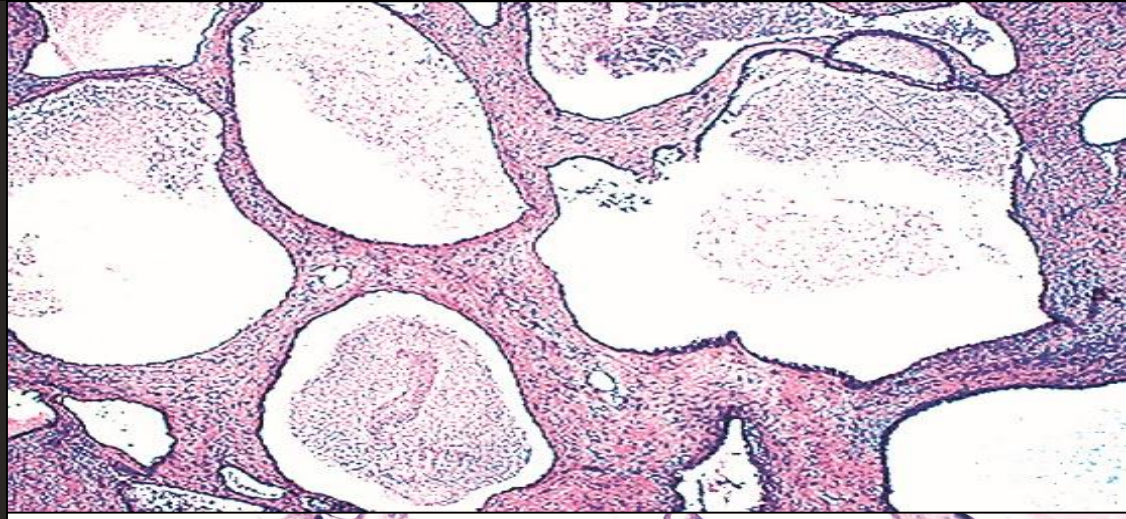
Author information

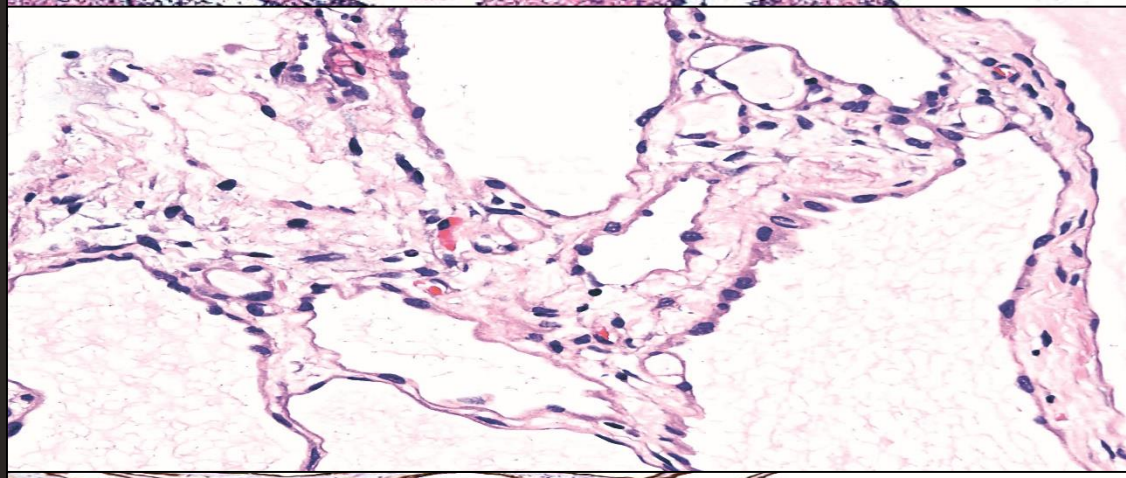
Abstract

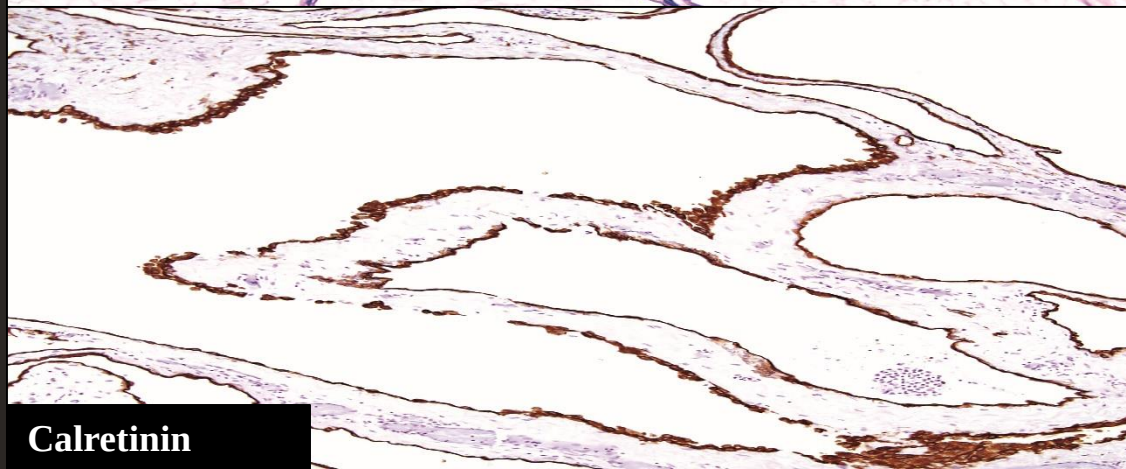
Multicystic mesothelioma is a well recognized but rare serosal tumor which mainly arises from the peritoneum in women and is considered as a benign lesion. This is the second case report of pericardial multicystic mesothelioma, which took a fatal clinical course. A 63-year-old man presented with pitting edema, shortness of breath, and hoarseness. Radiological investigations revealed solid and cystic tumor of the pericardium which was continuously extending into the mediastinum and the liver. Pericardial biopsy showed micro-cystic tumor lined by single layer of mesothelial cells without atypia, and the diagnosis was multicystic mesothelioma. Curative surgery could not be performed, and three years and four months later, the patient died because of the direct compression of the heart by the tumor. At autopsy, the tumor was found to be directly extending into the right pleural cavity and the right lung, besides the mediastinum and the liver. Neither malignant transformation nor metastatic tumor was identified.

Differential Diagnosis of Pericardial Cyst– Multicystic Mesothelioma





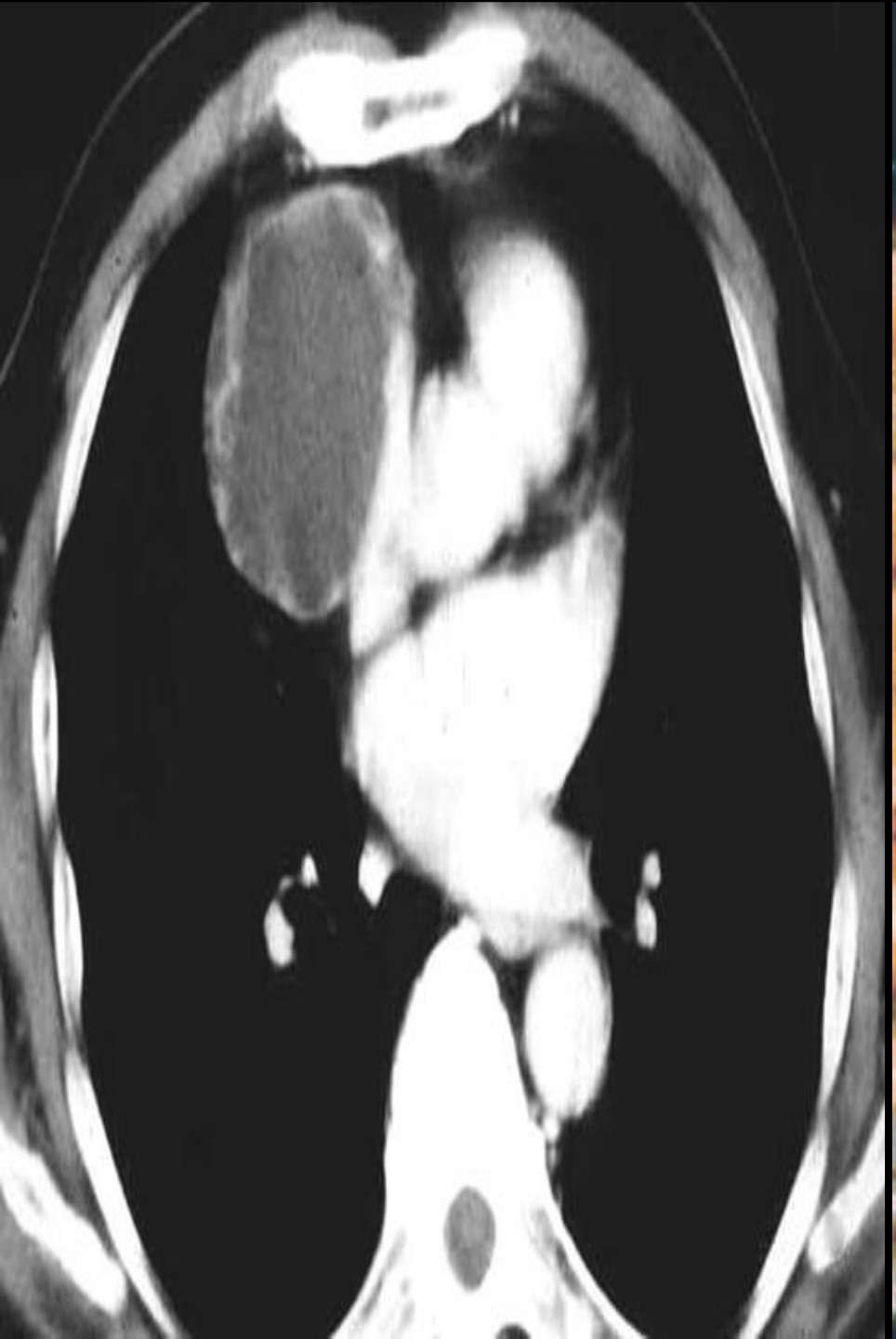


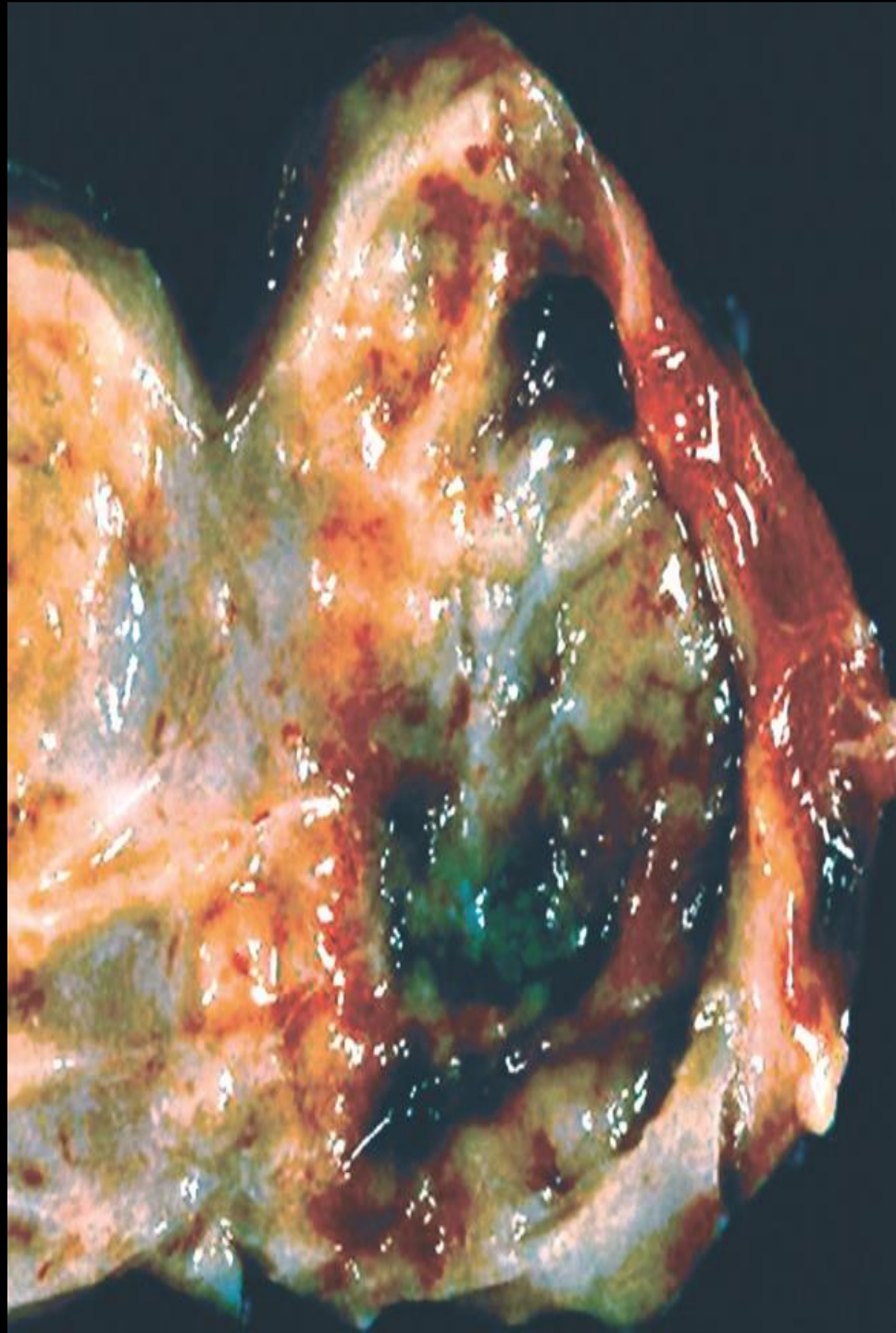


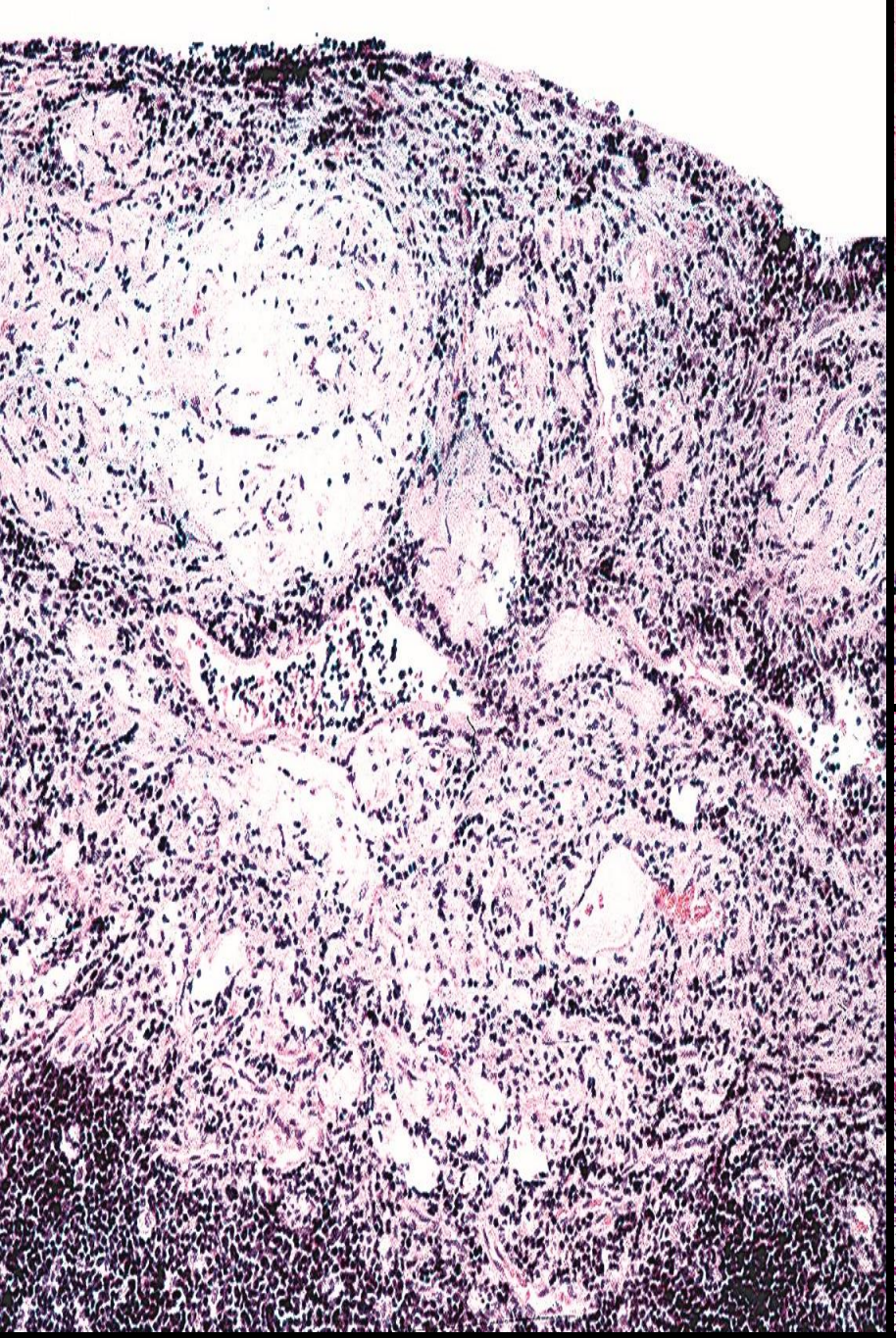
Calretinin

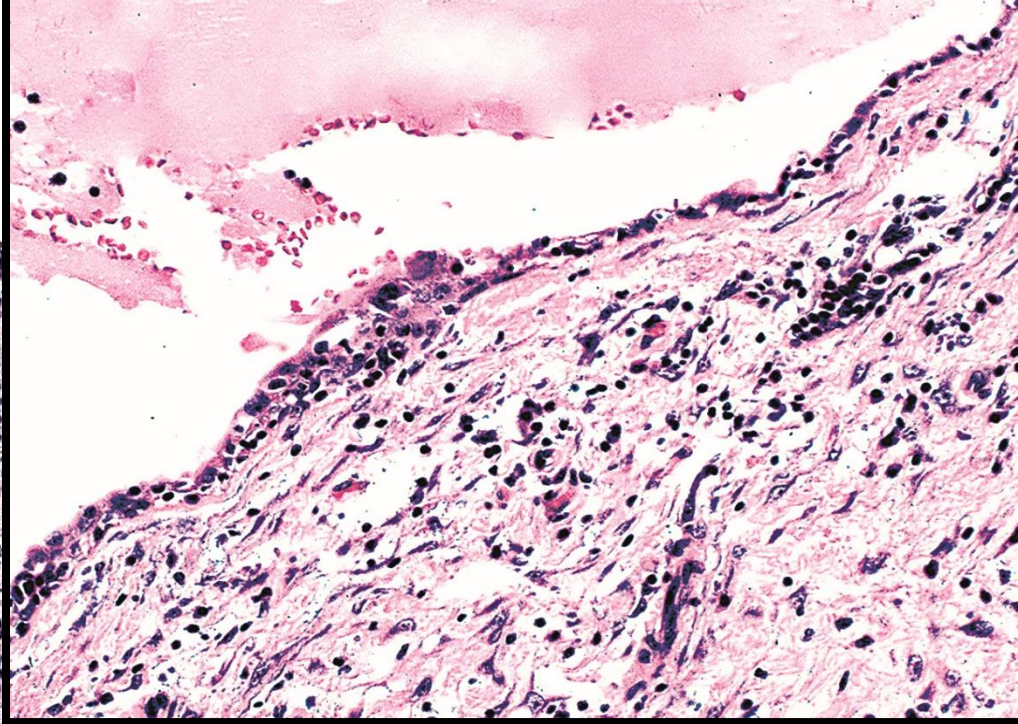
Unilocular Thymic Cysts

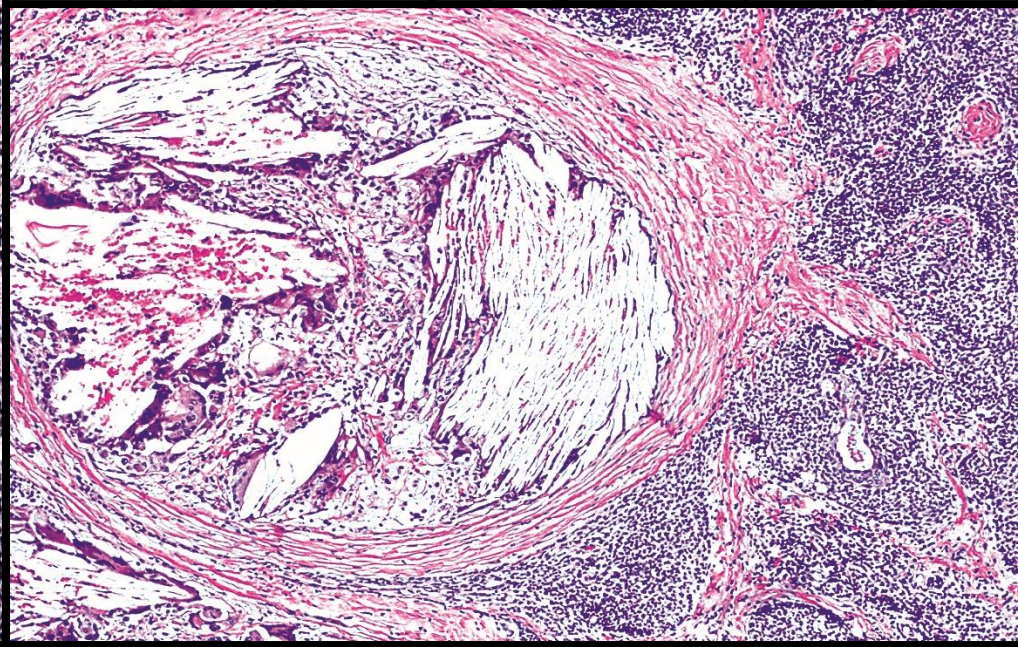
- May be present in the anterior or middle mediastinum, as an irregular or rounded density on plain films of the chest
- CT scans demonstrate a cyst with variable dense contents and an irregular wall; multiloculation may be present
- Microscopy shows a squamous lining with thymic tissue sometimes incorporated into the wall of the cyst; cholesterol clefts and calcification are common







