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-1예 보고-

성삼병원 병리과, 영남대학교 의과대학 병리학교실[1]

구 미 진 · 최 준 혁[1] · 배 영 경[1]

= **Abstract** =

Imprint Cytologic Features of Poorly Differentiated Synovial Sarcoma

- A Case Report -

Mi Jin Gu, M.D., Joon Hyuk Choi, M.D.[1], and Young Kyung Bae, M.D.[1]

Department of Pathology, Holy Trinity hospital, Yeungnam University College of Medicine[1], Daegu, Korea

Poorly differentiated synovial sarcoma is a variant of synovial sarcoma. We report a case of poorly differentiated synovial sarcoma imprinted after resection. The patient was a 47-year-old woman with a right shoulder pain for 6 months. The cytologic features showed malignant round to oval, monotonous tumor cells with high nuclear to cytoplasmic ratio. Some tumor cells showed perivascular distribution and nuclear molding. Vague rosette-like structures were seen. On immunohistchemical stains, tumor cells were diffusely positive for CD99 and focally positive for epithelial membrane antigen. Ultrastructural examination showed desmosomes and microvilli.

Key words: Synovial sarcoma, Cytology, Imprint.

Corresponding Author : Mi Jin Gu, M.D
Department of Pathology, Holy Trinity Hospital, 567-9, Shinmae-dong, Susung-gu, Taegu 706-170, Korea
Tel : 053-790-0638
Fax : 053-790-0557
E-mail : white_kmj@yahoo.co.kr

INTRODUCTION

Synovial sarcoma is a specific soft tissue sarcoma demonstrating dual epithelial and mesenchymal differentiation. Poorly differentiated synovial sarcoma is a variant of synovial sarcoma. The poorly differentiated synovial sarcoma have three subtypes; large cell epithelioid, high grade spindle cell, and small cell variant.[1-2] The small cell variant has diagnostic difficulty, because it shows striking similar cytologic findings with other small round cell tumors. The cytologic features of poorly differentiated synovial sarcoma has not been well described until recently. We are going to describe the imprint cytologic features of a case of small cell variant of poorly differentiated synovial sarcoma. The review of differential diagnostic points between poorly differentiated synovial sarcoma and other small round cell tumors is presented.

CASE REPORT

1. Clinical Findings

A 47-year-old woman was admitted to the hospital because of the right shoulder pain for 6 months. Her medical and family history were unremarkable. On physical examination, a hard mass was palpated in the right clavicular area. On MRI, a well demarcated lobulated, 6.5cm-sized mass was noted in the right subclavicular area. The mass was located between pectoralis major muscle and pectoralis minor muscle. The mass showed isosignal intensity on T1-weighted image and high signal intensity on T2-weighted images. After contrast enhancement, the mass was almost homogeneously enhanced except focal cystic areas. Under the impression of soft tissue malignancy, mass excision was performed. Grossly, the submitted specimen consisted of clavicle and soft tissue, covered by fat and fascia. On cut sections, the mass, measuring 6.5×6.5×6.0 cm in size, was well circumscribed lobulated yellow tan-gray solid and fish flesh in appearance with areas of focal hemorrhage and cysts (Fig. 1).

Multiple touch imprints preparation were made, and then fixed in alcohol, and hematoxylin-eosin and Papanicolaou stains were done.

Fig. 1. Macroscopic finding : The cut surface shows lobulating solid mass with yellow to gray-white appearance and variegated, friable focus.

2. Cytologic Findings

The smear was hypercelluar and showed individually scattered or clustered, round to oval, uniform and monotonous malignant cells with high nuclear to cytoplasmic ratio. Some of the clusters showed cells with nuclear molding. The nuclear chromatin was finely granular and one or two small nucleoli were seen. Vague rosette-like structures and perivascular pseudorosettes were seen. Mitotic figures were occasionally seen (Fig. 2). The background was composed of macrophages, lymphocytes, and a few metachromatic fragments. Immunohistochemical stains of the smears showed diffuse positivity for CD99 (Fig. 3A).

