Ewing’s sarcoma cells in pleural fluid

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A 17-year-old male with effusion in the pleural cavity and a tumor on the left 7th rib was diagnosed by exfoliative cytological and histological examination of pleural fluid and biopsy specimen from the chest wall tumor.

In the pleural effusion, small round cells with nuclear atypia were demonstrated as a mixture of monolayered clusters and single cells, with scanty and indistinct cytoplasm. The nucleus was round, supported by thin and smooth nuclear membrane, and hyperchromatic, showing finely granular chromatin pattern with one or two small but distinct nucleoli. PAS stain demonstrated intracellular glycogen. Histologically, biopsy specimen from the chest wall tumor yielded a diagnosis of round cell tumor, compatible with Ewing’s sarcoma.

Differential diagnosis of small round cell tumors was discussed from a morphological point of view.

Key words: Ewing’s sarcoma—pleural effusion—cytology

Dissemination of tumor cells in the body cavity is a very rare phenomenon in cases of soft tissue sarcoma. So we seldom encounter cases in which sarcoma cells appear in the body fluids. In addition, when sarcoma cells do appear, they frequently show epithelioid features, so it is difficult to differentiate them from carcinoma cells and others.

Ewing’s sarcoma cells characterized by small round cells should be distinguished from other types of small round cell tumors, for example neuroblastoma, rhabdomyosarcoma, Askin’s tumor, lymphoma, small cell carcinoma etc.

Case Report

A 17-year-old male complained of progressive pain in the left chest wall since April 1988 for two months before admission. Chest X-ray and CT scan (Fig. 1, 2) taken in June 1988 showed left sided pleural effusion and an osteolytic lesion in the left 7th rib with a soft tissue swelling around it.

In the pleural fluid, clusters of small round cells with nuclear atypia were demonstrated. In addition to this, a needle aspiration cytology and biopsy of the main chest wall tumor testified to presence of a tumor composed of small round cells identical to those of pleural fluid,
and which were interpreted as Ewing's sarcoma, taking the clinical findings into consideration. The patient received radiotherapy (60 Gy Lynac) and chemotherapy. The tumor and effusion almost completely disappeared and the patient was discharged.

After one and a half months there was recidivation with multiple metastases in both lungs and distant bone metastases. The patient failed to respond to radiotherapy and chemotherapy, and expired.

**Cytological findings**

Cytological examination of the pleural effusion disclosed that the atypical small round cells are grouped to make clusters in flat fashion, with numerous single cells (Fig. 3). The special structures such as rosettes were not seen. Atypical cells were characterized by scanty and indistinct cytoplasm, and round nuclei with thin and smooth nuclear membrane and finely granular chromatin with a couple of small, but prominent nucleoli. The cytoplasm was frequently filled with a PAS-positive substance, which was digested by diastase, revealing that the cells were rich in glycogen (Fig. 4). Aspiration smear from the main chest wall tumor showed loose clusters of small round cells with a few rosette-like formations (Fig. 5) and scattered single cells on a hemorrhagic background. The cellular features were the same as above.

**Histological findings**

The biopsy specimen from the main tumor showed diffuse proliferation of small round cells characteristic in high N/C ratio, hyperchromatic nuclei and cytoplasm rich in glycogen, without any organoid features (Fig. 6). A considerable amount of PAS-positive substance was detected in the cytoplasm which was digested with diastase revealing glycogen (Fig. 7). In immunohistochemical studies, tumor cells were all negative for antibodies for keratin, EMA, S-100 and NSE.

Electron microscopical material was procured from the treated tumor tissue, which showed cytoplasm rich in electron dense granules measuring 25 nm in thickness, without rosette-like arrangement or lake-like aggregation, which are interpreted as free ribosomes rather than glycogen granules. Neurosecretory granules and neurotubules were not detected, revealing no evidence of differentiation to neuroendocrine cells.
Discussion

Recent immunohistochemical and electronmicroscopical studies of Ewing's sarcomas suggest that they should be included in neuroectodermal tumors composed of small round cells, including neuroblastomas, Askin's tumors and so on.

Our case is compatible with Ewing's sarcoma, because it was a small round cell tumor characterized by rich in glycogen in the cytoplasm, and an appearance of rosette-like structures in the cell clusters in the pretreated tumor, though the fact that the recurrent tumor showed a depletion of glycogen could not be explained accurately.

Concerning the exfoliative cytological findings of sarcoma cells especially those in the body fluid, we have only limited knowledge because of its rarity. In cases of Ewing's sarcoma, the cells in effusion are difficult to differentiate from neuroblastoma, non-Hodgkin's lymphoma and other small cell tumors. The cytological findings in this case suggested diagnosis of small round cell tumor, however they were only consistent with, but not diagnostic of Ewing's sarcoma. Both neuroblastomas and Ewing's sarcomas have similar cellular features with occasional rosettes, however, the finding of thin delicate fibrils in the rosette is a feature more commonly associated with neuroblastoma. Large amount of glycogen deposits generally favor a diagnosis of Ewing's sarcoma rather than neuroblastoma, in spite of some reported cases of neuroblastoma with intracellular glycogen.

Clinicopathologically, our case had a resemblance to Askin's tumor, on account of the tumor localized mainly in the thoracopulmonary region in the initial stage of the disease. However, during the course of the disease, the patient developed distant bone metastases, excluding the diagnosis of Askin's tumor which did not seem to disseminate so widely. The morphological pictures of Ewing's sarcomas and Askin's tumors are very similar, however, pseudorosettes and the presence of intracellular glycogen excludes the diagnosis of Askin's tumor.

Of non-Hodgkin's lymphomas, the diffuse large cell types are most important in differential diagnosis. Lymphoma cells often appear as scattered single cells without clusters and many times as naked nuclei. The chromatin is generally coarser and more unevenly distributed than that of the Ewing's sarcomas. Rosette-like structures are not seen.

In embryonal rhabdomyosarcomas, the cells tend to form clusters, in which individual cells may show varying degrees of rhabdomyoblastic differentiation including thick eosinophilic cytoplasm with occasional cross striation. The nuclear size shows some variation, with coarse chromatin.

Oat-cell carcinomas of the lung also must be considered in differential diagnosis, in spite of their rare occurrence in persons under twenty. In oat cell carcinoma the cytoplasm is more scanty than in Ewing's sarcoma cells. Nuclear molding is commonly seen in cells appearing in clusters. Nuclei are generally naked, varying in size and with irregular outlines. Chromatin is more coarse and sometimes pyknotic. Nucleoli are usually not identifiable.

In conclusion, the differential diagnosis of small round cell tumors especially those appearing in the body fluid, is virtually impossible without the combined knowledge of all clinical data and cytochemical, immunocytochemical and electronmicroscopical studies.

References


Fig. 3 Pleural effusion cytology showing loose clusters of small rounded uniform cells with indistinct cytoplasm.

Fig. 4 PAS stain showing intracytoplasmic deposits.

Fig. 5 Aspiration cytology from the chest wall tumor showing rosette like formation with peripheral disposition of nuclei. (Papanicolaou stain × 200)

Fig. 6 Histology of the main tumor showing diffuse proliferation of small and round tumor cells with hyperchromatic nuclei and scanty cytoplasm. (H&E stain × 400)

Fig. 7 PAS stain showing glycogen deposits in the cytoplasm.