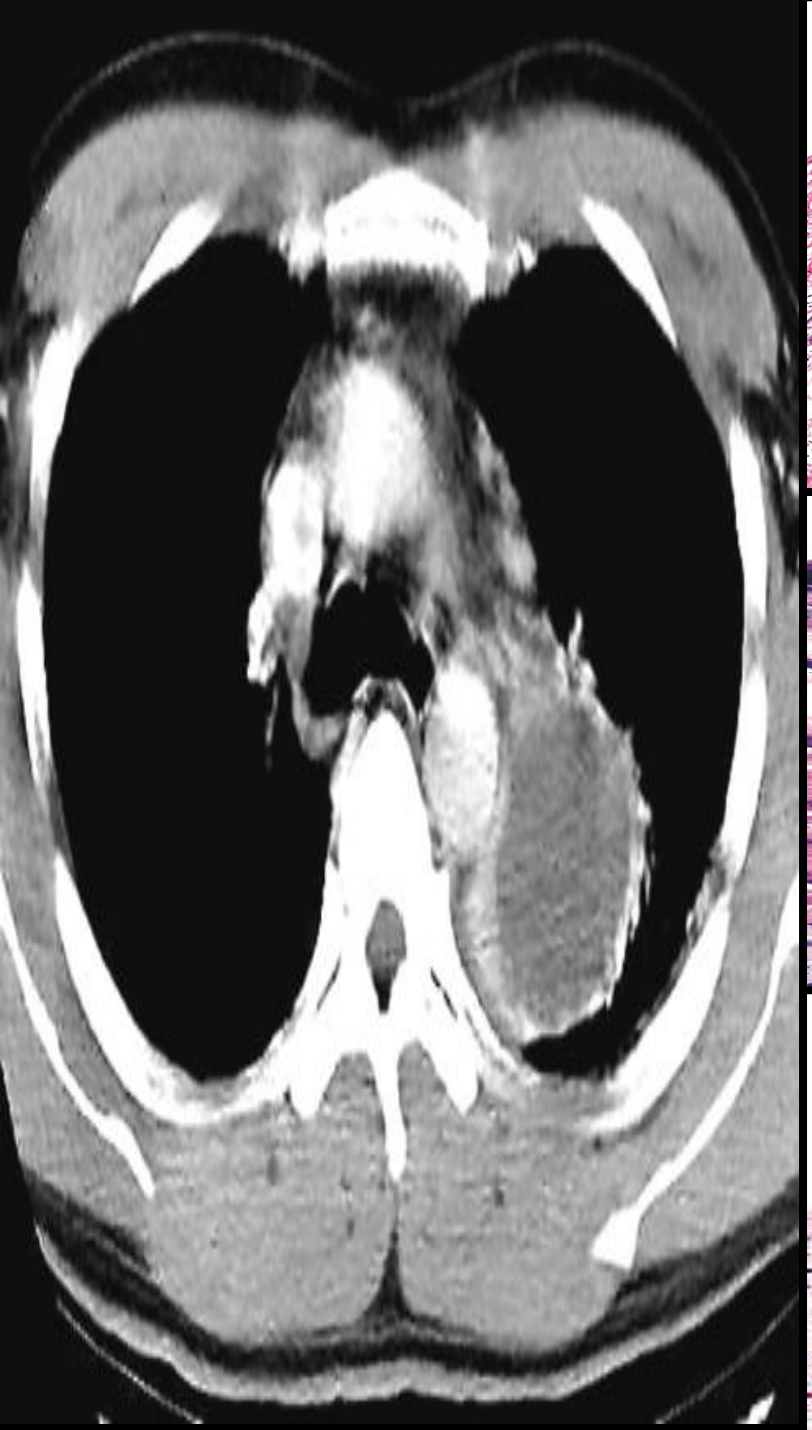
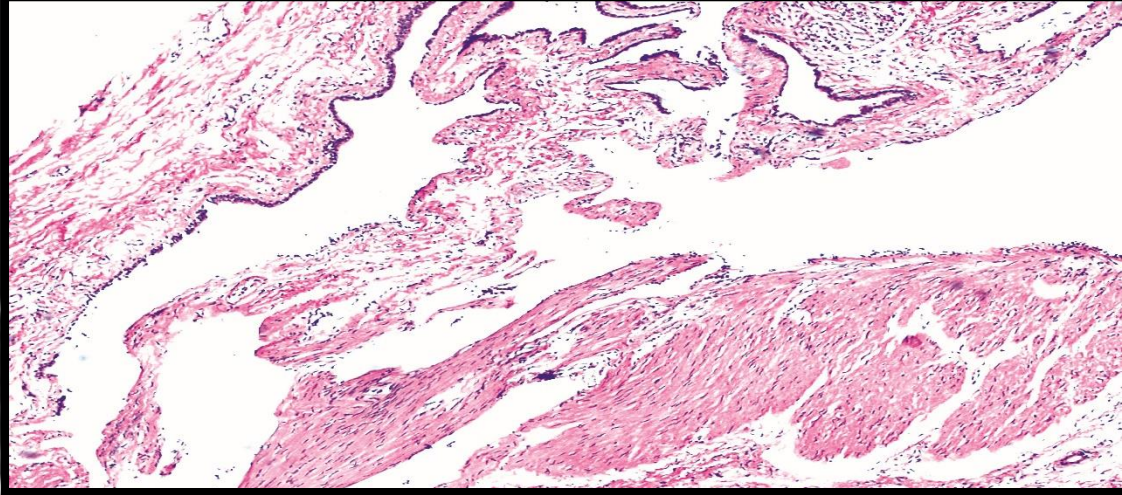
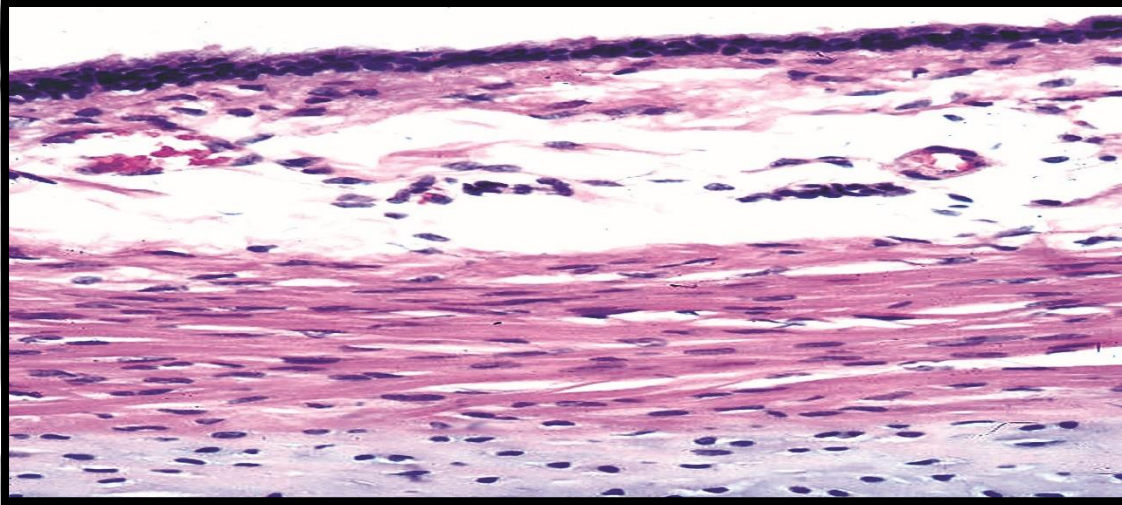
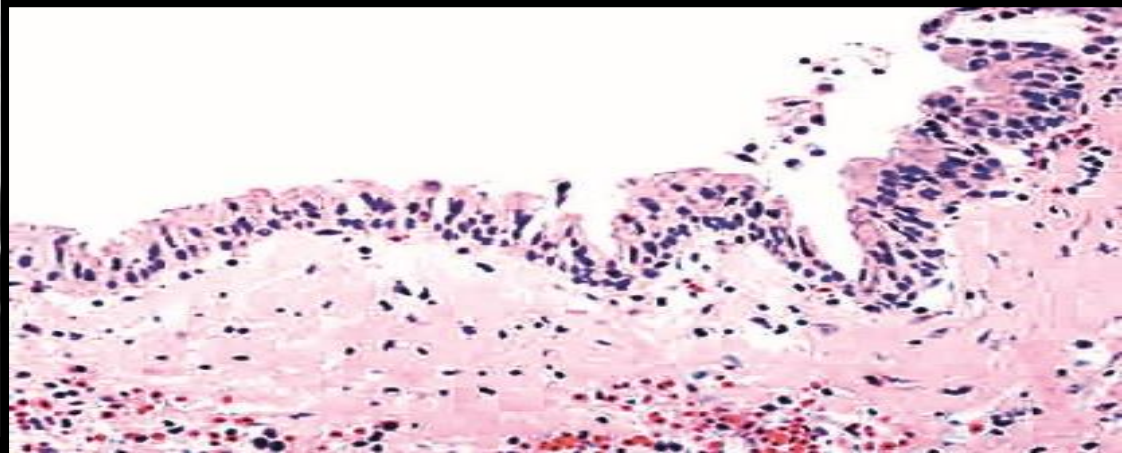




Unilocular Thymic Cyst

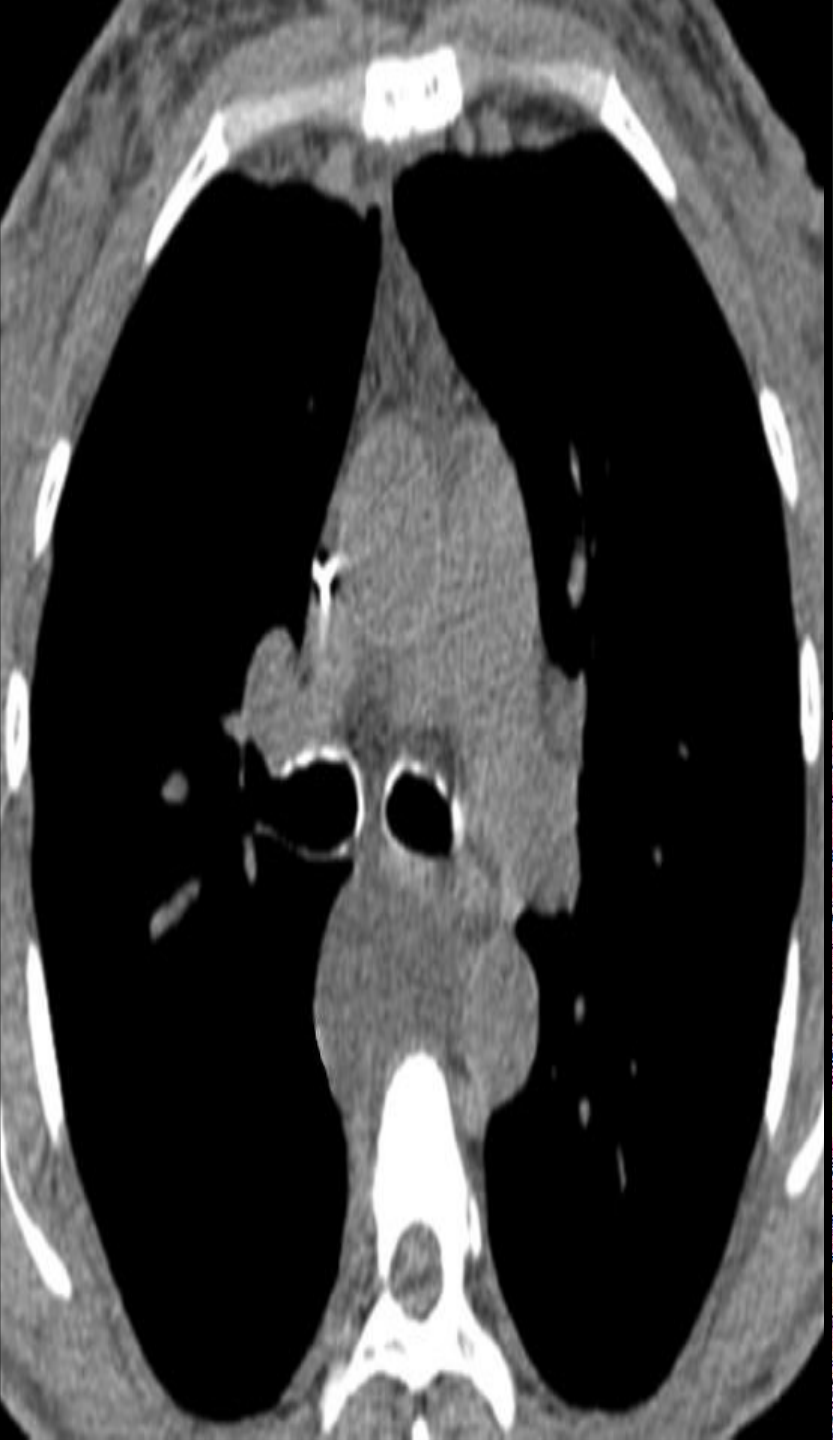
Bronchogenic Cysts

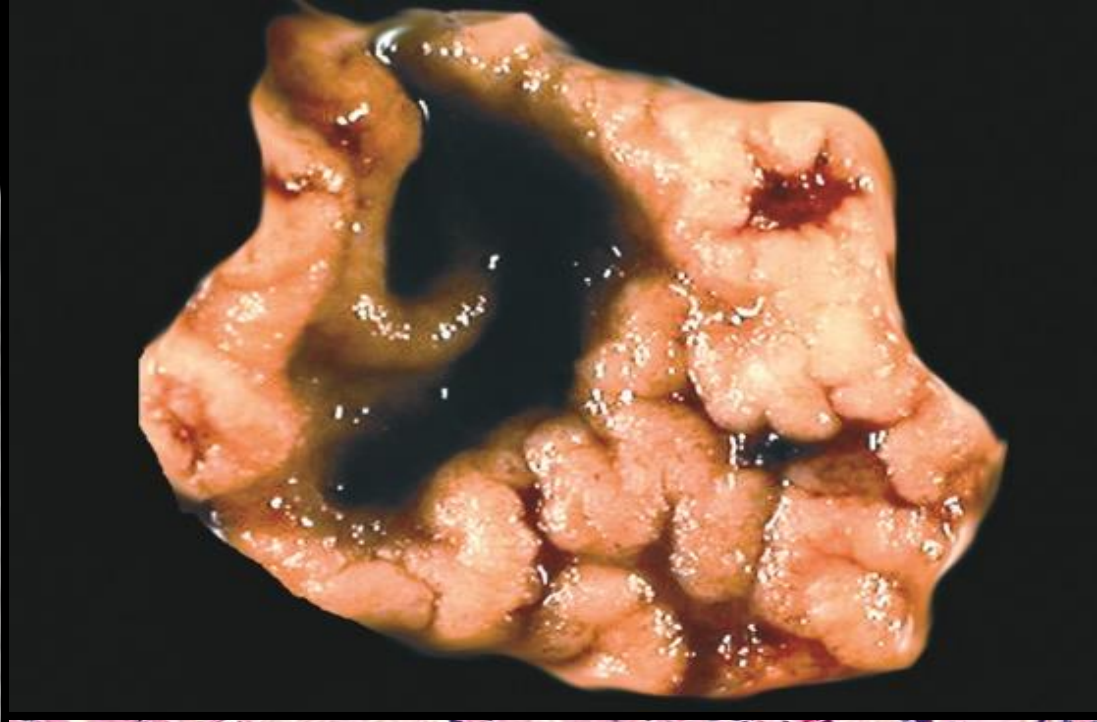
- **Rounded masses, usually in the *middle* mediastinum**
- **Patients may or may not complain of cough and expectoration of foul-tasting material ("motor oil"), depending on whether the cyst connects to a major bronchus**
- **CT scans may show calcified cartilaginous tissue in bronchogenic cysts**
- **Microscopy demonstrates the presence of cartilage, smooth muscle, and ciliated bronchial-type epithelium**

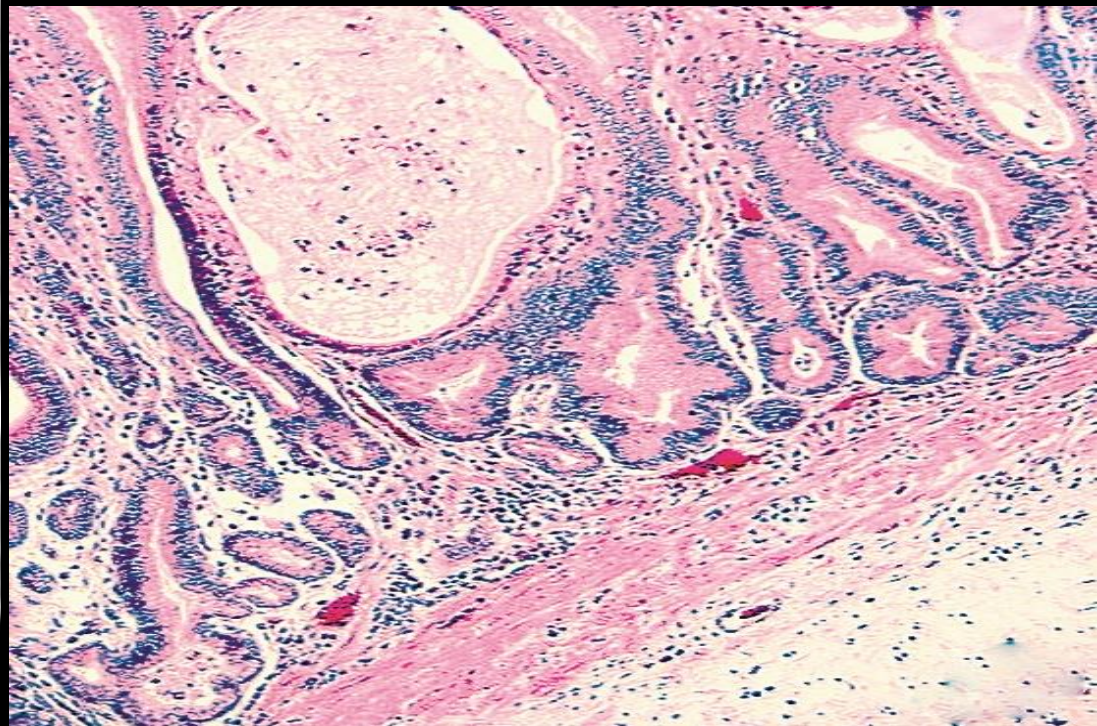





Enteric Duplication (Gastroenteric) Mediastinal Cysts

- Probably derived from misplaced foregut rests
- Typically seen in children < 15 years old, who present with dysphagia, cough, or vomiting
- Characteristically present in the posterior mediastinum as spheroid masses that may show internal loculation
- Specialized gastric-mucosal, squamoid, or simple columnar epithelial linings (or mixtures thereof) may be present







Mullerian (Hattori) Cysts of the Posterior Mediastinum

- Paravertebral in location, in women
- Unilocular, with an epithelial lining resembling that of endosalpingiosis
- Immunoreactive for CA-125, ERP, PRP, PAX8, and WT1
- Simple excision is curative

Mullerian cysts of the posterior mediastinum: report of two cases and review of the literature

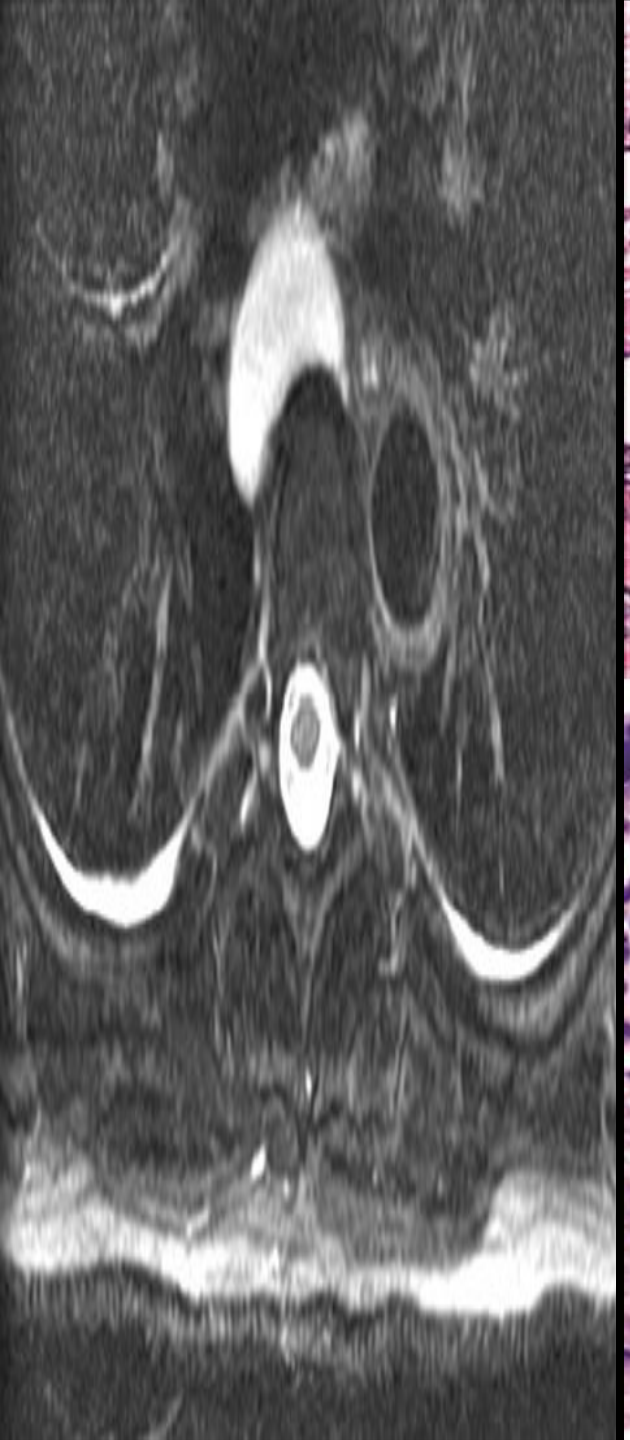
Matthew Simmons[1], Lizette Vila Duckworth[1], Kurt Scherer[2], Peter Drew[1], Demaretta Rush[1]

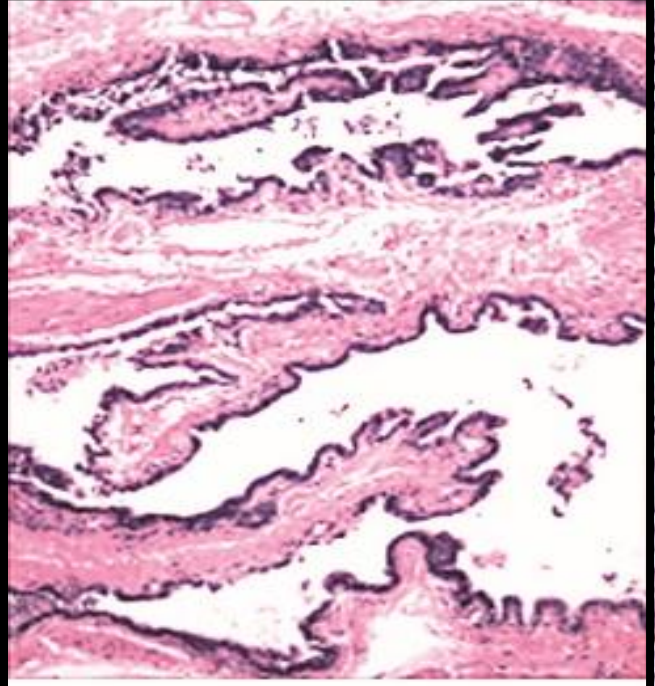
[1]University of Florida College of Medicine, Department of Pathology, Immunology, and Laboratory Medicine, Gainesville, Florida, USA; [2]University of Florida College of Medicine, Department of Radiology, Gainesville, Florida, USA

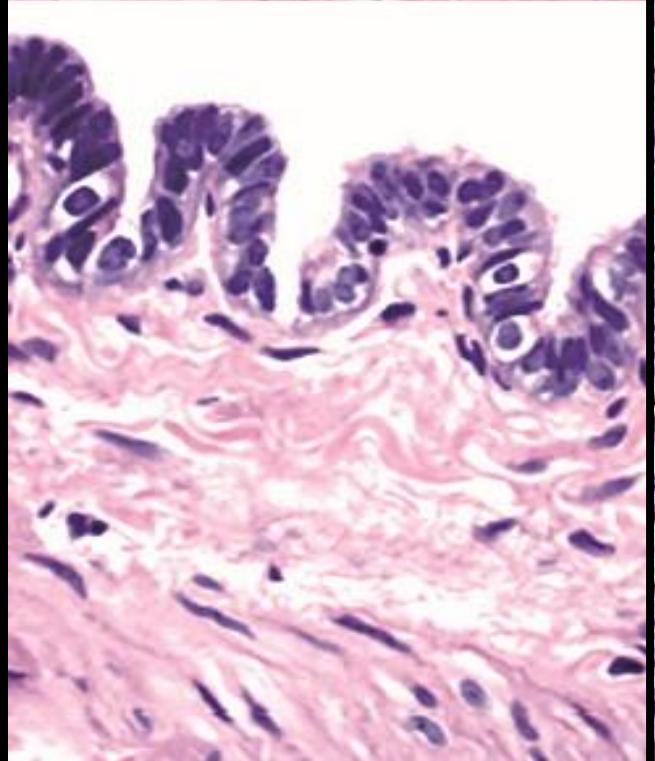
ABSTRACT

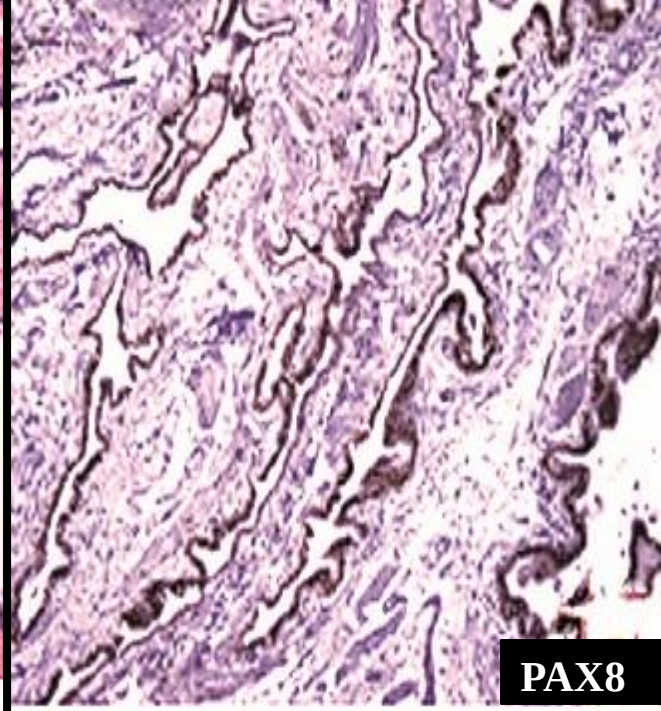
Cystic lesions can be occasionally be found in the mediastinum, and typically include bronchogenic cysts, esophageal duplication cysts, and neuroenteric cysts. In 2005, Hattori described the first mediastinal cyst with Mullerian differentiation. Since that time, three other authors have described similar cysts occurring in the posterior mediastinum. Here we present two cases of patients with ciliated cysts with Mullerian differentiation with expression of estrogen receptor, progesterone receptor, PAX8 and Wilm's tumor 1, occurring in the posterior mediastinum and review the related literature.