3. Histologic Findings

Histologic examination showed closely packed anaplastic tumor cells. The tumor cells were uniform, small, round shaped and had finely dispersed chromatin with small nucleoli. Some cells were somewhat oval or spindle in shape. The tumor cells were arranged in

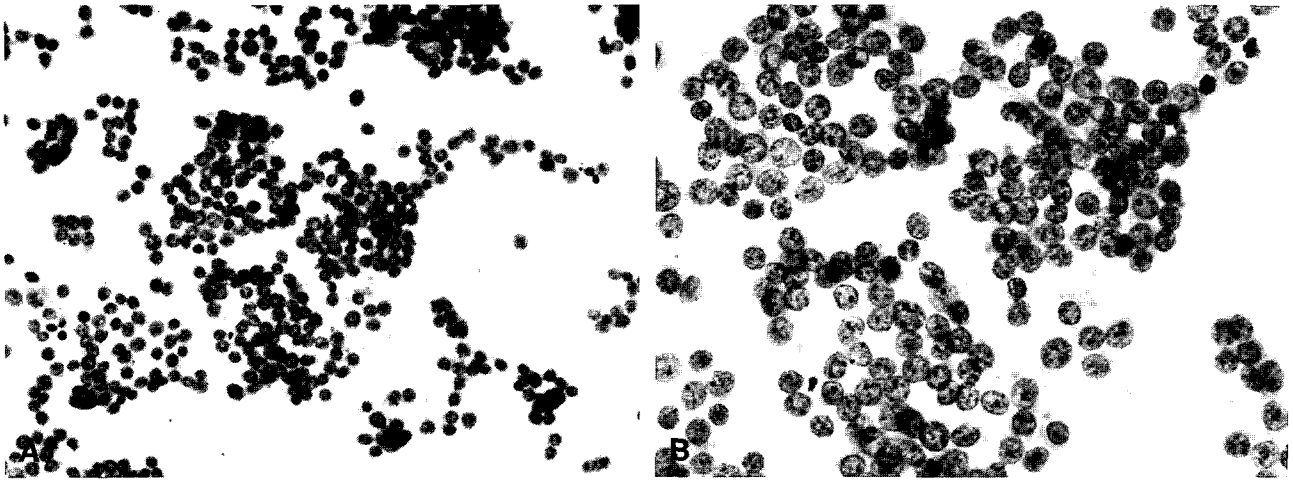

Fig. 2. Imprint cytologic findings : The smear shows small round tumor cells with high nuclear to cytoplasmic ratio. Mitotic figures and rosette - like structure are seen (A & B : H - E).

sheets, alveolar, and cord-like pattern. Focal myxoid stroma was present. Mitotic rates were about 20 per high power field. Necrosis was rarely seen (Fig. 4). Immunohistochemical stains for excised tumor showed diffuse positivity for CD99 and focal positivity for epithelial membrane antigen (Fig. 3B). Tumor cells were negative for cytokeratin (AE1/AE3), desmin, and S-100 protein. Ultrastructurally, basement membrane around the tumor cells and microvilli projecting into the intercellular spaces were found (Fig. 5). The patient was treated with six cycles of MAID regimen (doxorubicine, dacarbazine, ifosfamide, and mesna). One year later, follow-up chest computed tomography (CT scan) showed multiple, small lung nodules, consistent with metastatic tumor.

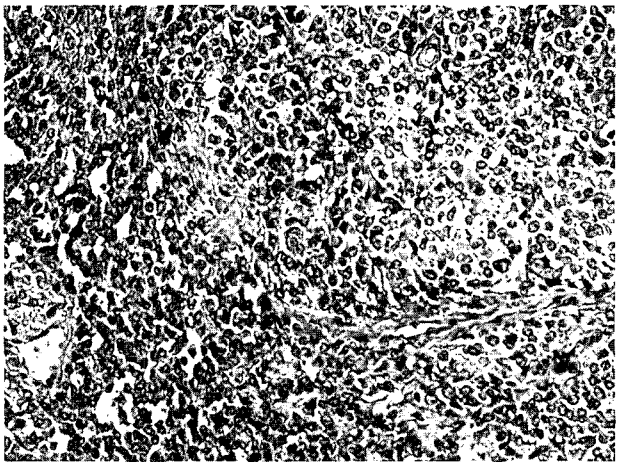

Fig. 3. Histologic findings : The neoplasm shows closely packed small round cells with high nuclear to cytoplasmic ratio and small nucleoli.

