

TUMORS OF THE PLEURA (OTHER THAN DIFFUSE MALIGNANT MESOTHELIOMA)

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EWING'S SARCOMA

PRIMITIVE NEURAL ECTODERMAL TUMOR (PNET)

DESMOPLASTIC SMALL ROUND CELL TUMOR (DSRCT)

EWING'S SARCOMA/PNET

- Ewing's sarcoma is the second most common bone tumor occurring in children and young adults accounting for 10-15% of primary bone tumors and can involve the chest area (ribs 13%) with extension into soft tissues
- Extraskelatal Ewing's sarcoma arises in soft tissue and reported cases of chest/chest wall primaries

EWING'S SARCOMA/PNET

- Thoracopulmonary primitive neuroectodermal tumor (PNET) or Askin tumor first described in 1979 is also "a round small blue cell tumor" occurring in the first 2 decades of life with rare cases reported in older patients (69 yr. male)

SMALL ROUND BLUE CELL TUMORS

In past Ewing's/Extraskelatal Ewing's, peripheral primitive neuroectodermal tumors (PNET) and Askin's tumor were thought to be different neoplasms

SMALL ROUND BLUE CELL TUMORS

- Tumors that showed more uniform primitive cells with scant cytoplasm and cytoplasmic glycogen were usually classified as Ewing's sarcomas
- Tumors composed of primitive cells that showed more variable nuclear size/shape, more abundant cytoplasm and variable amounts of cytoplasmic glycogen were classified as PNET or if occurred in the thoracopulmonary area, as Askin's tumor

SMALL ROUND BLUE CELL TUMORS

- Currently Ewing's sarcoma and PNET (Askin tumor) are classified together as ES/PNET
- Although have different differentiation in neuroectoderm, share similar translocation t(11;22)(q24;q12) with EWS-FLI-1 fused gene

EWING'S/PNET & DSRCT

- Desmoplastic small round cell tumor (DSRCT) first described in the abdomen, pelvis and paratesticular area with cases reported as primary pleural tumors
- Both ES/PNET & DSRCT occur in children and young adults (mean age 15 yrs.), reported cases in infants and older adults; slightly more in M than F

EWING'S/PNET & DSRCT

- Symptoms varied from unilateral chest pain, cough, pleural effusion, dyspnea and tachypnea
- ES/PNET & DSRCT are not associated with elevated catecholamine metabolite
- Tumor growth reported as localized with a case presenting as a pedunculated mass but more often infiltrative and diffuse with tumor encasing the lung, studding pleural surfaces
- Tumor size reported up to 10cm

EWING'S/PNET & DSRCT

ES/PNET:

- Most often composed of undifferentiated small cells with scant to moderate amounts of cytoplasm, oval to round nuclei, uniform chromatin and inconspicuous nucleoli with the tumor cells arranged in a nested pattern, rosette formation and a delicate stromal vascular network

Stains:

- POSITIVE for S-100, Synaptophysin, CD99
- Variable staining for glycogen (Pas, Pas/D) with more uniform positive staining found in Ewing's sarcoma

EWING'S/PNET & DSRCT

DSRCT:

- Small cells arranged in more organoid pattern of cords and nests in a fibrous stroma
- Scattered larger cells with rhabdoid features, multinucleated giant cells, signet-ring cells have been reported
- Cystic spaces, small tubules with lumens and "papillary-like" structures also been reported

Stains:

- POSITIVE for Vimentin, Desmin, Keratin, Synaptophysin, CD99, WT-1 (no staining for glycogen)

EWING'S/PNET & DSRCT

Cytogenetics:

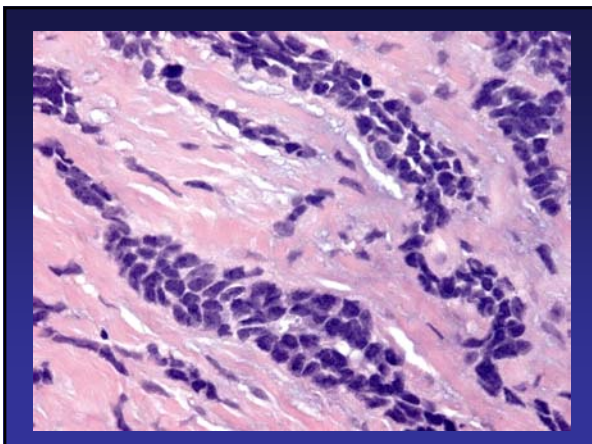
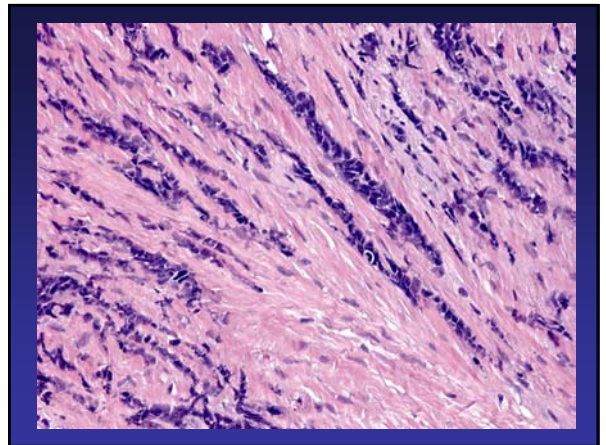
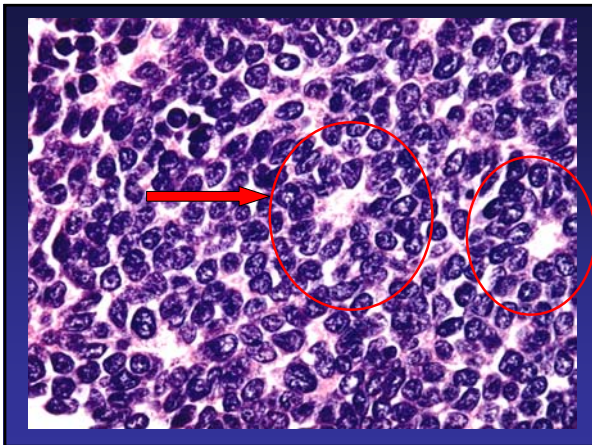
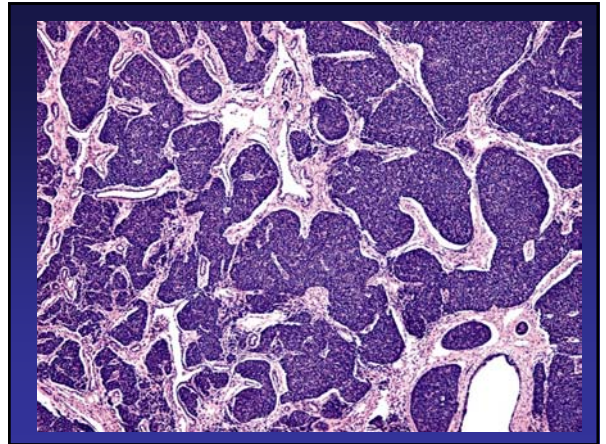
ES/PNET & DSRCT share the Ewing sarcoma gene translocation t(11;22) [Ewing sarcoma "family" of tumors]

ES/PNET fusion gene EWS/FL1 t(11;22)(q24;q12)

DSRCT fusion gene EWS/WT1 t(11;22)(p13;q12)

ES/PNET CYTOGENETICS

- ES/PNET fusion gene **EWS-FLI-1** and **t(11;22)(q24;q12)** occurs in **85%**
- **t(21;22)(q22;q12)** fusion gene **EWS-ERG** occurs in **10%** of tumors
- other translocations: **t(7;22)** EWS-ETV1, **t(17;22)** EWS-E1AF and **t(12;22)** EWS-FEV are rare



EWING'S/PNET & DSRCT

Treatment & Prognosis:

- Very aggressive tumors, usually large size at time of diagnosis, complete surgical resection
- Post-operative chemotherapy & radiotherapy (using protocols for Ewing's sarcoma) have improved survival
- Reported increased complications and risk after radiotherapy > second malignancy (second sarcoma, myelodysplastic syndrome and acute leukemia) pulmonary fibrosis

EWING'S/PNET & DSRCT

Treatment & Prognosis:

- Several current large studies have advocated adjuvant chemotherapy with delayed resection after 4 courses of treatment > complete resection, microscopically negative margins > 5 year survival rates of 56%
- No benefit was found in adding radiotherapy if tumor could be completely resected

EWING'S/PNET & DSRCT

Staging proposed by NCI prognostic significance:

- Stage I: <5 cm., completely excised
- Stage II: <5cm., grossly appear completely excised but show microscopic positive margins
- Stage III: >5cm., non-resectable
- Stage IV: metastatic disease to extra-pleural sites
- Low stage better survival

THANK YOU !