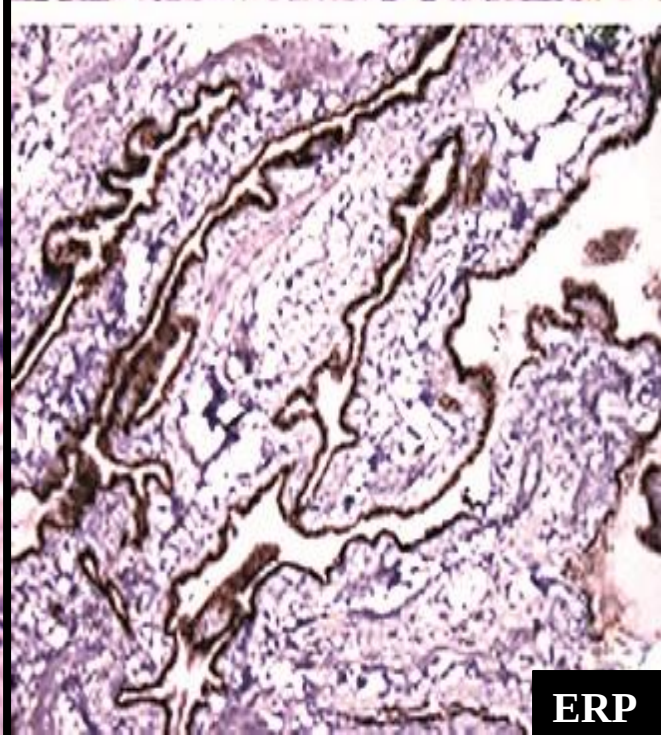
J Thorac Dis 2013;5(1):E8-E10. DOI: 10.3978/j.issn.2072-1439.2012.07.10








PAX8


ERP

Acquired Non-Neoplastic Mediastinal Cyst– Multilocular Thymic Cyst

Multilocular Thymic Cysts

- Usually present in the anterior mediastinum as irregular or rounded densities in radiographic studies
- CT scans demonstrate variably dense contents and internal multiloculation
- Cholesterol clefts are inconspicuous, and mural lymphoid tissue is abundant
- Multilocular thymic cysts may rarely undergo malignant transformation

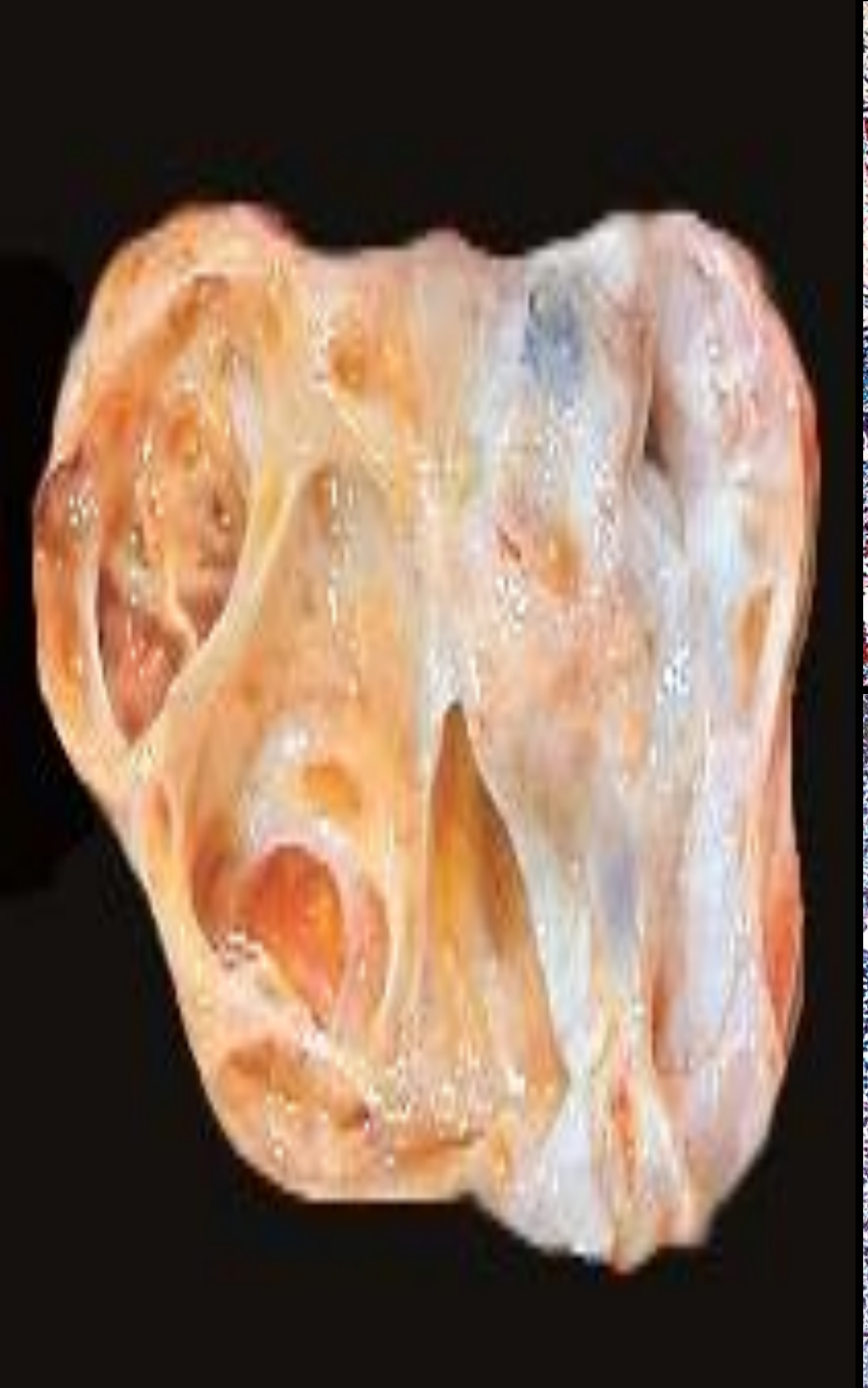
Am J Surg Pathol. 1991 Apr;15(4):388-98.

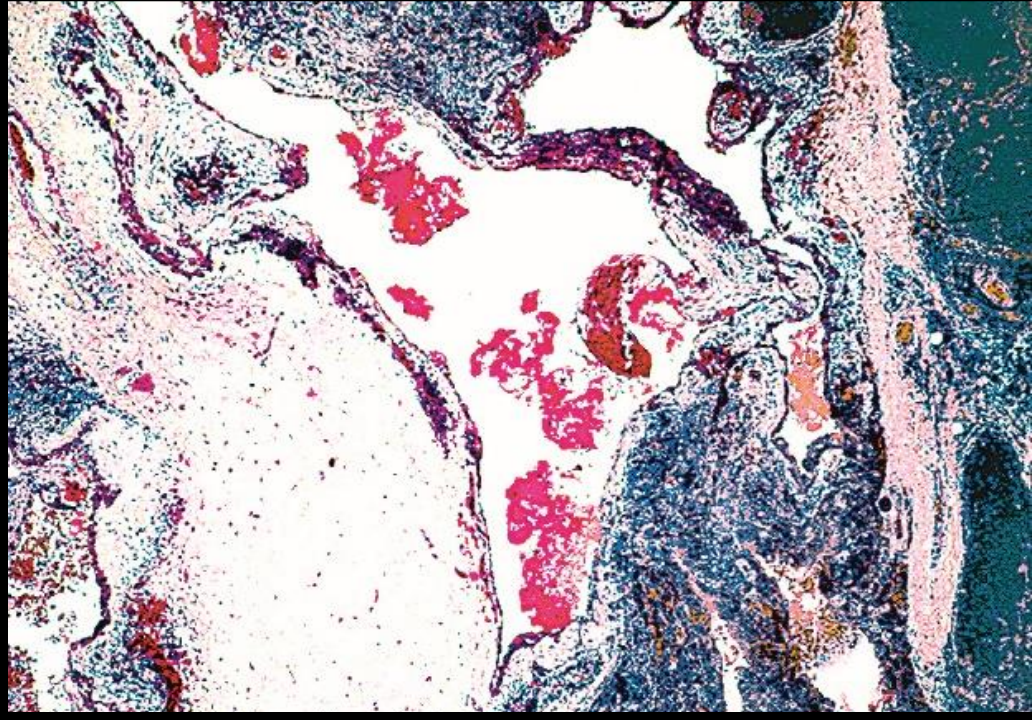
Multilocular thymic cyst: an acquired reactive process. Study of 18 cases.

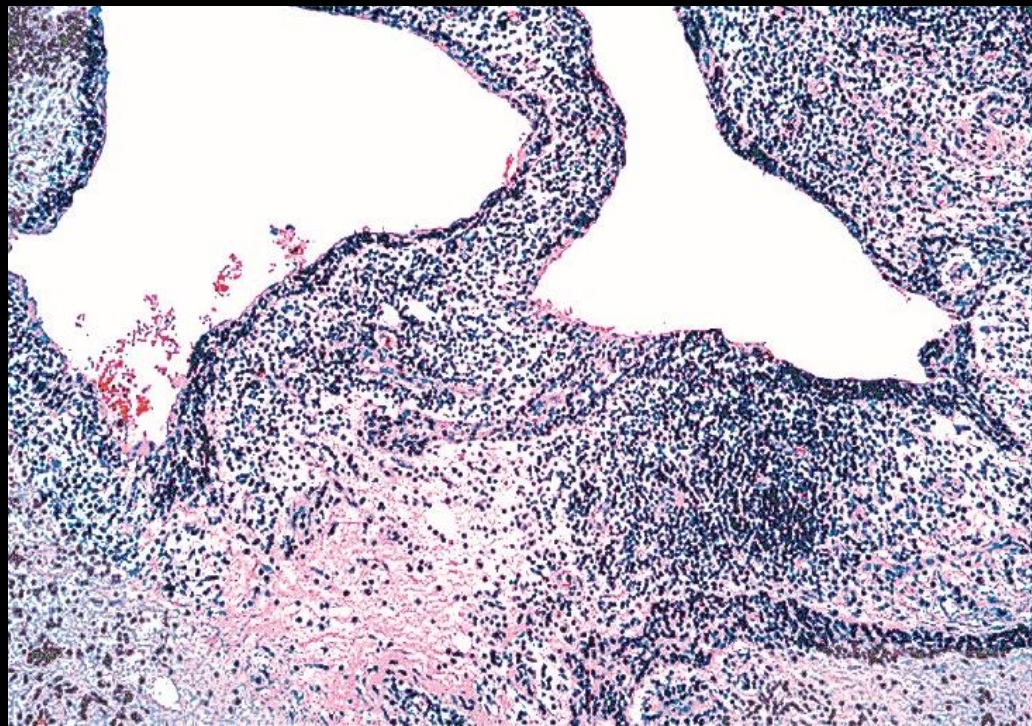
Suster S[1], Rosai J.

Abstract

The clinical and pathologic features in 18 cases of multilocular thymic cyst (MTC) of the anterior mediastinum unassociated with Hodgkin's disease or seminoma were studied. The majority of cases were asymptomatic and discovered incidentally on routine chest x-ray. Several patients presented with acute symptoms of chest pain or discomfort, sometimes associated with dyspnea. Two cases had an incidental thymoma, and two had an incidental thymic carcinoma. The main histologic features of MTC included the following: multiple cystic cavities partially lined by squamous, columnar, or cuboidal epithelium (some having features of Hassall's corpuscles); scattered nests and islands of non-neoplastic thymic tissue within the cyst walls, often continuous with the cyst lining; severe acute and chronic inflammation accompanied by fibrovascular proliferation, necrosis, hemorrhage, and cholesterol granuloma formation; and reactive lymphoid hyperplasia with prominent germinal centers. These features suggest that MTC most likely results from the cystic transformation of medullary duct epithelium-derived structures (including Hassall's corpuscles) induced by an acquired inflammatory process. The changes are similar to those sometimes seen in association with thymic Hodgkin's disease and thymic seminoma, which are also probably due to the inflammation that accompanies these tumors rather than to the tumors themselves. We believe that MTC is pathogenetically analogous to a variety of cystic conditions of the head and neck region, for which the common denominator seems to be the induction of cystic transformation in ductular epithelial formations of branchial pouch or related derivation by an acquired inflammatory process.







Proliferating Thymic Cysts

- Unusual examples of multilocular thymic cyst in which the squamoid lining epithelium proliferates irregularly into the cyst wall, yielding an image which simulates that of squamous carcinoma
- Probably represents "pseudoepitheliomatous hyperplasia" of the lining epithelium, with an unknown cause

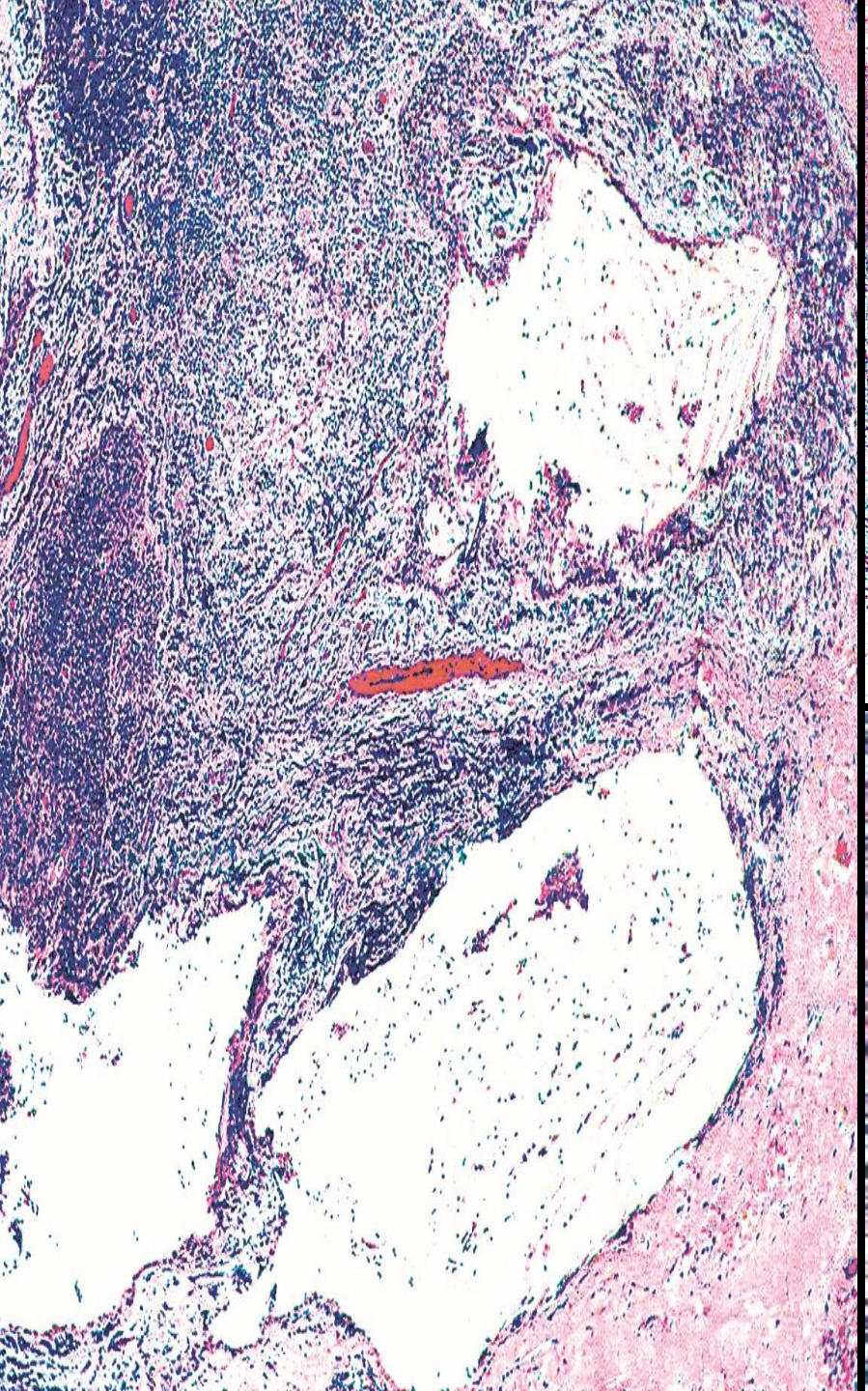
Hum Pathol. 1991 May;22(5):455-60.

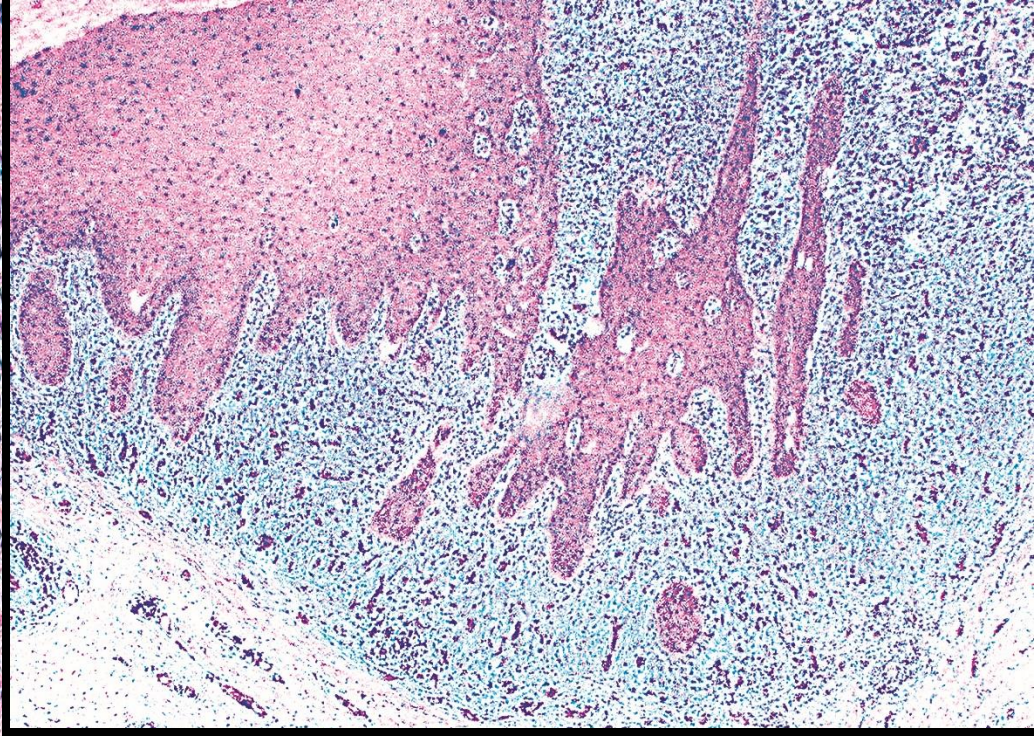
Multilocular thymic cysts with pseudoepitheliomatous hyperplasia.

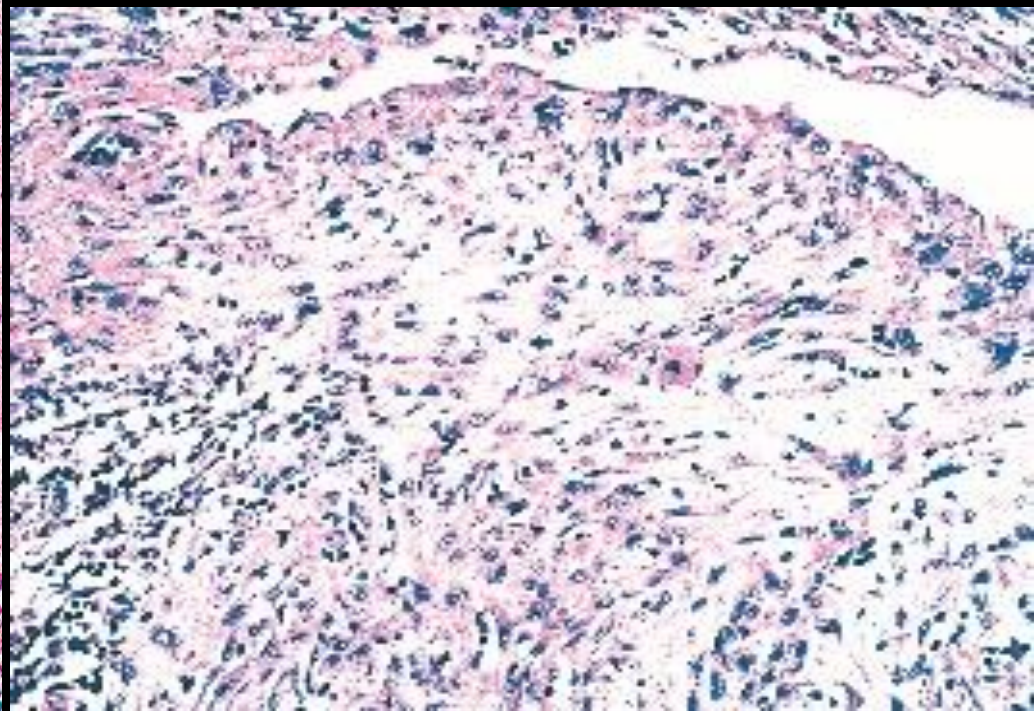
Suster S[1], Barbuto D, Carlson G, Rosai J.

Abstract

Six cases are described of benign thymic cysts of the anterior mediastinum showing focal pseudoepitheliomatous hyperplasia of the lining epithelium. The patients' ages ranged from 11 to 54 years; five cysts occurred in males and one in a female. Histologically, the lesions were characterized by exuberant proliferation of the cyst lining epithelium that grew as sheets and tongues of atypical squamous cells with large, hyperchromatic nuclei, prominent nucleoli, and scattered mitotic figures. The walls of the cyst adjacent to the areas of epithelial proliferation showed abundant hemorrhage, necrosis, and severe inflammatory changes. All cases were treated by local surgical excision. There was no evidence of recurrence or metastases over a follow-up period of up to 8 years (average follow-up, 4 years). It is proposed that pseudoepitheliomatous hyperplasia may develop in thymic cysts as an expression of regeneration of the lining epithelium in response to the inflammatory, hemorrhagic, and necrotizing changes which often accompany these lesions. This should not be mistaken for malignancy, and should be distinguished from the exceptional cases of true thymic neoplasms seen in association with thymic cysts.



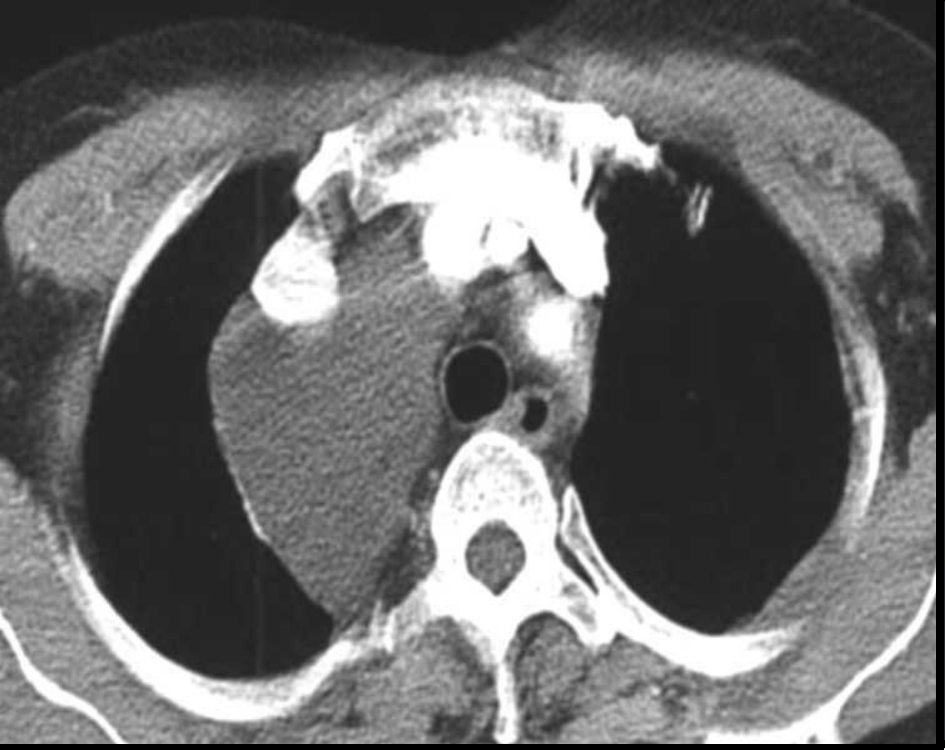


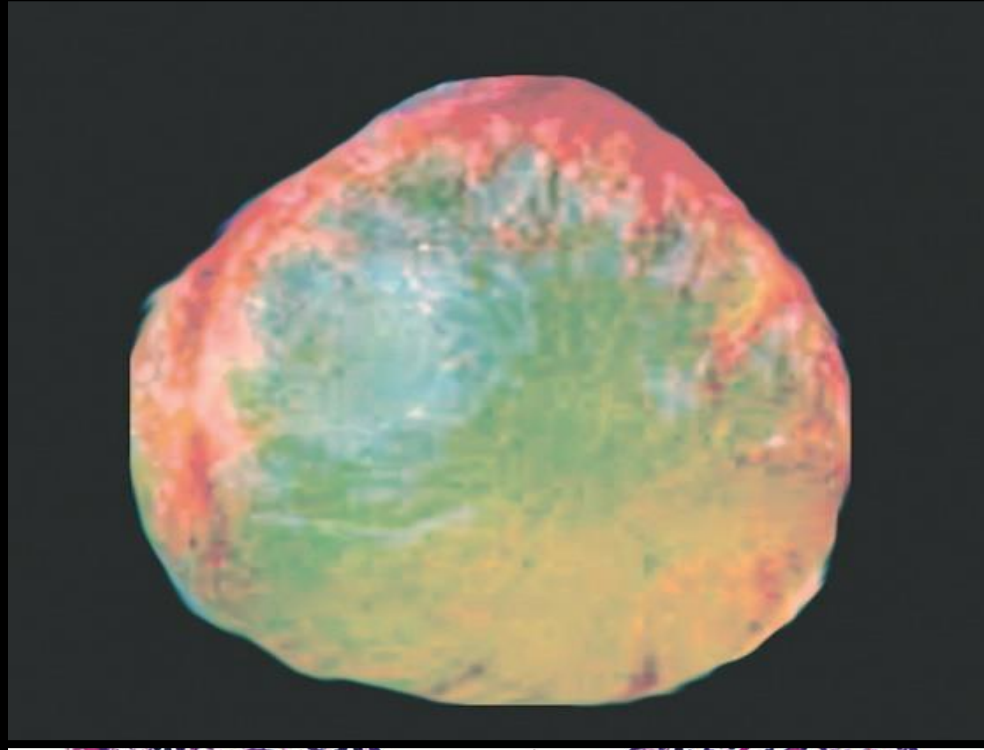


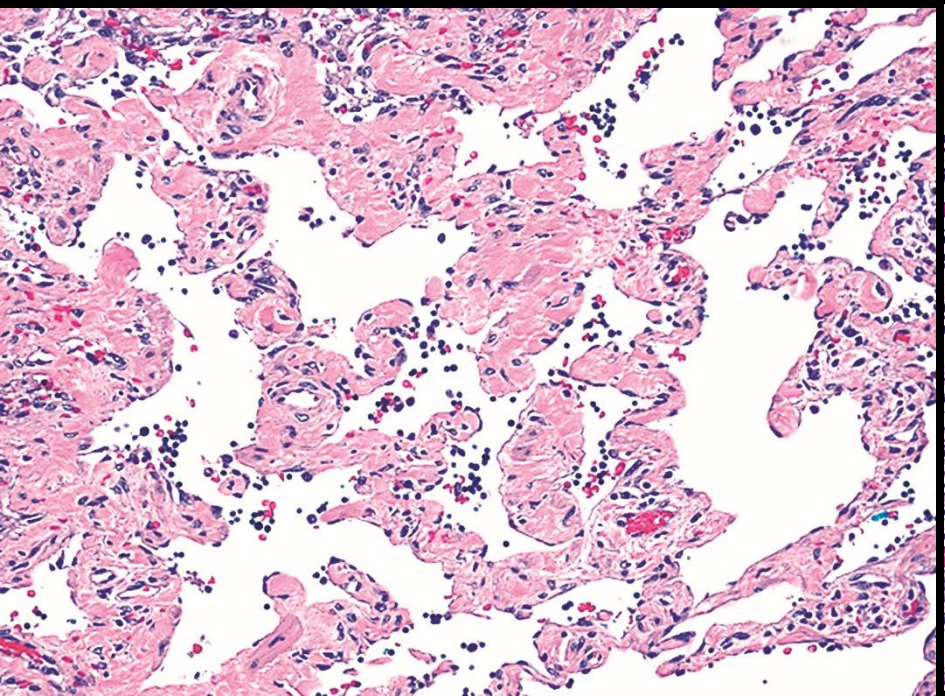
Neoplastic & Paraneoplastic Cystic Lesions of the Mediastinum

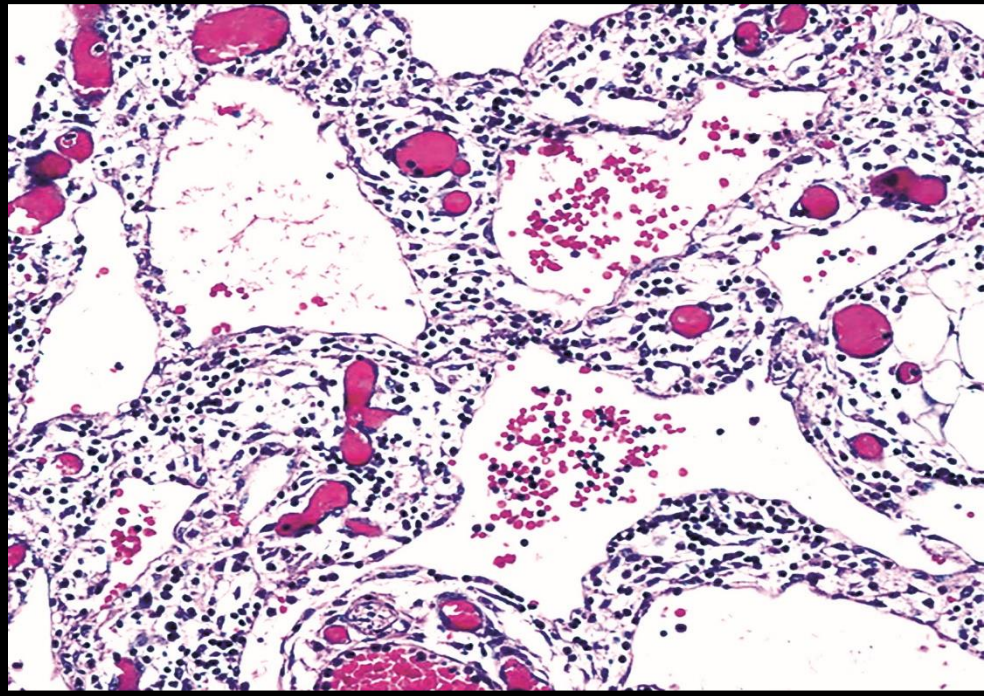
Mediastinal Lymphangiomas

- May be seen in all 3 mediastinal compartments, as unilocular or multilocular masses on imaging studies
- Predominate in children
- Interanastomosing vascular channels, associated with infiltrates of lymphocytes, & sometimes containing internal micropapillations









Thymic Cysts in Hodgkin or Non-Hodgkin Lymphoma

- Usually seen after therapy of some kind (radiation; chemotherapy) but may occur as a spontaneous tumor-related phenomenon as well
- A central cystic cavity is surrounded by atypical lymphoid tissue containing diagnostic Reed cells or, alternatively, non-Hodgkin lymphoma

Thorax. 1995 Oct;50(10):1118-9.

Management of residual thymic cysts in patients treated for mediastinal Hodgkin's disease.

el-Sharkawi AM[1], Patel B.

Abstract

The pathogenesis of residual thymic cysts after treatment for mediastinal Hodgkin's disease is uncertain. Their presence after adequate treatment often presents the oncologist and the thoracic surgeon with a therapeutic dilemma. Two patients with residual thymic cysts after curative treatment for mediastinal Hodgkin's disease are described and the management discussed.

Med Pediatr Oncol. 1988;16(4):293-4.

Concurrent development of a thymic cyst and mediastinal Hodgkin's disease.

Kaesberg PR[1], Foley DB, Pellett J, Hafez GR, Ershler WB.

Abstract

A case is presented of a young adult female who presented with nodular sclerosing Hodgkin's disease and a mediastinal mass that proved to be a thymic cyst. Prior to this illness, a chest x-ray had been obtained that did not show a mediastinal mass. This case illustrates that thymic cysts may arise simultaneously with mediastinal Hodgkin's disease, rather than as a result of treatment or being present congenitally.

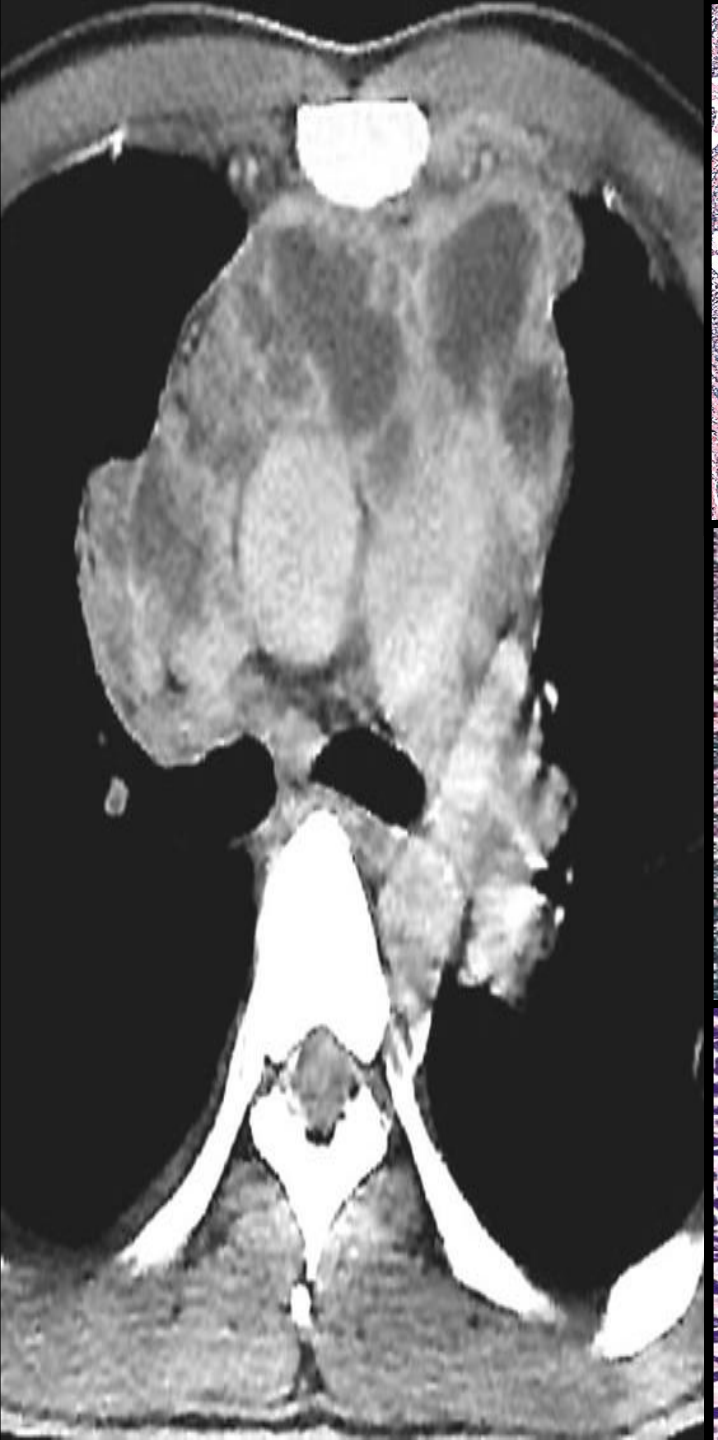
Med Pediatr Oncol. 1994;22(1):70-2.

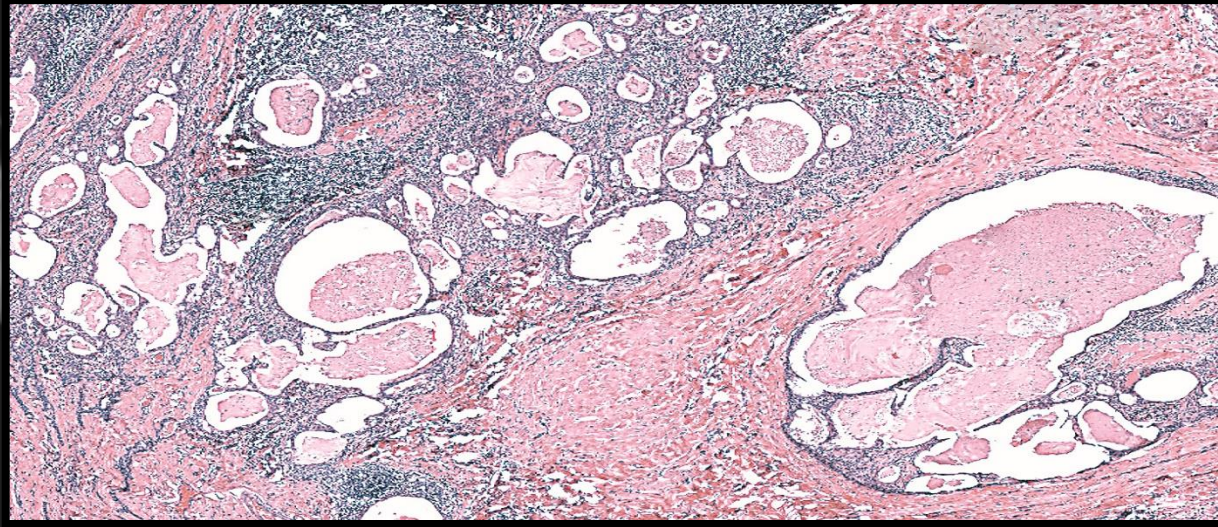
Thymic cyst appearing after treatment of mediastinal non-Hodgkin lymphoma.

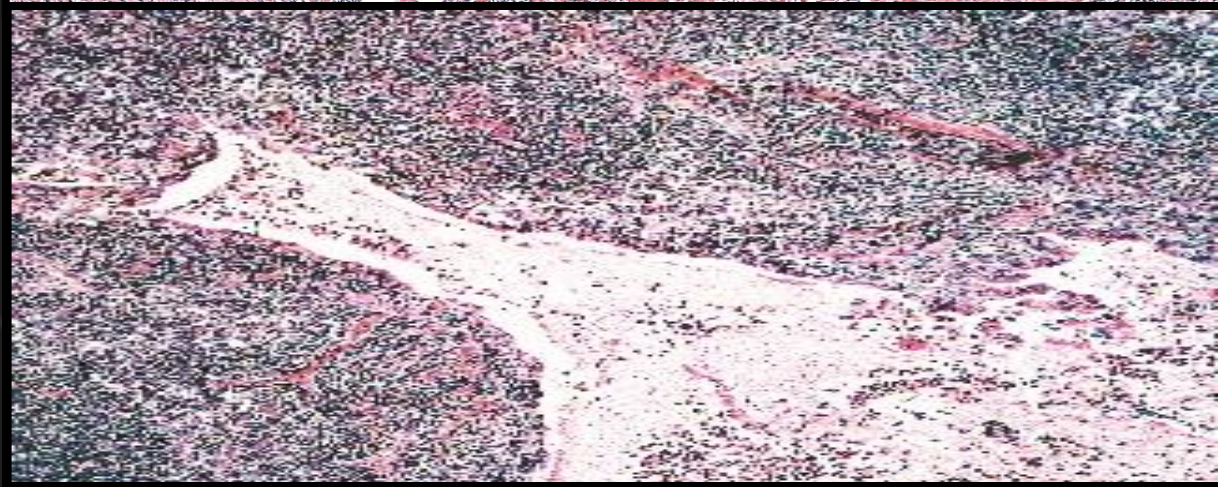
Borgna-Pignatti C[1], Andreis IB, Rugolotto S, Balter R, Bontempini L.

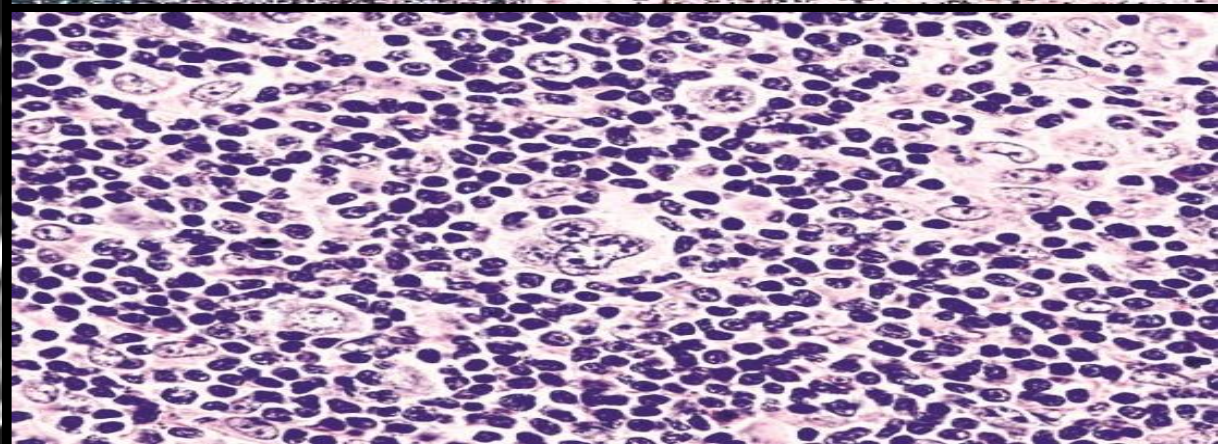
Abstract

We report the first case of a thymic cyst appearing in the course of treatment for non-Hodgkin lymphoma of the anterior mediastinum. The patient was a 9-year-old child in whom an abnormal contour of the left cardiac border persisted after chemotherapy, suggesting residual disease. The mass was found at thoracotomy to be a benign thymic cyst. The lesion was not present 2 years previously, and most likely represented cystic degeneration of the thymus, secondary to lymphomatous involvement. CT scan was not helpful in distinguishing the cystic lesion from residual lymphoma.







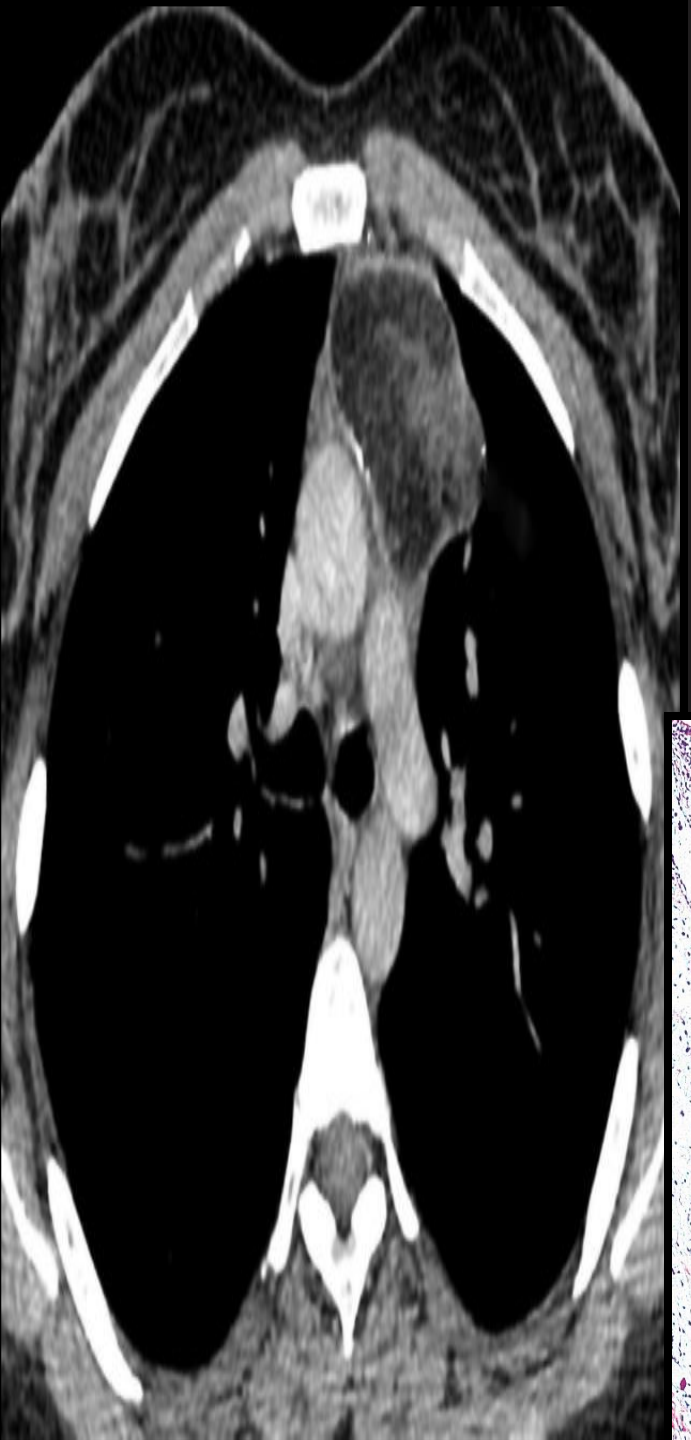


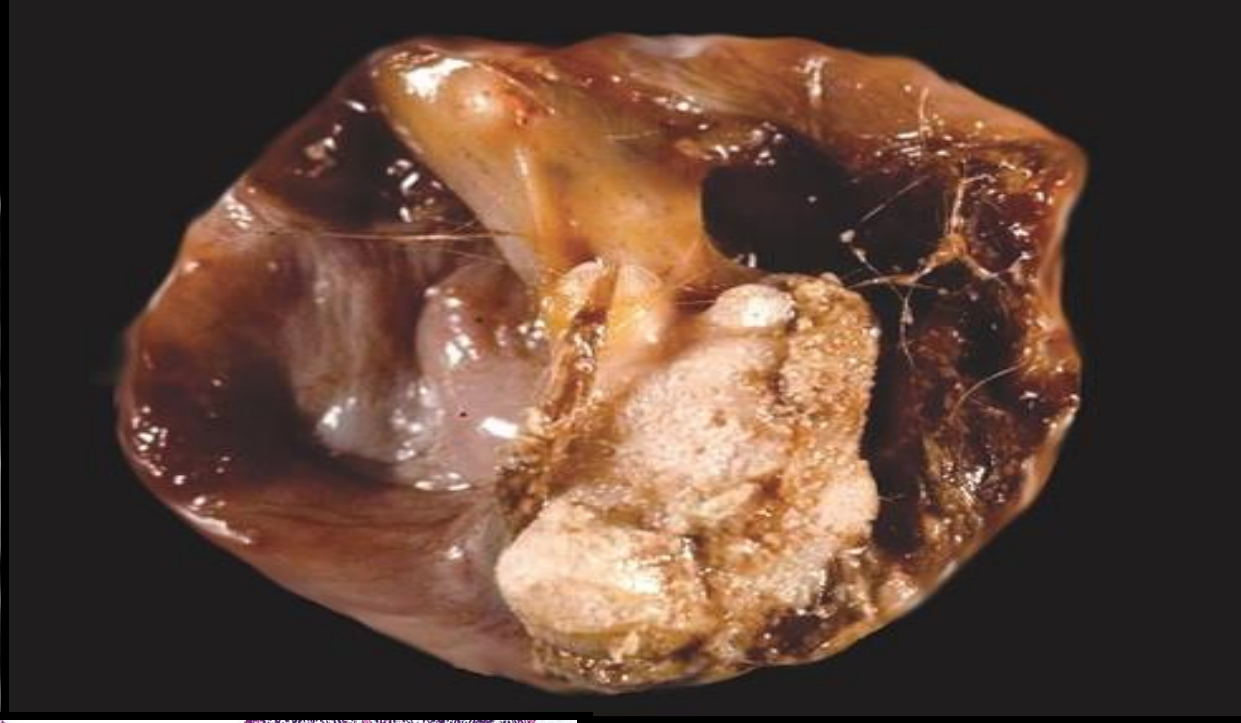
Other Potentially-Cystic Neoplasms of the Anterior Mediastinum

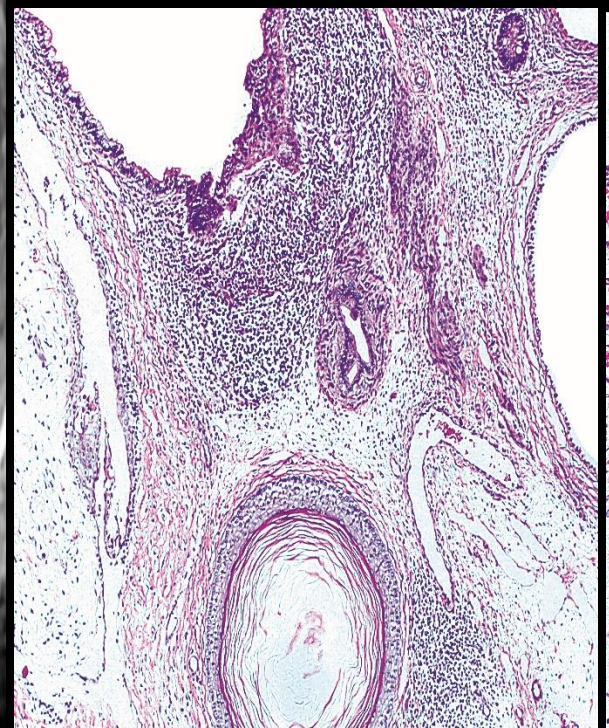
- **Teratoma**
- **Thymoma**
- **Carcinoma *ex* thymic cyst**
- **Cystic *de novo* thymic carcinoma**
- **Seminoma**
- **Thymic carcinoid tumor**

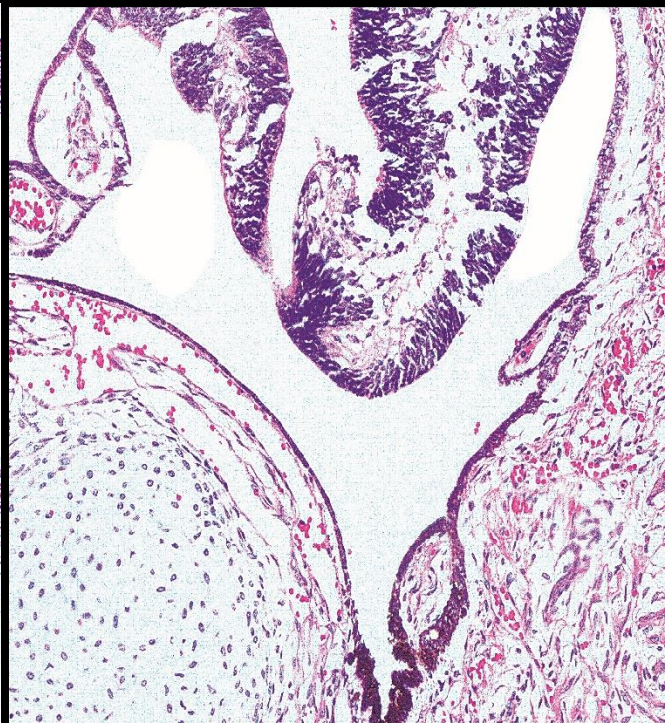
Intrathymic Cystic Teratomas

- Predominantly seen in children and young adults, typically presenting with nondescript symptoms & signs or as lesions found incidentally on chest radiographs
- "Eggshell" calcification of the mass is possibly seen in plain-film radiographs
- At least 2 of 3 germ layers must be represented in the lesional tissue
- Immature neuroepithelial components are not prognostically important before the age of 15 years









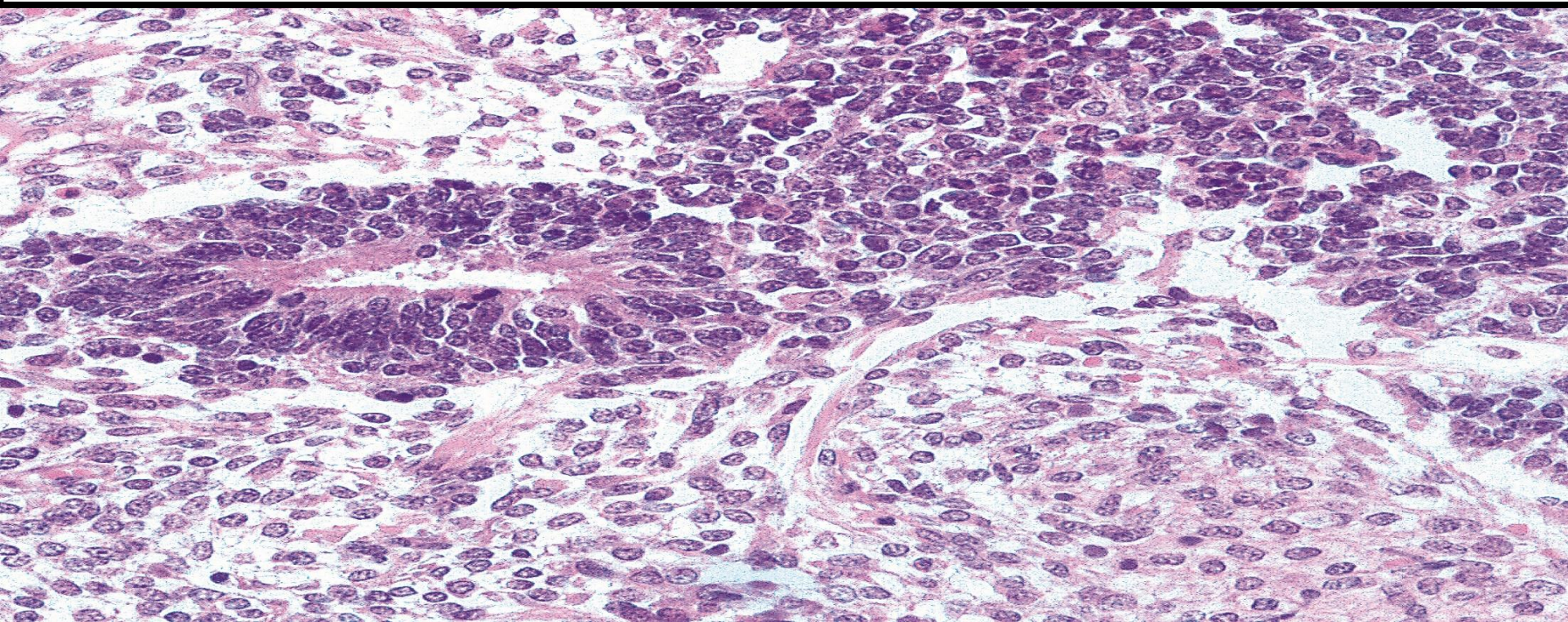
Cancer. 1982 Jan 15;49(2):398-402.

Benign clinical behavior of immature mediastinal teratoma in infancy and childhood: report of two cases and review of the literature.

Carter D, Bibro MC, Touloukian RJ.

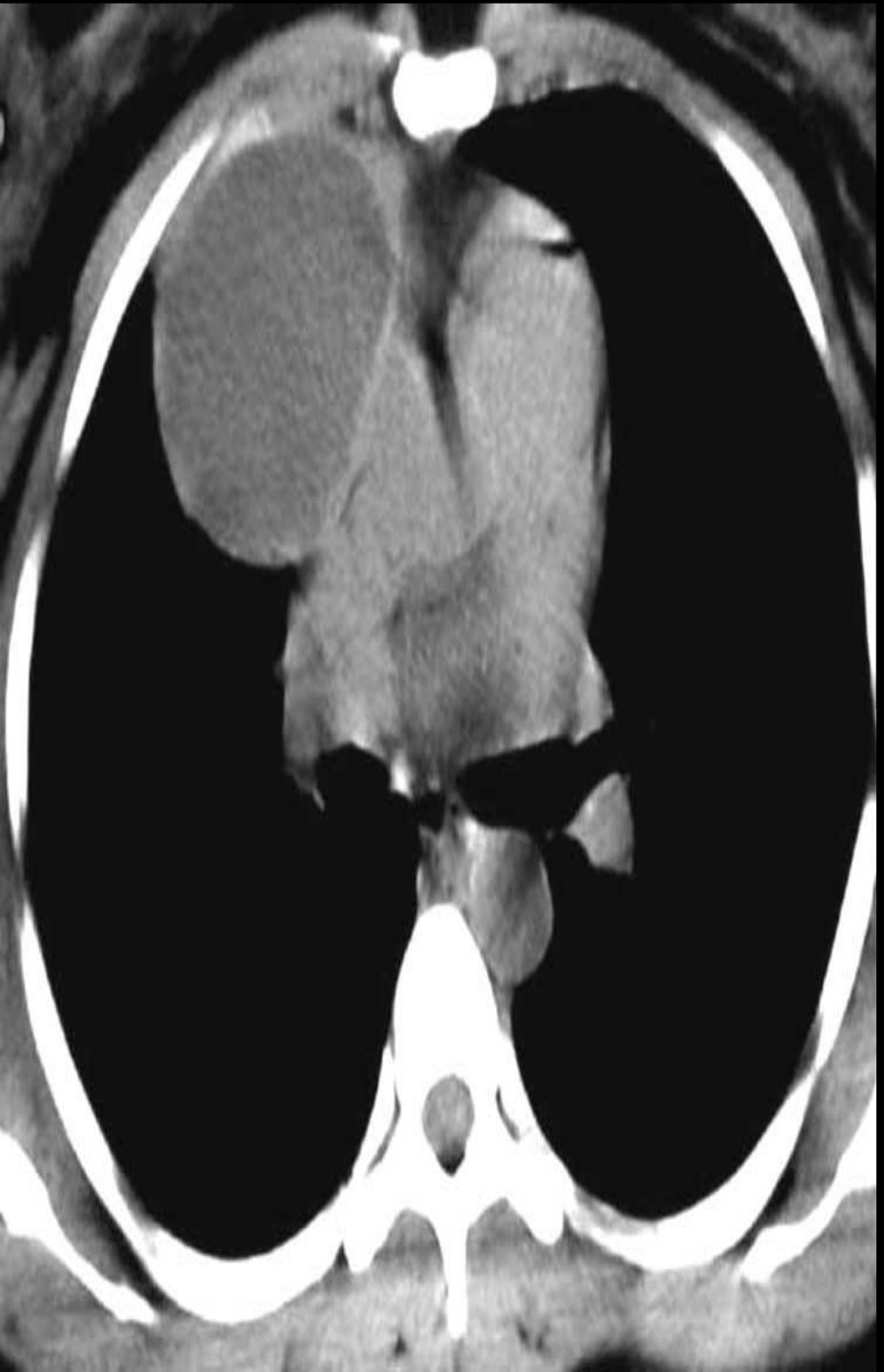
Abstract

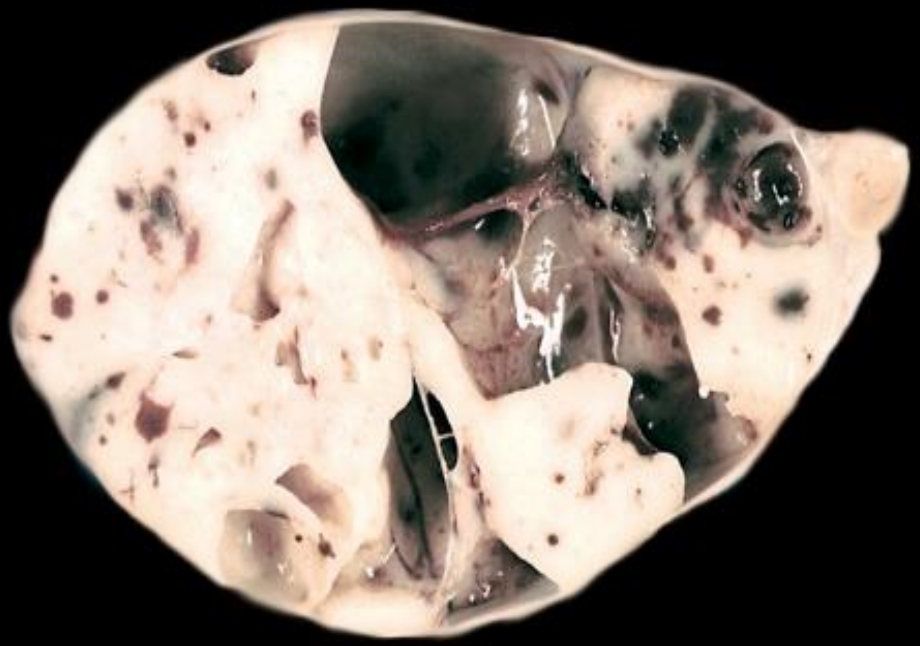
Germ cell tumors of the mediastinum can be divided into three categories: 1) mature teratomas which have all elements at a mature level; 2) immature teratomas which are similar to the mature teratomas, but also contain immature epithelial or mesenchymal elements or blastema; and 3) embryonal tumors which contains elements which are recognized as dysgerminoma, embryonal carcinoma with or without yolk sac elements, and choriocarcinoma. Immature teratomas are the rarest type, accounting for only about 1% of mediastinal teratomas. Two cases of immature teratoma of the mediastinum occurring in infants are reported. One tumor was completely excised. The child is well without evidence of disease two years later. The other immature teratoma was unresectable. Biopsy showed it to be similar to the teratoma that was excised. No postoperative treatment was given. The tumor has not changed appreciably in size, but the child has grown normally for six years so that the tumor mass, which initially filled his chest, is now evidenced as mediastinal widening. A review of the reported cases of immature teratomas in the mediastinum shows that the prognostic value of the histologic appearance of these tumors has not been developed to the same degree as it has for teratomas in the ovary or the sacrococcygeal region. The immature teratomas that occur in infants behave as mass lesions as do the mature teratomas. Immature teratomas in the mediastinum of children in their late teens and in young adults behave as highly malignant tumors similar to the embryonal carcinomas.

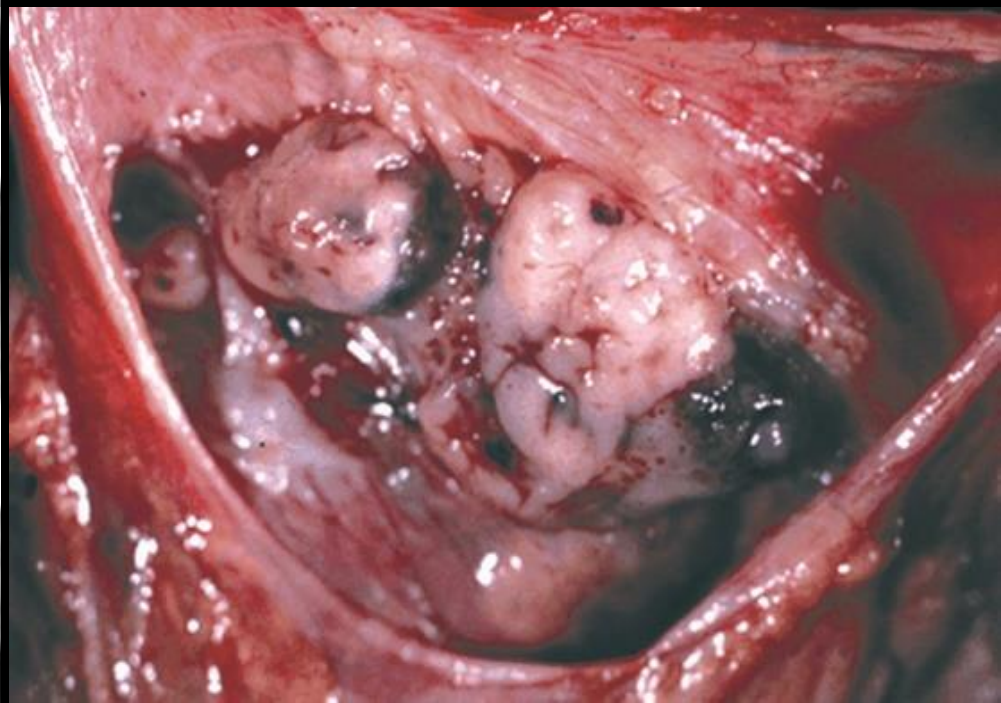


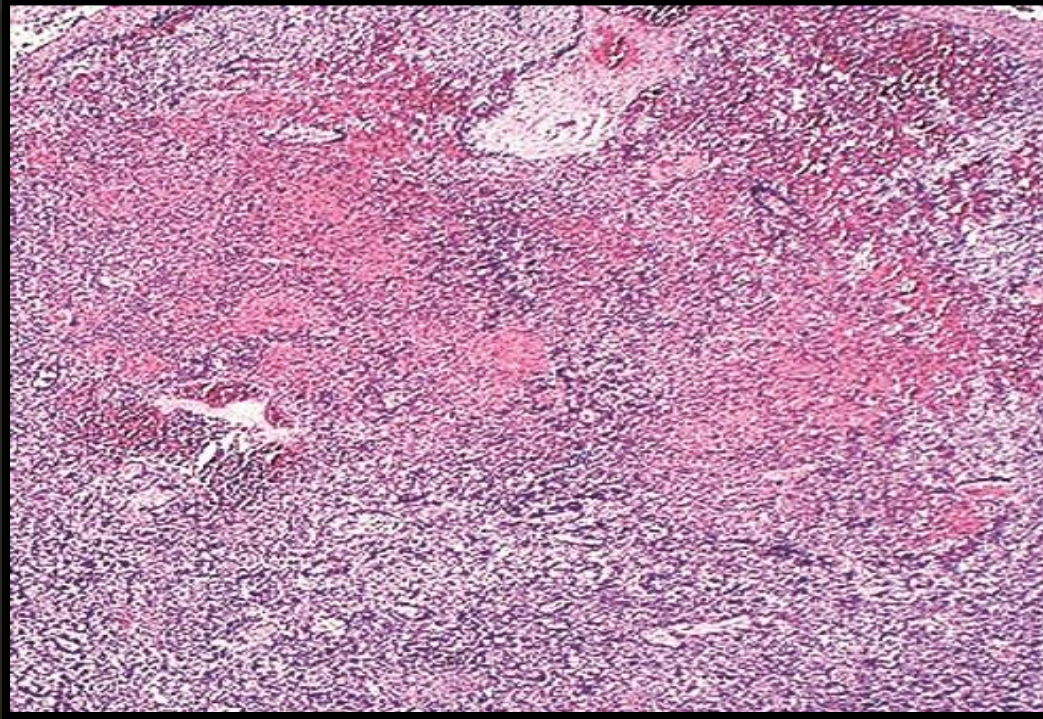
Cystic Thymoma

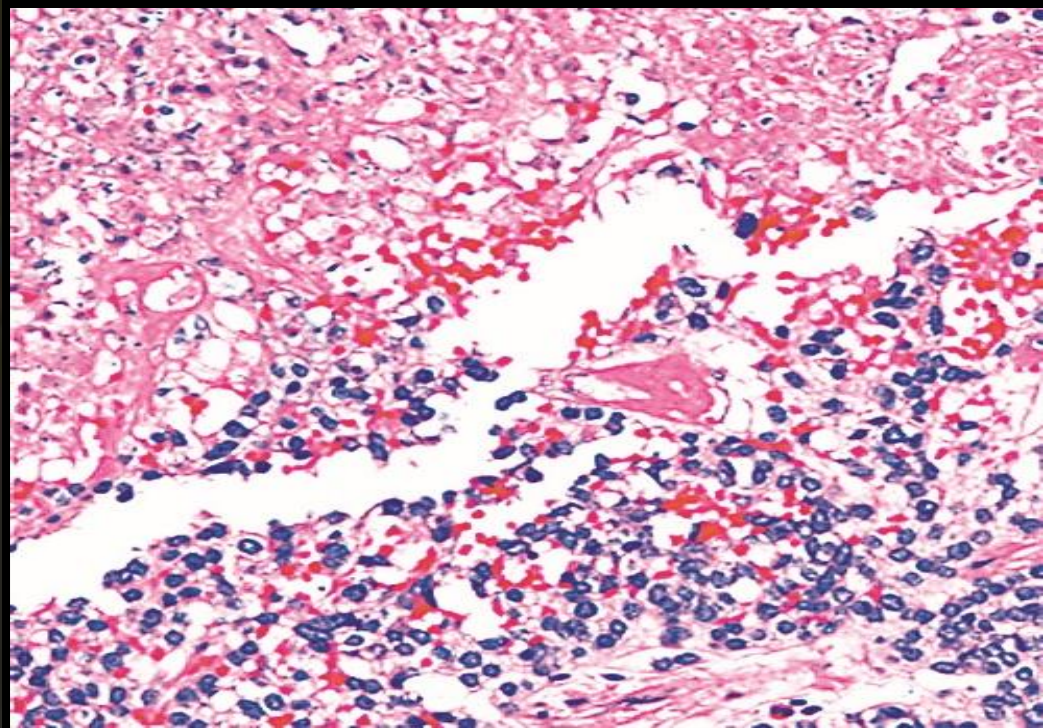
- Spontaneous cystic change may be so marked in thymoma that the initial pathologic impression is that of thymic cyst
- Thorough sampling of the lesional wall may well be necessary to identify neoplastic tissue
- Occasional tumors manifest a striking degree of hemorrhage and necrosis, but these findings do not influence prognosis











Carcinomas & Thymic Cysts

- A rare event that appears to be associated only with the multilocular form of thymic cyst
- Enlarging mural nodules are visible in the cyst radiographically
- Histotypes of the carcinomas in this setting include keratinizing & non-keratinizing squamous carcinoma; basaloid carcinoma; mucoepidermoid carcinoma; papillary carcinoma; & sarcomatoid carcinoma
- *De novo* thymic carcinomas also may become cystic

Am J Surg Pathol. 2011 Jul;35(7):1074-9. doi: 10.1097/PAS.0b013e31821c7402.

Thymic carcinoma associated with multilocular thymic cyst: a clinicopathologic study of 7 cases.

Weissferdt A[1], Moran CA.

Abstract

We present 7 cases of thymic carcinoma associated with a multilocular thymic cyst (MTC). The patients were 5 men and 2 women aged 22 to 71 years (mean, 49.3 y). Clinically, 6 patients presented with chest, sternal, or upper extremity pain, and in 1 patient the tumor was an incidental finding. Grossly, 4 tumors were described as multilobulated solid-cystic masses, whereas 3 cases were described as solid tumors with a white-yellow cut surface and areas of hemorrhage and necrosis. The tumor size ranged from 7.0 to 10.0 cm (mean, 8.1 cm). Histologically, 4 cases were classified as squamous cell carcinoma, and 1 each as sarcomatoid (spindle) cell carcinoma, papillary carcinoma, and basaloid carcinoma. In addition to the tumor component, prominent MTC changes were observed in the adjacent remnant thymic tissue. Immunohistochemical studies were conducted in 2 cases of squamous cell carcinoma. The neoplastic cells were positive for cytokeratin (CK), CK5/6, and p63, and showed variable reactivity for CK7 and CD5. Clinical follow-up showed that 4 patients were alive and well, 2 to 63 months after diagnosis, and 3 patients were alive with disease, 13 to 33 months after diagnosis. This study expands the morphologic spectrum of thymic carcinoma associated with MTC, detects a higher incidence than previously believed, and highlights the importance of adequate sampling and proper evaluation of all cystic lesions of the anterior mediastinum so as not to mistake malignancy for a benign cystic process.

Histopathology. 2015 Jun 1. doi: 10.1111/his.12748. [Epub ahead of print]

Cystic well differentiated squamous cell carcinoma of the thymus A clinicopathological and immunohistochemical study of 6 cases.

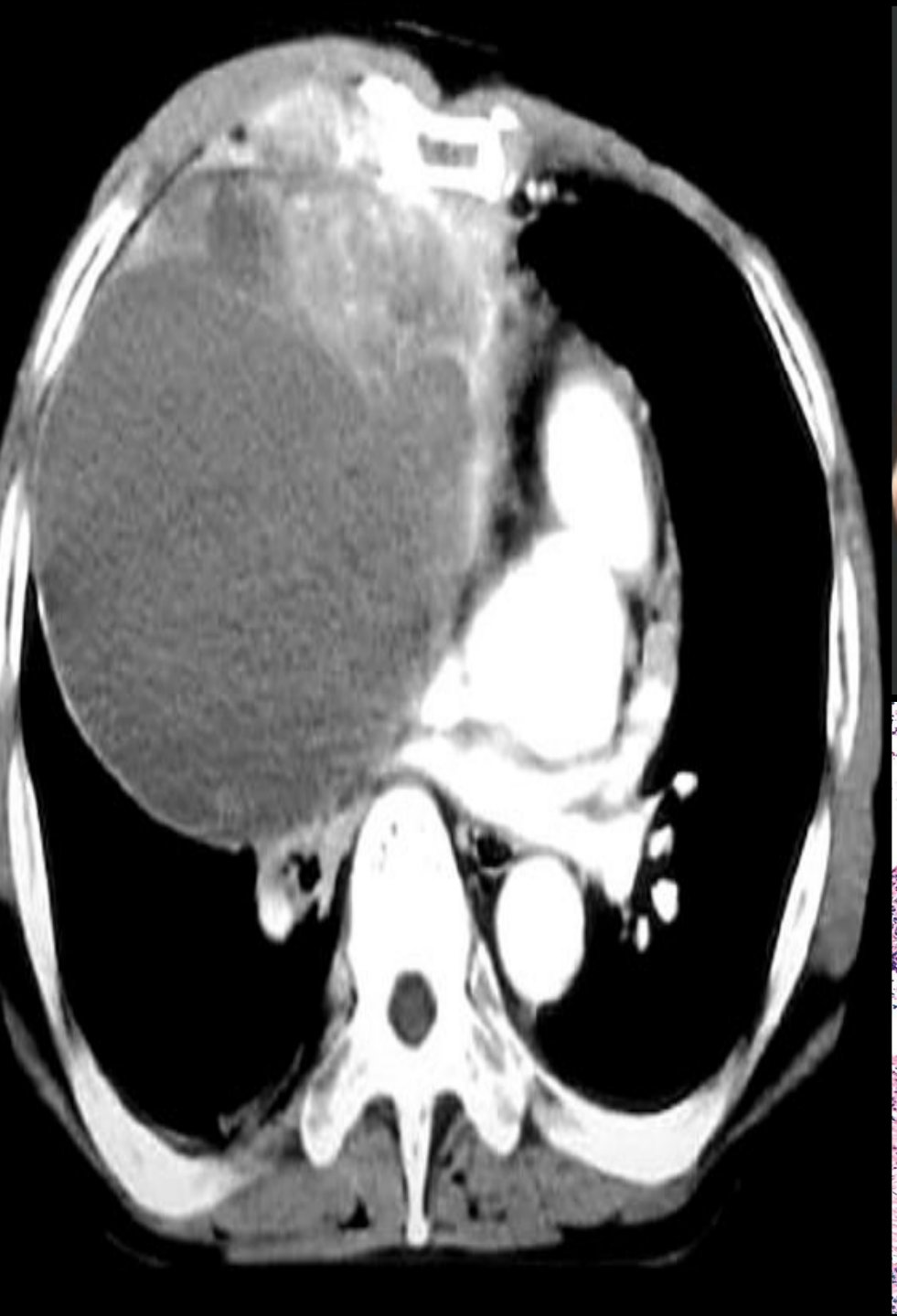
Weissferdt A[1], Kalhor N[1], Moran CA[1].

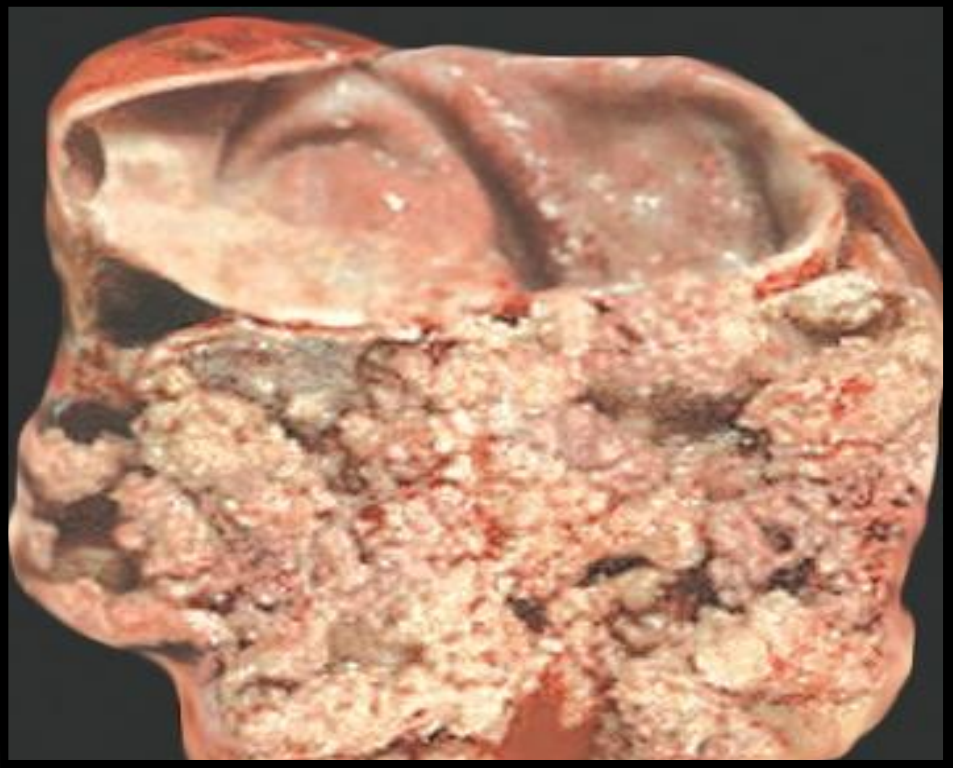
Abstract

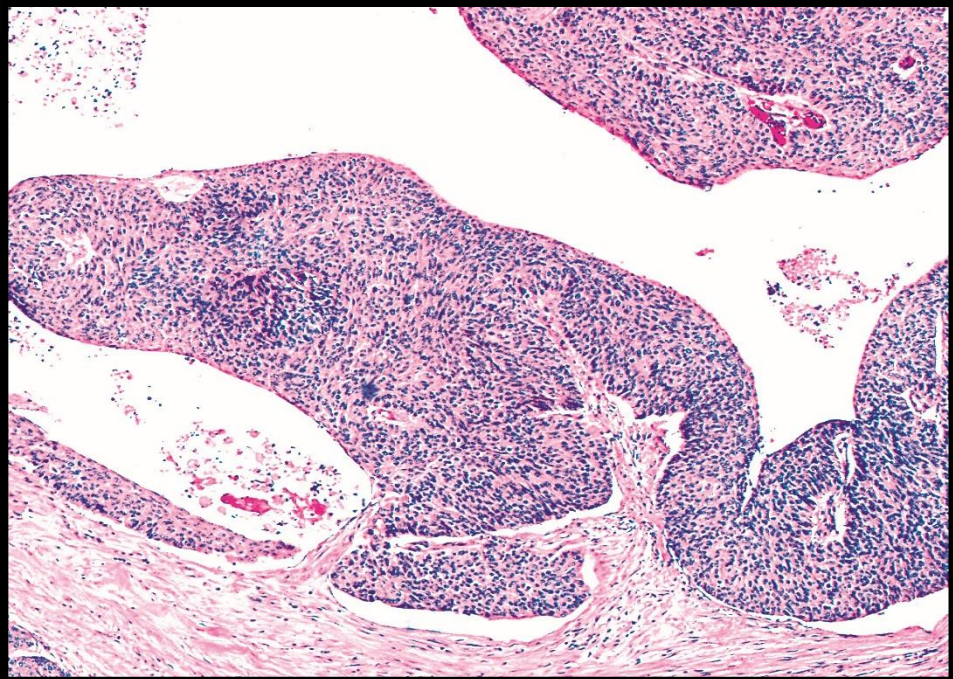
AIMS: Six cases of cystic well differentiated squamous cell carcinomas of the thymus are presented.

METHODS AND RESULTS: The patients were six men aged between 48 and 75 years (average 61.5 years) who were symptomatic with chest pain, shortness of breath, and dyspnoea. Diagnostic imaging showed anterior mediastinal masses and surgical resection was accomplished in all. Grossly, the tumours measured 4 to 9 cm in greatest diameter (average: 6.5 cm) and were described as ill-defined lesions with a prominent cystic component and focal areas of hemorrhage and necrosis. Histologically, they were characterized predominantly by their cystic architecture. The cyst walls were lined by squamous epithelium showing different degrees of cellular atypia. In focal more solid areas, the tumours showed evidence of keratinization. By immunohistochemistry, tumour cells were positive for cytokeratin 5/6, p40, and Pax8. All tumours were staged as T1N0M0 using the Weissferdt-Moran staging system. Clinical follow-up showed that 4 patients have remained alive and well after a period ranging from 1 to 2 years. Two patients were lost to follow-up.

CONCLUSIONS: The current cases highlight an uncommon growth pattern of well differentiated squamous cell carcinoma of the thymus that may cause diagnostic difficulty with mediastinoscopic biopsies.







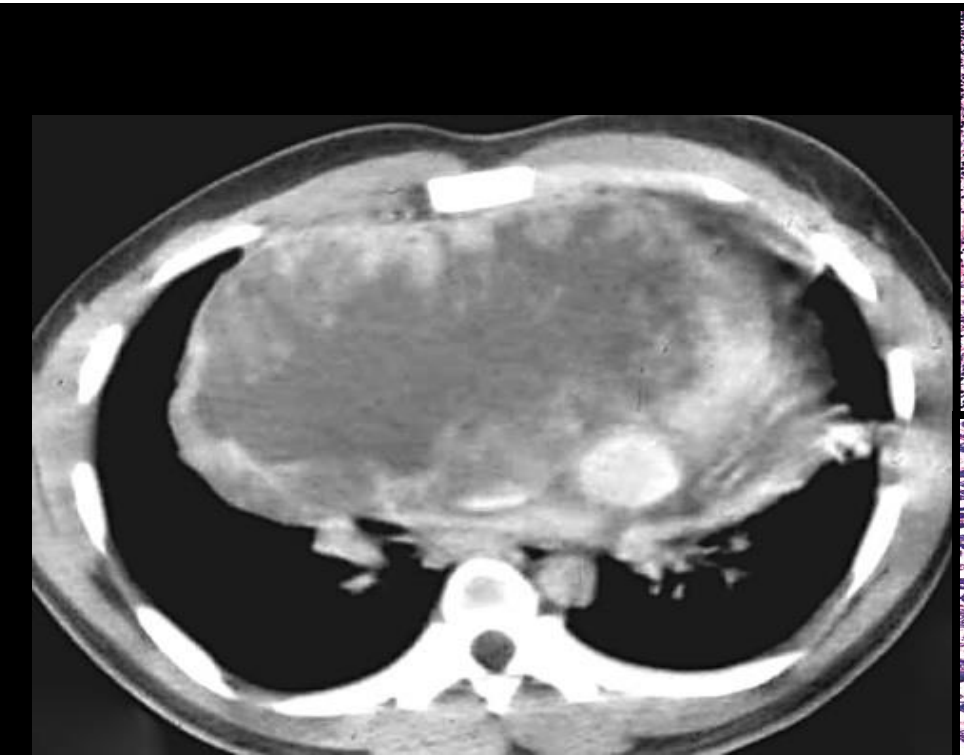
Am J Surg Pathol. 1995 Sep;19(9):1047-53.

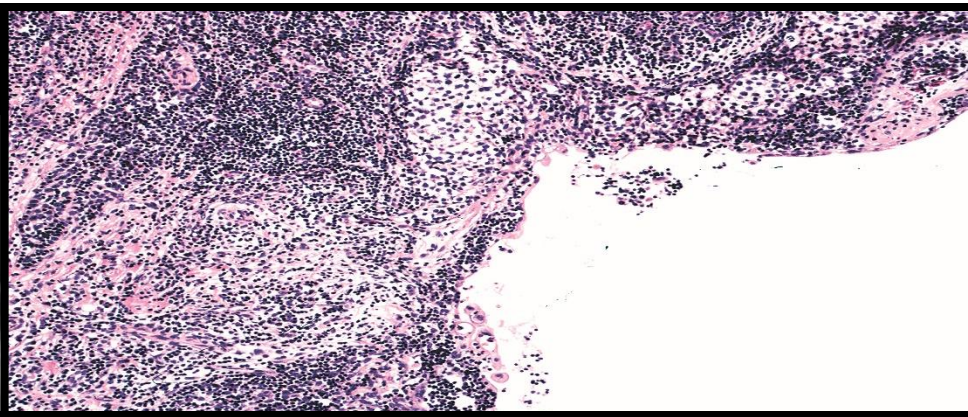
Mediastinal seminomas with prominent cystic changes. A clinicopathologic study of 10 cases.

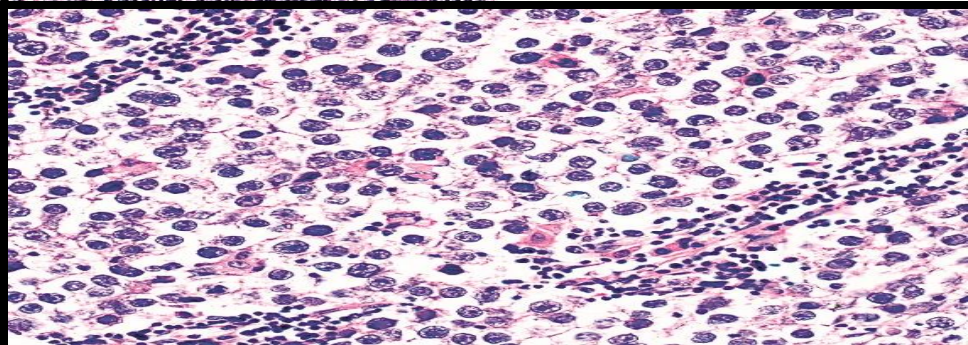
Moran CA[1], Suster S.

Abstract

We present 10 cases of thymic seminomas associated with prominent cystic changes. All patients were males, aged 16 to 79 years (median, 23.5). Clinically, two patients presented with chest pain/four were asymptomatic and the tumors were discovered on routine chest radiographs; one tumor was discovered incidentally at autopsy; and in three patients no clinical information was obtained. Grossly, the tumors were described as multilocular cystic lesions that ranged in size from 7 to 19 cm in greatest dimension, showing small focal areas of induration within the cyst walls. Histologically, the lesions were characterized by cystic spaces lined by squamous or cuboidal epithelium showing severe chronic inflammatory changes with areas of cholesterol cleft granulomas, lymphoid follicular hyperplasia, and scattered foci of residual thymic parenchyma within the walls of the cysts, resulting in a picture indistinguishable from acquired multilocular thymic cysts. Careful examination, however, revealed microscopic foci composed of a neoplastic proliferation of large polygonal cells with slightly eosinophilic to clear cytoplasm and large nuclei with prominent nucleoli. The atypical cells were admixed with an inflammatory background and were often accompanied by a florid granulomatous reaction. Periodic acid-Schiff histochemical reaction with diastase revealed moderate amounts of glycogen within the cytoplasm of the tumor cells. Immunohistochemical studies in five cases showed positive labeling of the tumor cells with placental alkaline phosphatase. Nine patients were treated by complete surgical excision of the mass, and additional postoperative radiation therapy was given to two patients. Follow-up information available for five patients showed all to be alive and well from 2 to 19 years after diagnosis (mean follow-up, 9 years). Four of the patients were lost to follow-up. The pathogenesis of the cystic process in these cases remained unsettled but may represent a reactive change secondary to epithelial hyperplasia of thymic epithelium. Thymic seminoma should be considered in the differential diagnosis of cystic lesions of the anterior mediastinum; extensive sampling of such lesions is therefore recommended for proper evaluation.







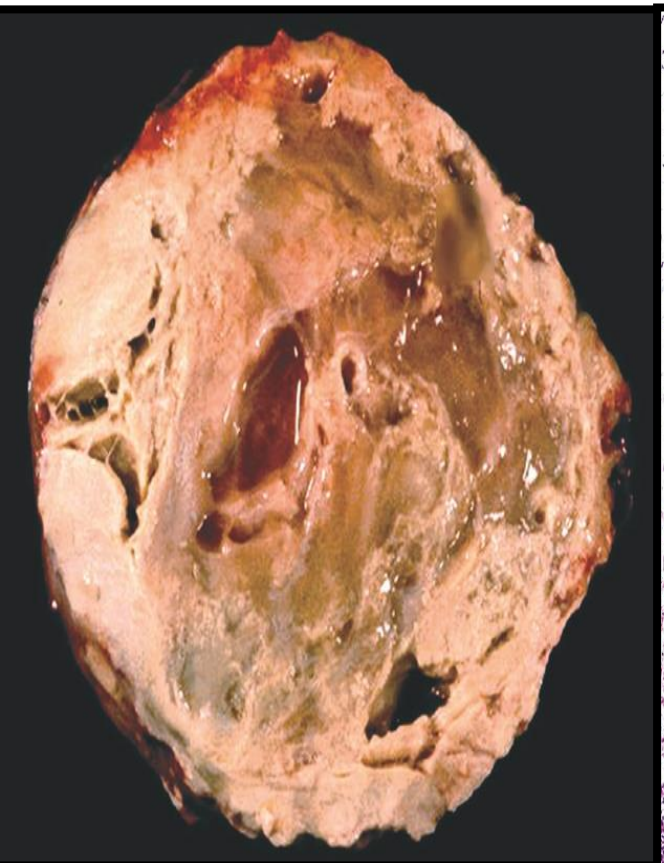
Am J Clin Pathol. 2006 Sep;126(3):377-80.

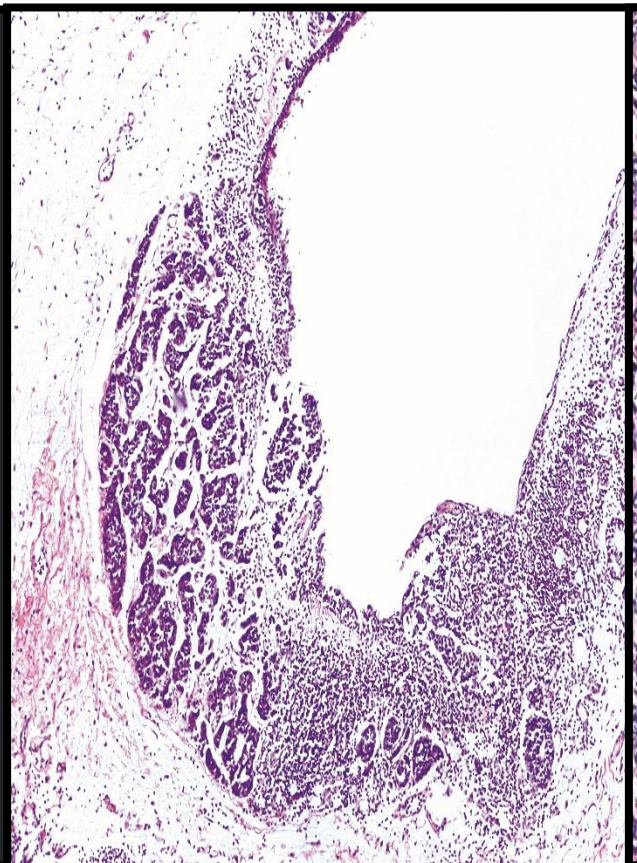
Cystic well-differentiated neuroendocrine carcinoma (carcinoid tumor): a clinicopathologic and immunohistochemical study of two cases.

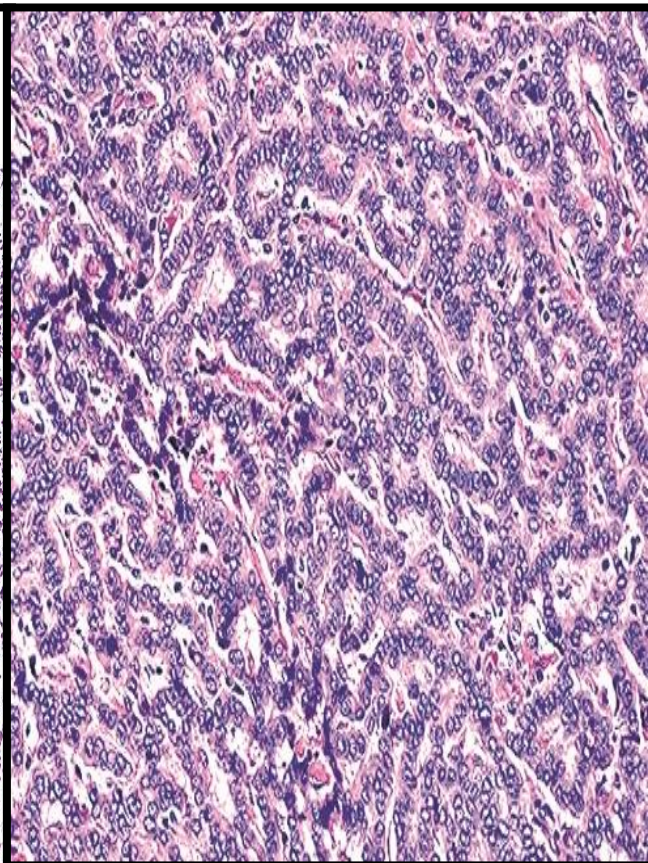
Moran CA[1], Suster S.

Abstract

Two cases of primary neuroendocrine carcinoma (carcinoid tumor) arising in the walls of a multilocular thymic cyst (MTC) are described. The patients were 2 men, ages 36 and 44 years. Clinically, the patients had chest pain, cough, and dyspnea. Radiographic evaluation demonstrated the presence of anterior mediastinal tumor in both patients, and complete surgical resection of the tumor mass was performed. The tumors measured approximately 6 and 8 cm in greatest dimension and were cystic with solid areas but did not show areas of necrosis or hemorrhage. Histologic examination revealed a cystic tumor with features similar to those previously described for MTCs. In addition, in the walls of the cystic structures, there was cellular proliferation arranged in a nesting growth pattern, similar to the more solid areas of the tumor. The tumor was characterized by a homogenous cellular proliferation with mild cellular atypia and no more than 2 mitotic figures per 10 high-power fields. Immunohistochemically, the tumor cells showed strong positive reactions for keratin and neuroendocrine markers, ie, chromogranin and synaptophysin. Both patients were alive after periods of 12 and 18 months.





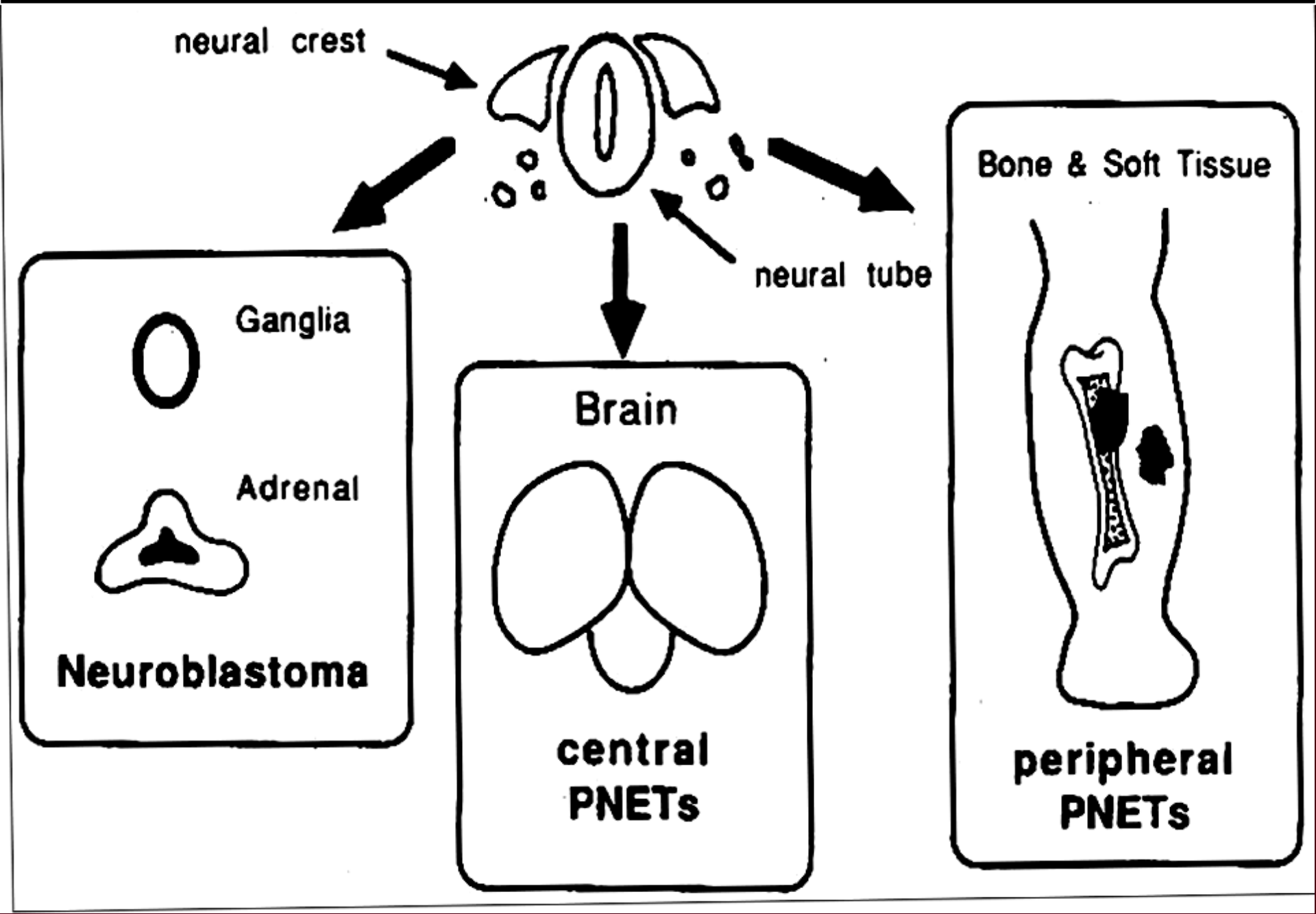


NEUROECTODERMAL TUMORS OF THE MEDIASTINUM

MEMBERS OF THE "EWING'S FAMILY" OF SMALL CELL TUMORS

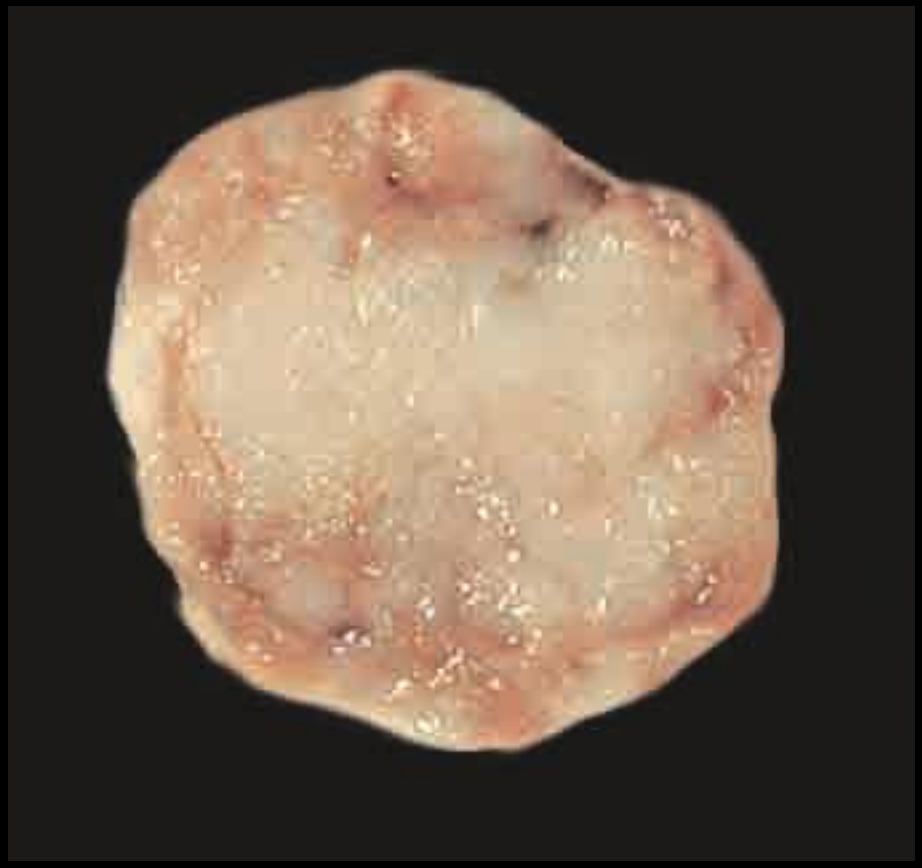
- **Prototypic Ewing's tumor/Primitive neuroectodermal tumor (monophenotypic)**
- **Peripheral and central polyphenotypic small cell tumors (including desmoplastic small cell tumor)**

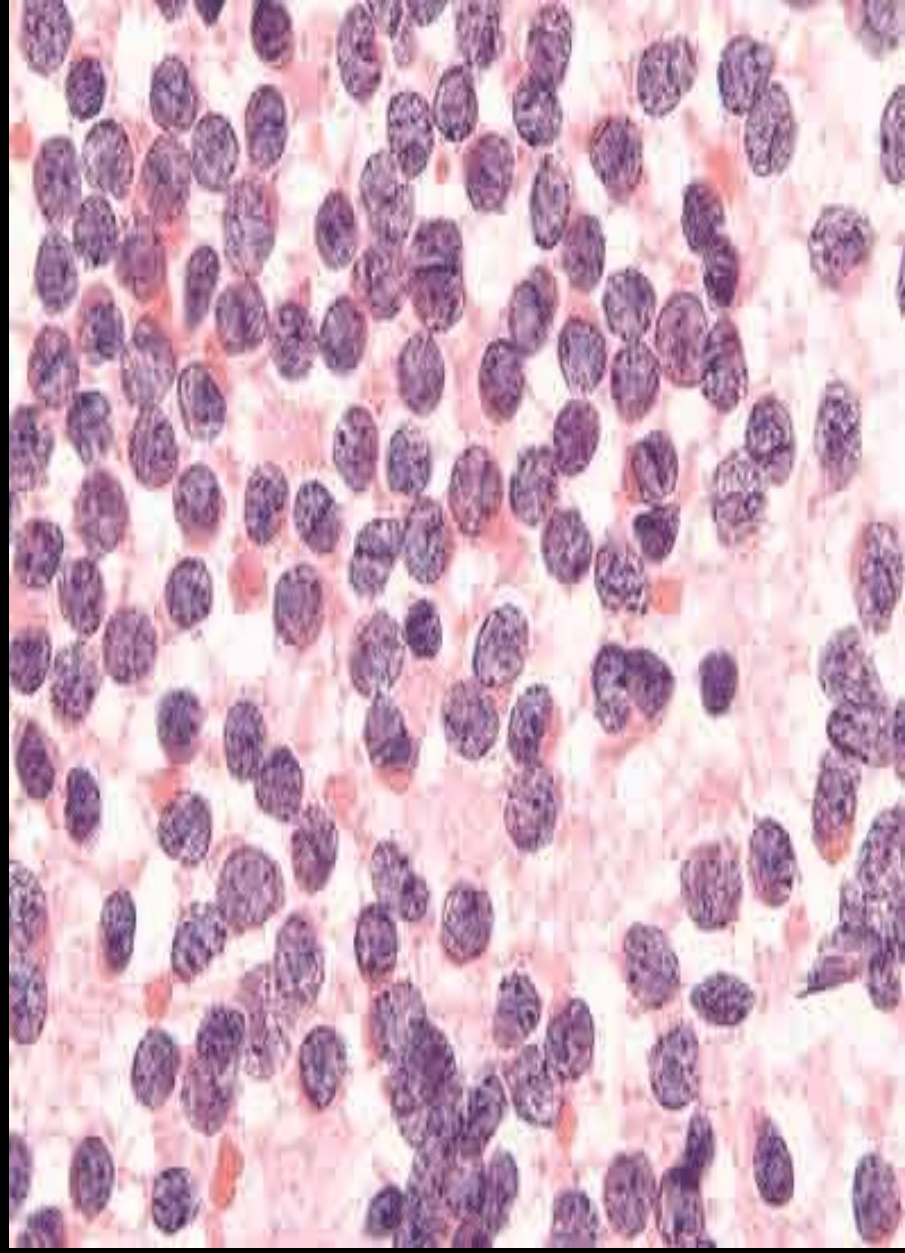
Neuroectoderm



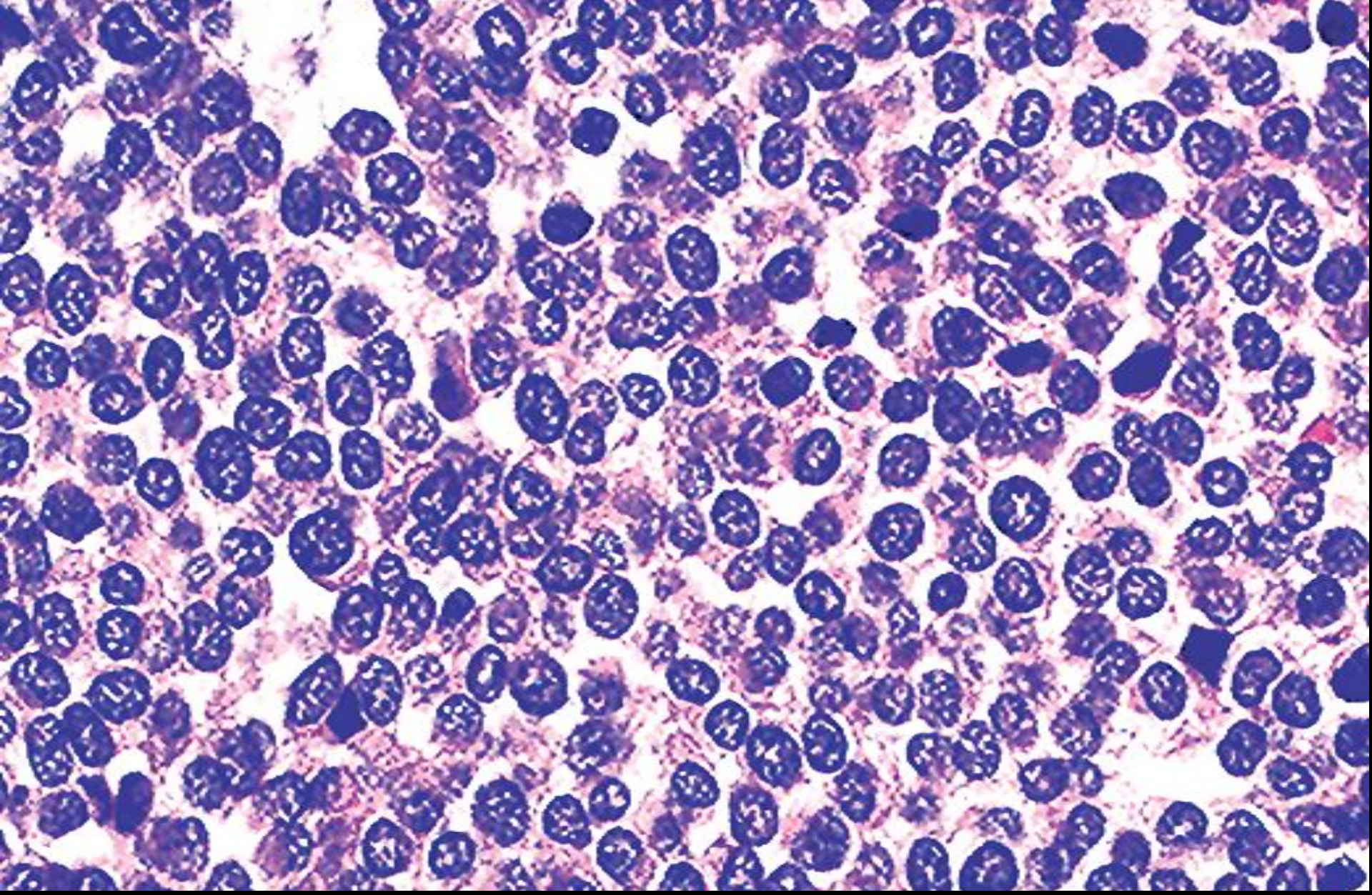
PRIMITIVE NEUROECTODERMAL TUMORS:
Clinical Features

- Patients generally under 35 years of age , with a slight male predominance
- Presenting symptoms and signs are principally represented by a mass, with or without pain
- Large intrathoracic lesions may cause cough & dyspnea, and those in the abdomen may lead to constipation, urinary retention, and a palpable mass
- Tumors may be bulky and measure up to 40 cm. in greatest dimension

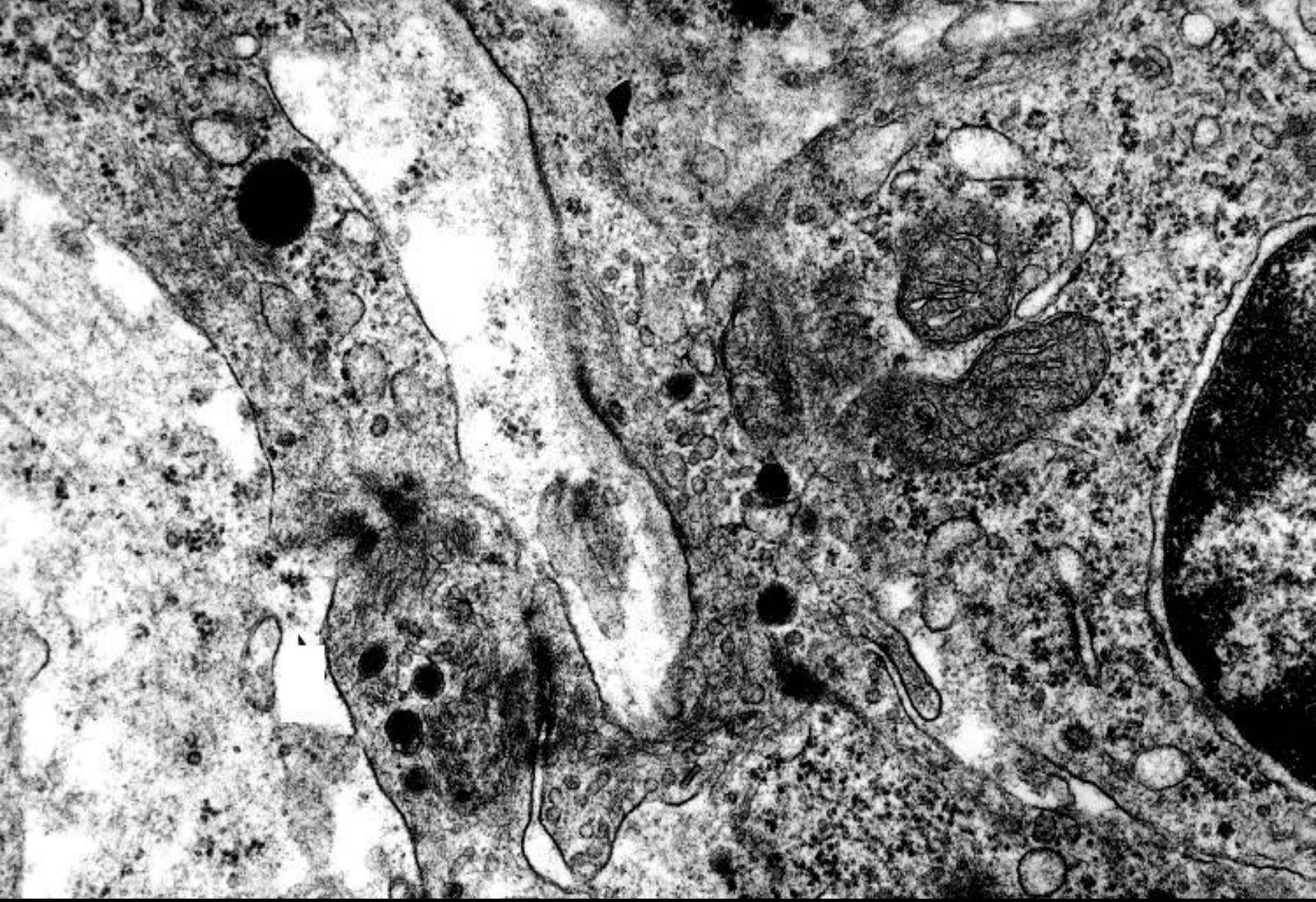




Primitive Neuroectodermal Tumor/Extraskeletal Ewing's Sarcoma of Mediastinum



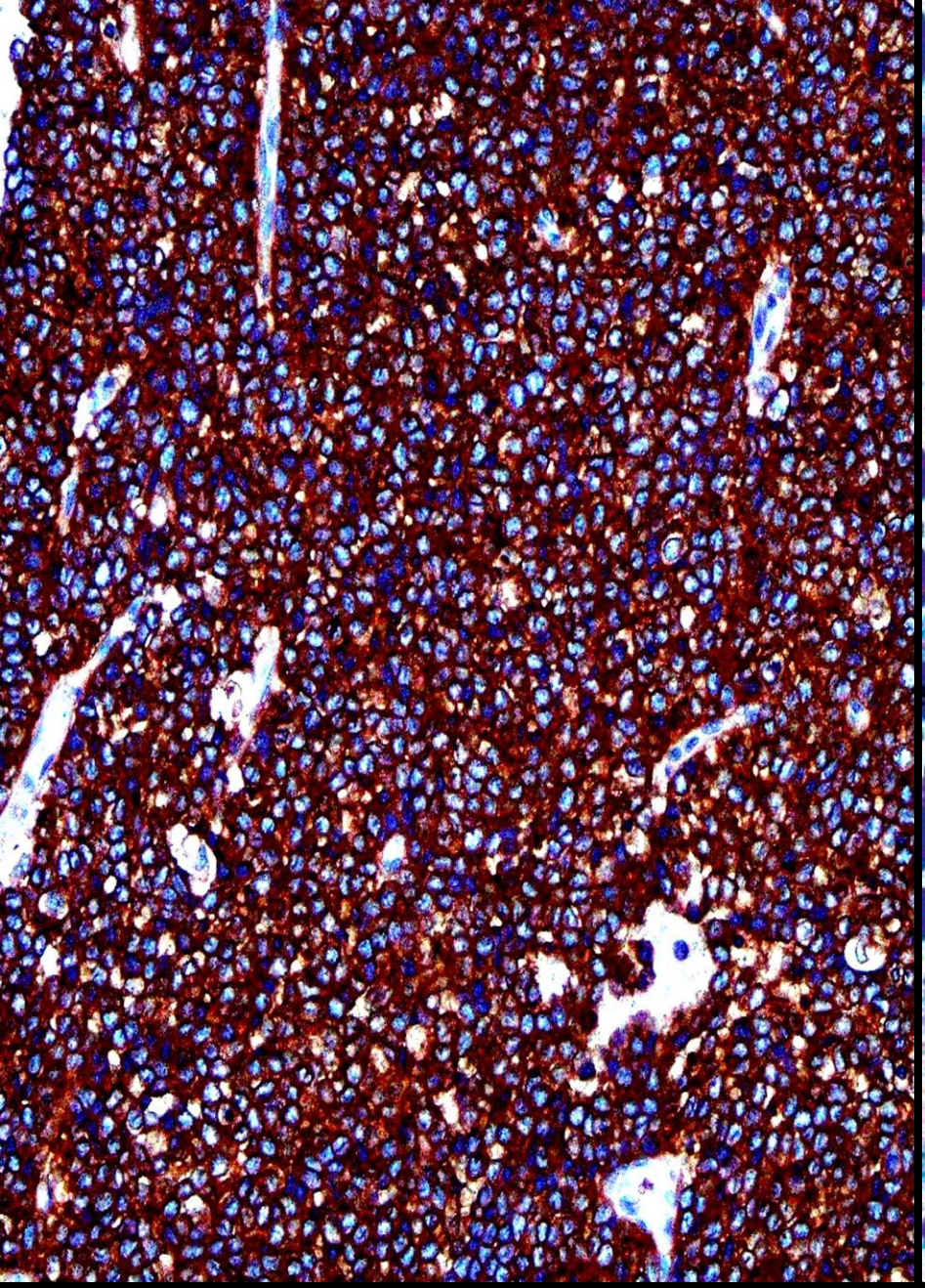
Primitive Neuroectodermal Tumor/Extraskeletal Ewing's Sarcoma of Mediastinum



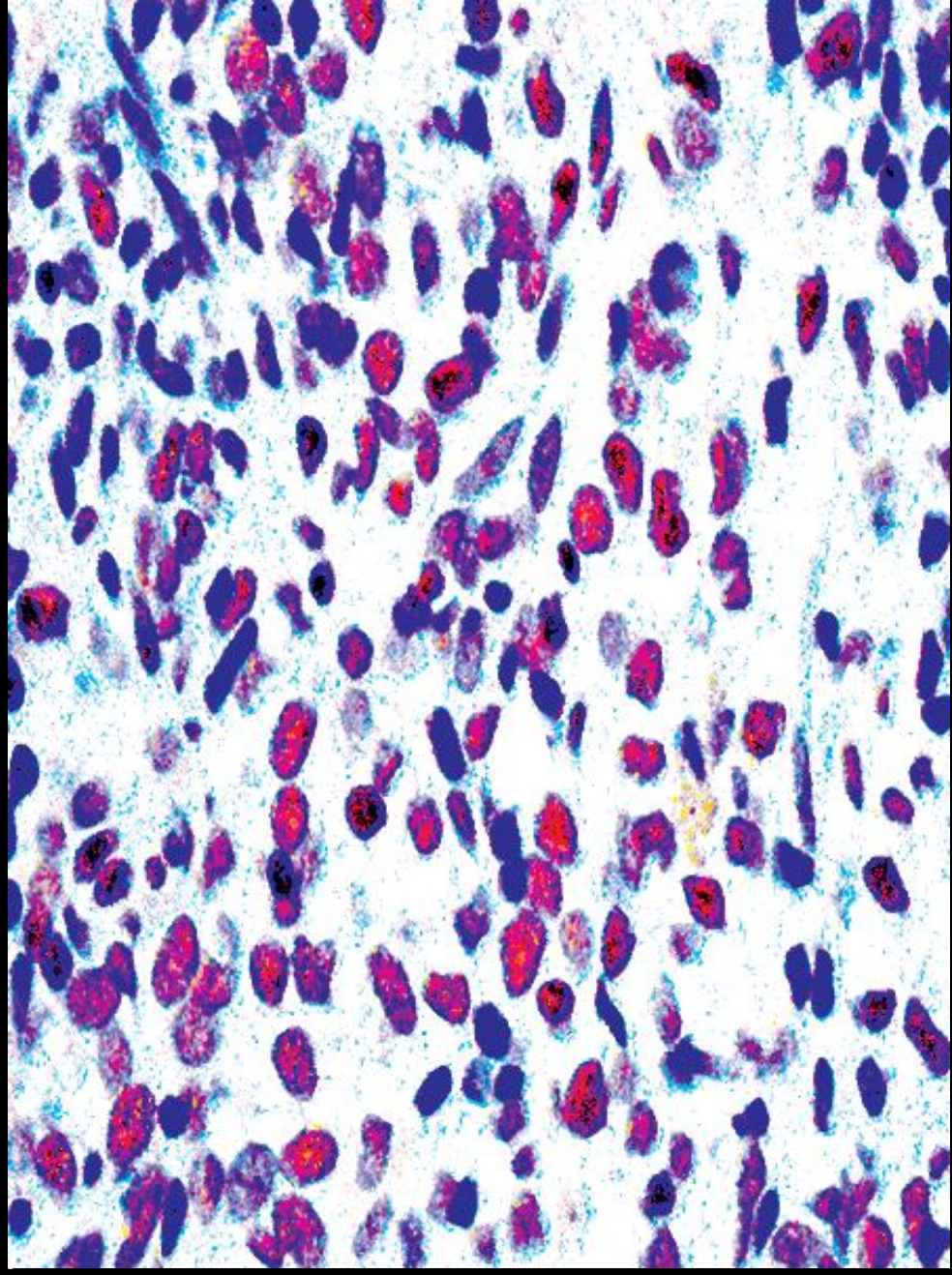
Primitive Neuroectodermal Tumor-- Ultrastructure

IMMUNOHISTOLOGY OF CLASSIC PNET

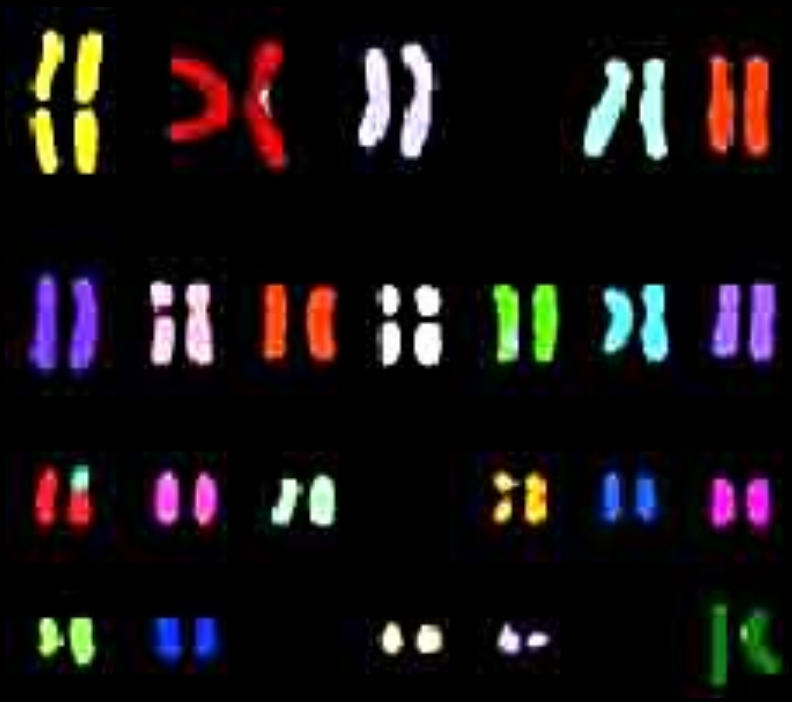
- **Keratin (-)**
- **Vimentin (+)**
- **Desmin (-)**
- **Muscle-specific actin (-)**
- **Neuron-specific enolase (+)**
- **CD56 or 57 (+/-)**
- **Synaptophysin (+/-)**
- **NB84 (+/-)**
- ***CD99 (+)***
- ***FLI-1 (+)***



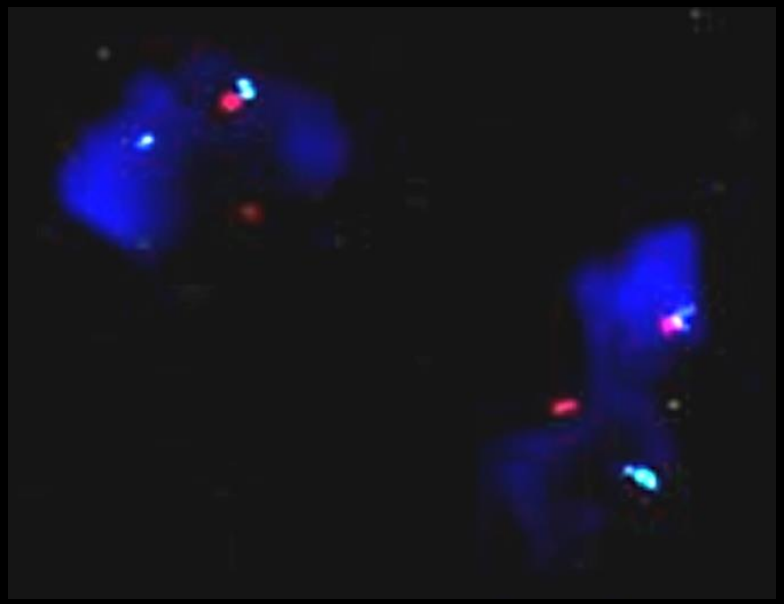
CD99



FLI-1



Spectral Karyotype– t(11;22)
In PNET



FISH with EWS telomere-centromere
probe set in PNET

Fusion Genes & Transcripts in PNET

- **Translocation of portions of chromosomes 11 & 22 bring the EWS & FLI-1 genes into apposition, creating a spliced "fusion" gene**
- **PCR, RT-PCR, or Western blotting can be used to detect the fusion gene itself, or its mRNA transcripts, or its protein product in fresh tumor tissue**

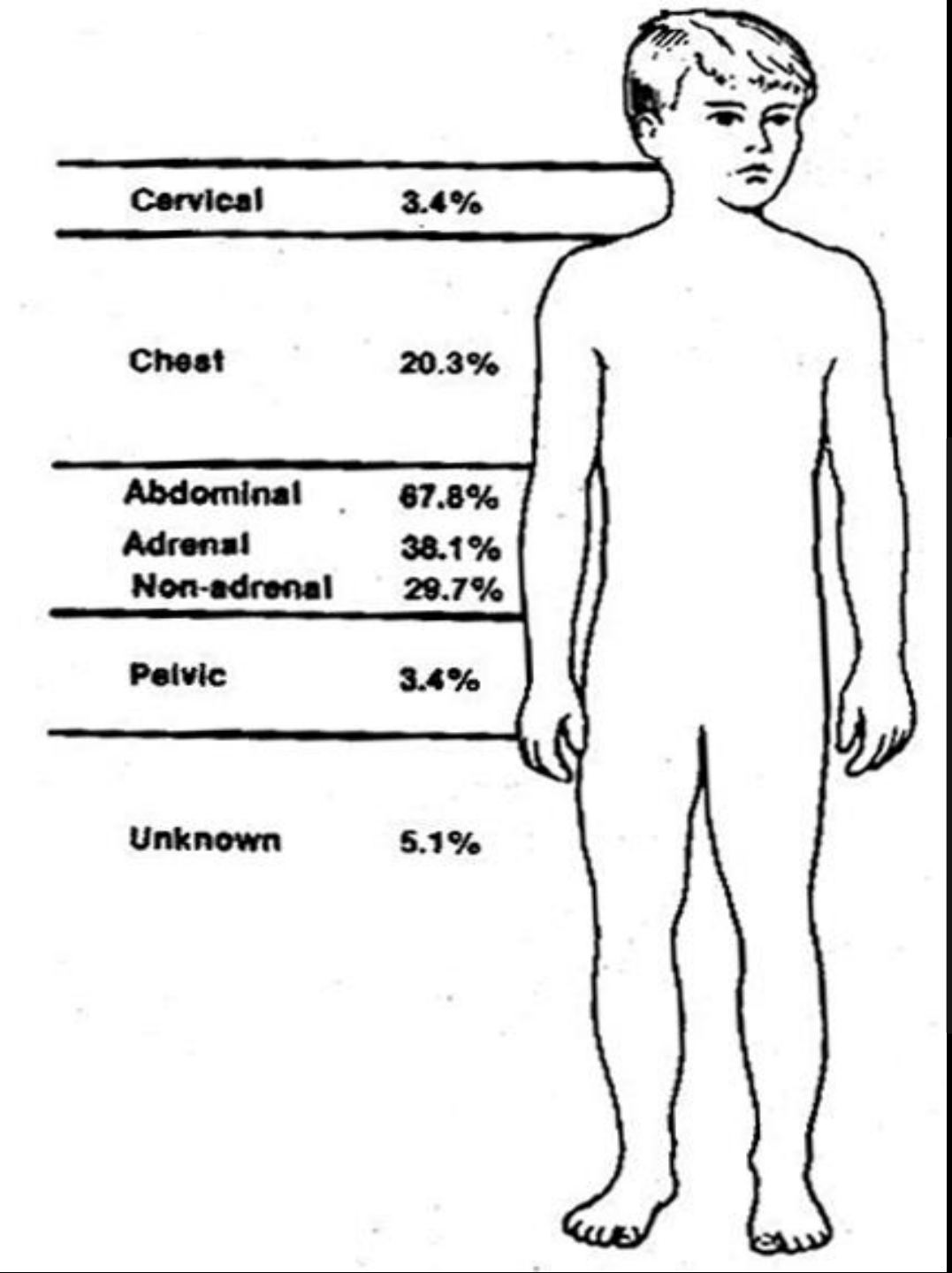
BEHAVIOR OF PRIMITIVE NEUROECTODERMAL TUMORS

- *AGGRESSIVE*
- **Approximately 60% of patients die in 5 years or less, despite intensive irradiation and chemotherapy**
- **Aggressive debulking surgery and combined multimodality adjuvant therapy is the currently recommended treatment approach**

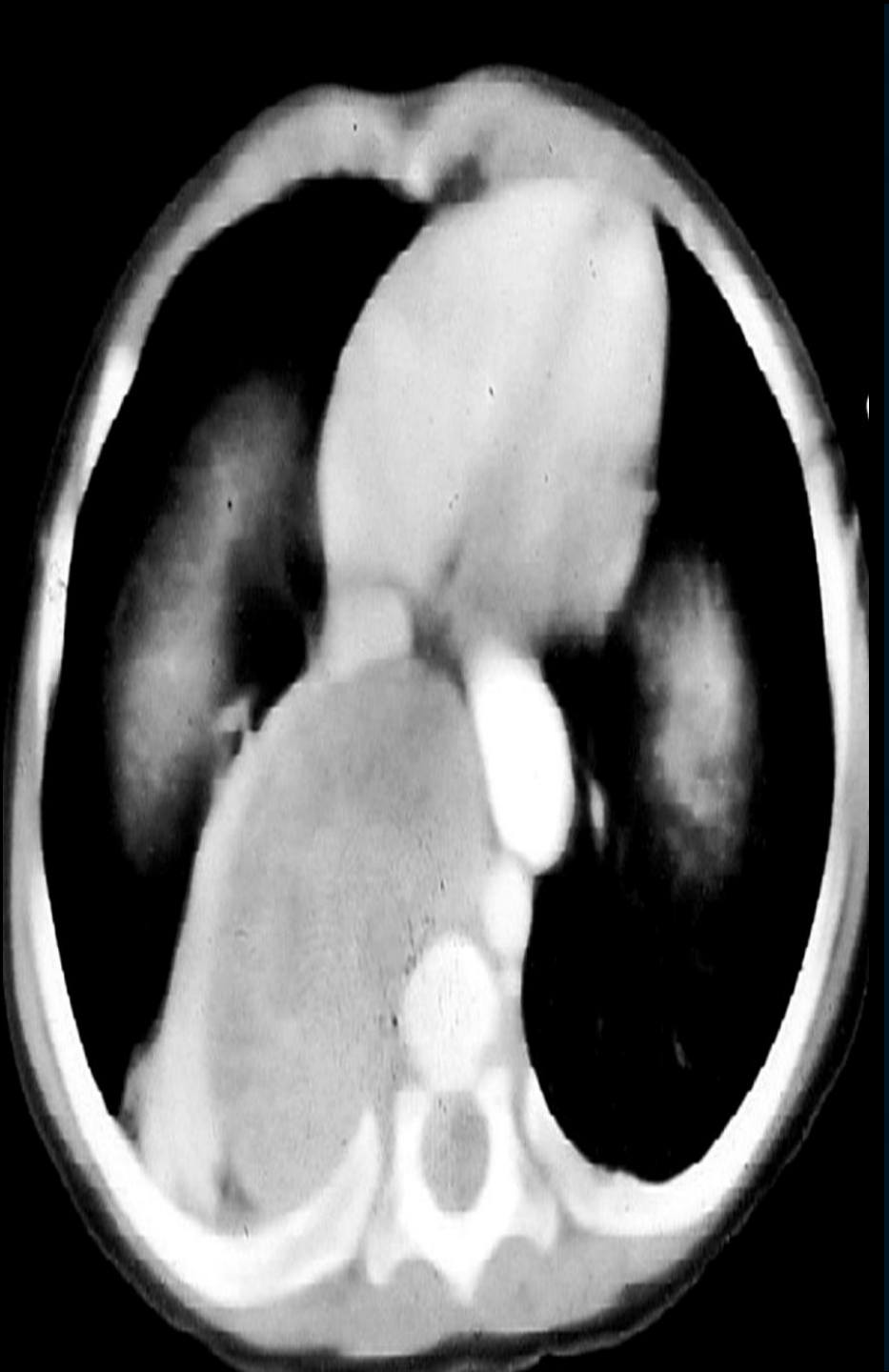
Differential Diagnosis Between Mediastinal PNET & Neuroblastoma

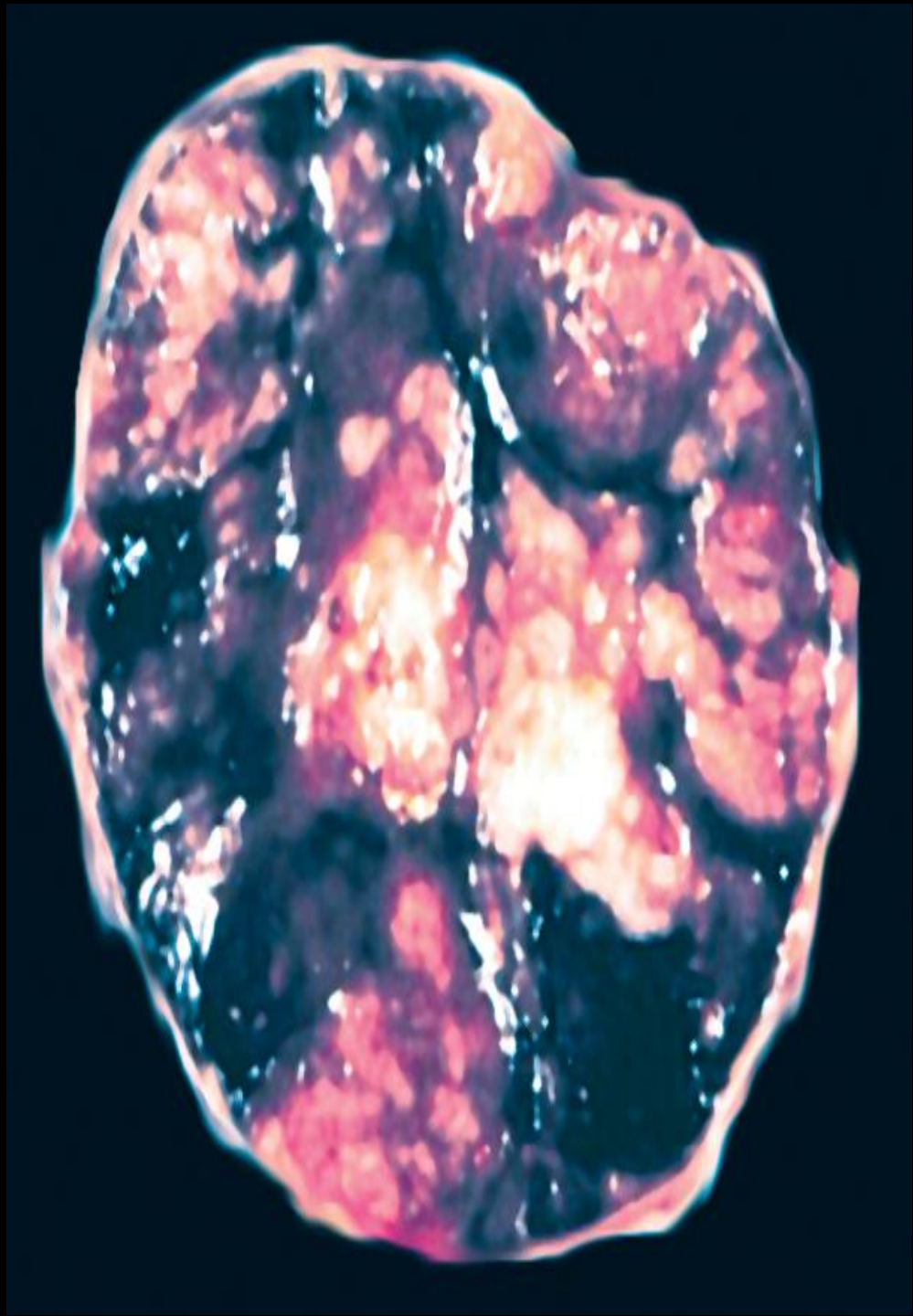
NEUROBLASTIC TUMORS:
Clinical Features

- **Majority occur in first decade of life, without predilection for either gender**
- **Symptoms and signs principally relate to the presence of an enlarging mass and interference with function of contiguous structures**
- **Minority of cases show paraneoplastic phenomena such as Cushing's syndrome, Verner-Morrison syndrome, and opsoclonus-myoclonus ("dancing feet-dancing eyes")**
- **Association with Beckwith-Wiedemann syndrome, Hirschprung's disease, neurofibromatosis, anencephaly, protein-losing enteropathy, and central pontine apnea**



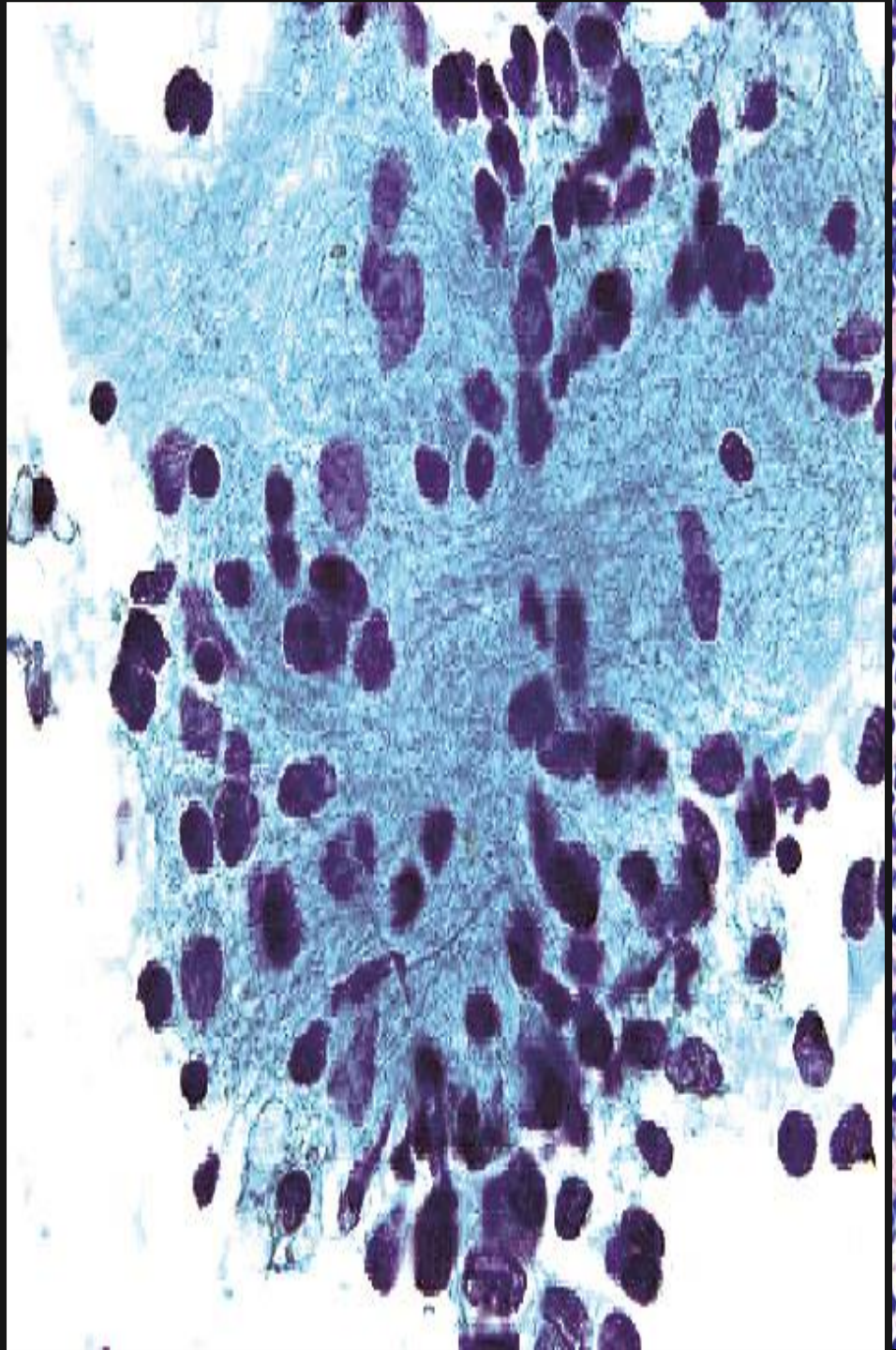
Anatomic Distribution of Neuroblastoma

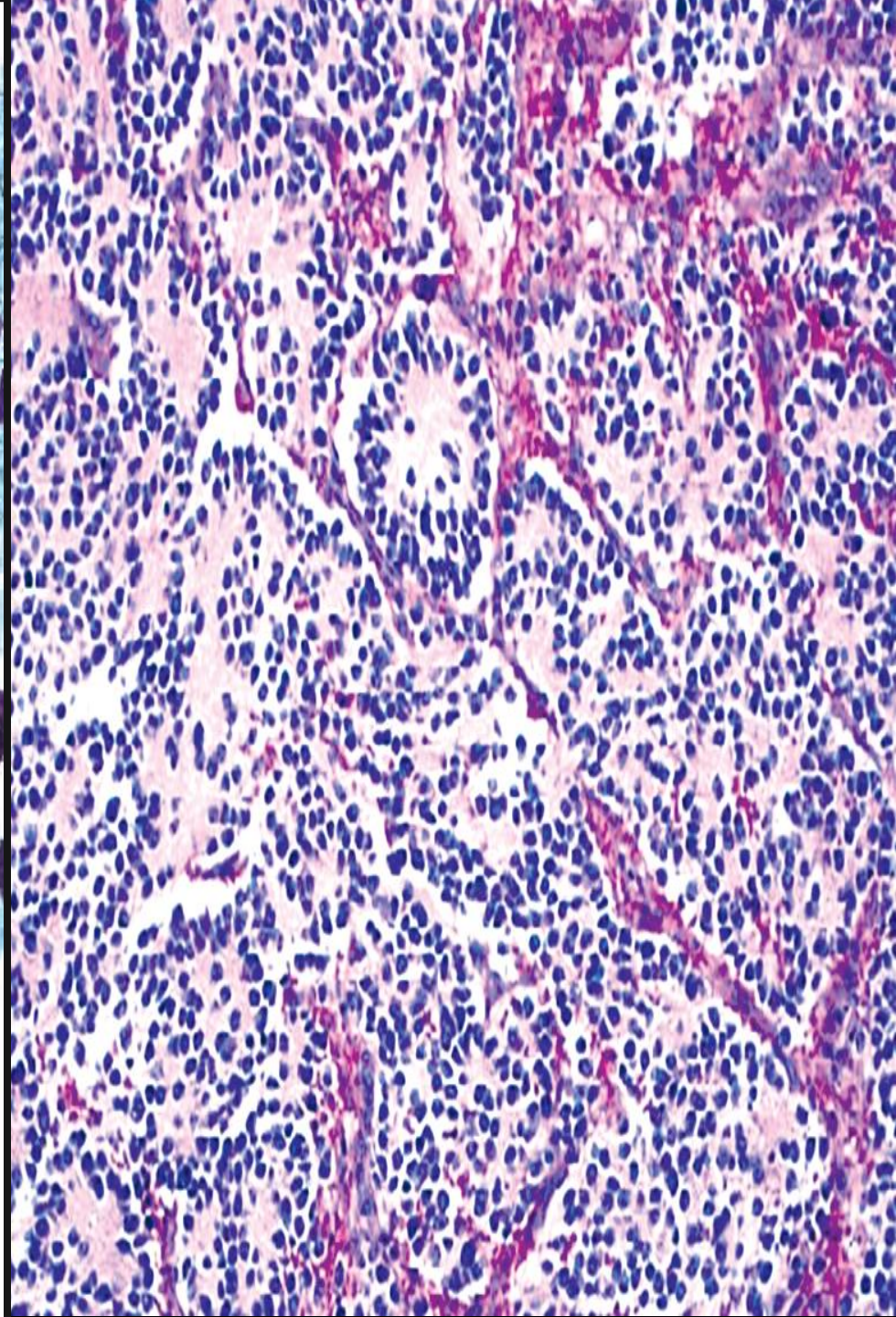


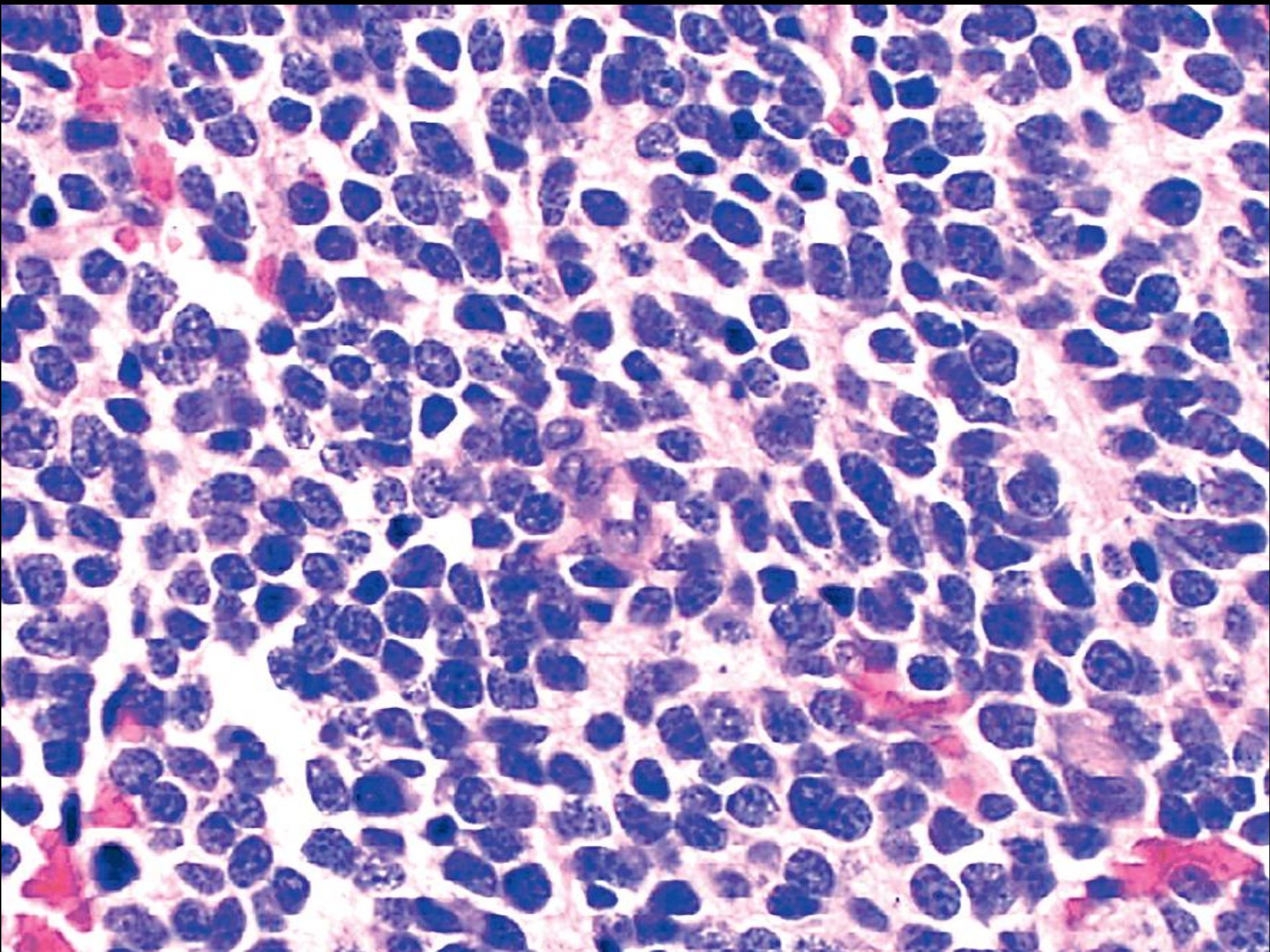


NEUROBLASTIC TUMORS:
Anatomic Locations & Function

- Abdominal tumors are most common; 38% are adrenomedullary lesions
- Intrathoracic neoplasms are next most frequent (20%), with predilection for the posterior mediastinum
- Only a minority of lesions are located in the cervical paraspinal region or in the pelvis
- Cervical, pelvic, and mediastinal tumors pursue more favorable courses, putatively because of higher level of biochemical differentiation of the neoplastic cells and augmented production of complex polysialogangliosides







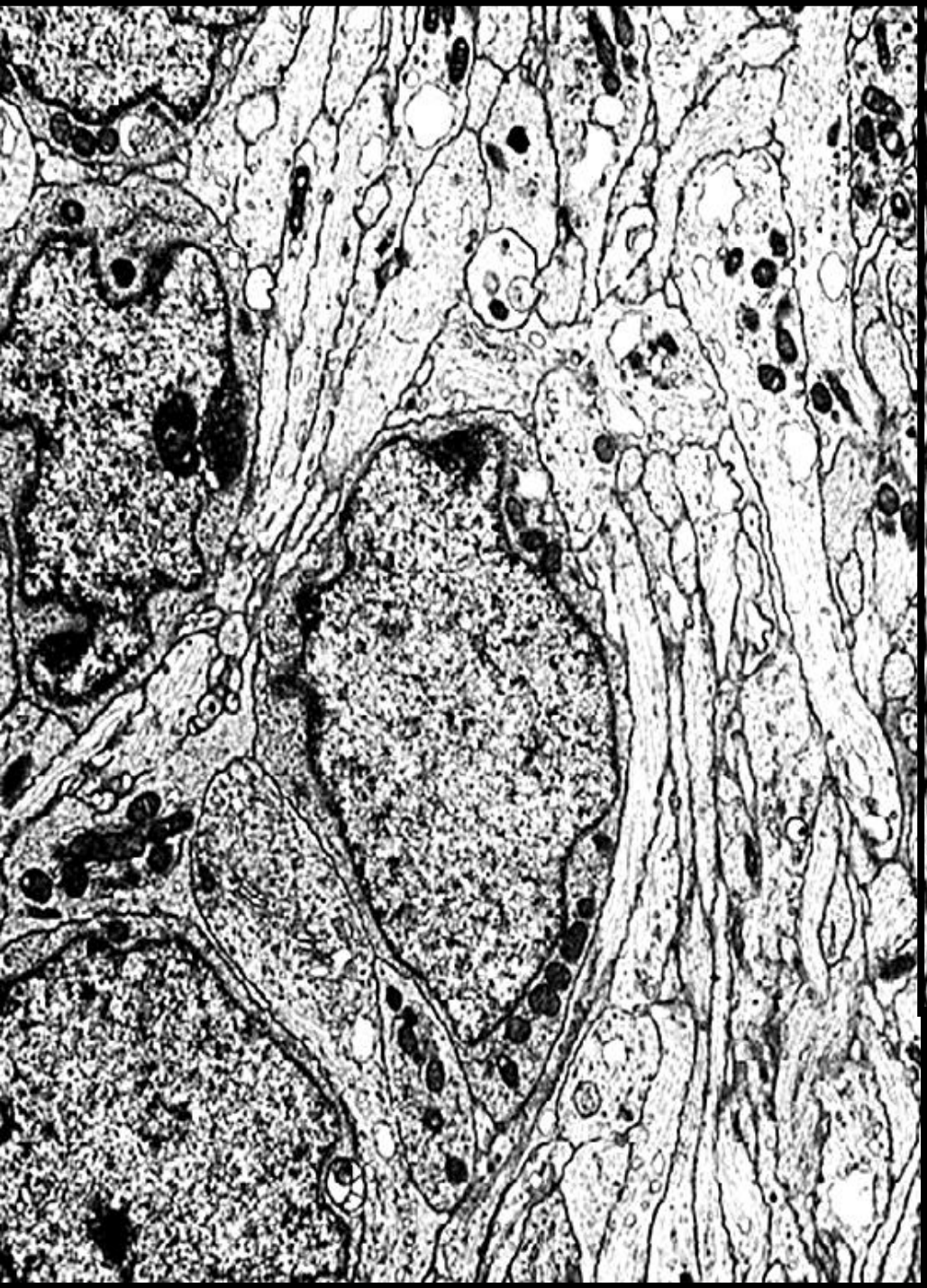
Neuroblastoma variants are all nonreactive for CD99 & FLI-1 immunohistochemically

Monoclonal Antibody MB2: a Potential Marker for Ewing's Sarcoma and Primitive Neuroectodermal Tumor.

Kahn HJ, Thorner PS

Fetal Pediatr Pathol 1989; 9: 153 – 162.

The small round-cell tumors of childhood present difficulties in diagnosis when differentiation is not apparent. Immunohistochemistry is helpful; however, the only antigen consistently detected in Ewing's sarcoma is vimentin, which may also be detected in the other types of small-cell neoplasms. The monoclonal antibody (MAb) MB2 is marketed as a B-lymphocyte marker that can be used on paraffin-embedded tissue. To determine its specificity, we performed immunohistochemical staining on pediatric tumors with MB2. These included 55 cases of small round-cell tumors (lymphomas, Ewing 's sarcoma, peripheral primitive neuroectodermal tumors [PNET], neuroblastomas, rhabdomyosarcomas, and nephroblastomas). MB2 positivity was detected in all B-cell lymphomas and in 7 of 9 cases of Ewing's sarcoma and all PNET. In neuroblastomas only differentiating ganglion cells were positive. In rhabdomyosarcomas only large rhabdomyoblasts were positive. Blastema of nephroblastomas was negative. Thus, in cases of poorly differentiated small round-cell tumors, MB2 was positive in all B-cell lymphomas, most Ewing's sarcomas and all cases of PNET. Lymphomas were distinguished by staining for leukocyte-common antigen and PNET by neuron-specific enolase. Therefore, the addition of MB2 to a discrete panel of antibodies may prove useful in the diagnosis of Ewing's sarcoma and PNET.



Neuroblastoma: Electron Microscopic Features

Cytogenetics & Molecular Pathology of Neuroblastic Tumors

- Deletion or loss of chromosome 1p (1p36 locus) is common in neuroblastoma
- Loss of heterozygosity for chromosome 14q is also seen in a subset of cases
- *NO* abnormalities in chromosomes 2, 11, 13, or 22
  - Majority of NBs are diploid, but a substantial number are near-tetraploid or near-triploid
- N-*myc* amplification and loss of *TRK-A* expression are thought to correlate with worsened prognosis of neuroblastoma cases

NEUROBLASTOMA