DISCUSSION

Synovial sarcoma is the fourth most common soft tissue sarcoma of unknown histogenesis in adults, comprising between 5.6% and 10% of primary adult soft tissue sarcoma.[2-5] It is often seen in adolescents and adults between 15 and 30 years of age and frequently occurs in lower extremity.[1-5] Males were affected more than females.[1] The reported 5-year survival ranges from 38% to 45%.[6] Histologically, synovial sarcoma is biphasic or monophasic. Poorly differentiated synovial sarcoma is a variant of synovial sarcoma. There are three types of poorly differentiated synovial sarcoma reported, including the large epithelioid cell, high grade spindle cell, and small cell variants.[2]

The recognition of poorly differentiated synovial sarcoma is important not only because it poses a special problem in diagnosis but also because it behaves more aggressively and metastasizes. The cytologic differential diagnosis of a poorly differentiated synovial sarcoma include primitive neuroectodermal tumor (PNET)/Ewing's sarcoma, malignant peripheral nerve sheath tumor (MPNST), rhabdomyosarcoma, neuroblastoma, malignant lymphoma, granulocytic sarcoma, and Wilms' tumor.[1-8]

PNET/Ewing's sarcoma shows uniform, monotonous,

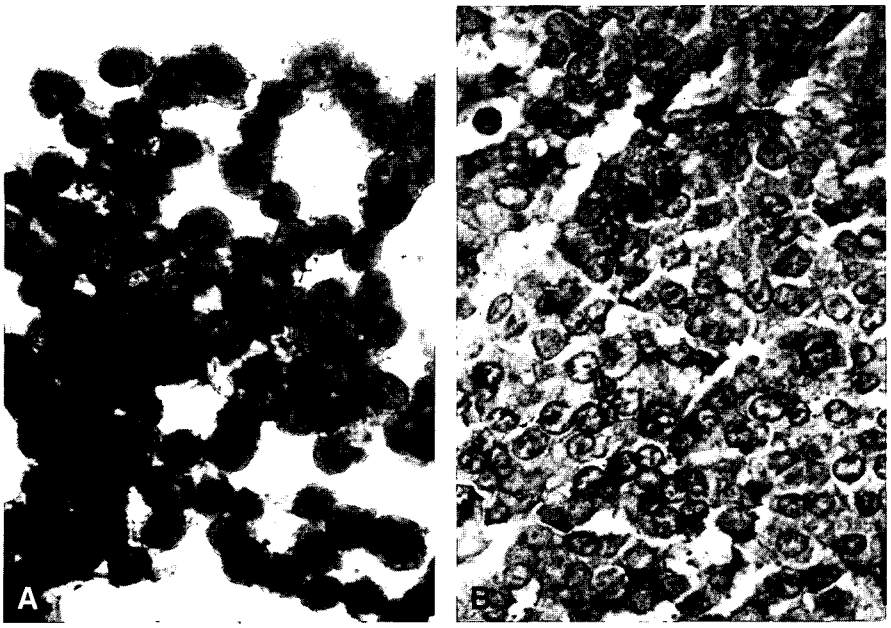

Fig. 4. Immunohistochemical stain : The tumor cells reveal positivity on CD99 **(A)** and EMA **(B)**.

small primitive round cells with high nuclear to cytoplasmic ratio. Nuclear molding and cytoplasmic vacuolization with membranous cytoplasmic bleb are occasionally seen.[1,7-8] Diff-Quik smears of the Ewing's sarcoma show dimorphic population, composed of chief cells and dark cells. But this pattern is not found in the Papanicolaou stain. Layfield et al.[8] reported that extremely scanty cytoplasm and cytoplasmic vacuole indicate Ewing's sarcoma. Tumor cells of the PNET/Ewing's sarcoma reveal positivity on CD99 and negativity on cytokeratin, EMA, and CD 56. Brahmi et al.[3] reported that CD99 was helpful to distinguish the PNET/Ewing's sarcoma group of neoplasm from other small round cell tumors. But poorly differentiated synovial sarcoma also shows positivity on CD99. CD56 is a useful marker because it is positive for poorly differentiated synovial sarcoma and negative for PNET.[7] Folpe et al.[2] reported that antibodies to low molecular weight cytokeratin, high molecular weight cytokeratin, and epithelial membrane antigen were positive in 30%, 50%, and 100% of poorly differentiated synovial sarcoma, respectively. And they reported that PNET and MPNST were negative for antibodies to high molecular weight cytokeratin. EMA is not a specific marker of synovial sarcoma, but its presence in a poorly differentiated round to spindle cell sarcoma can suggest synovial

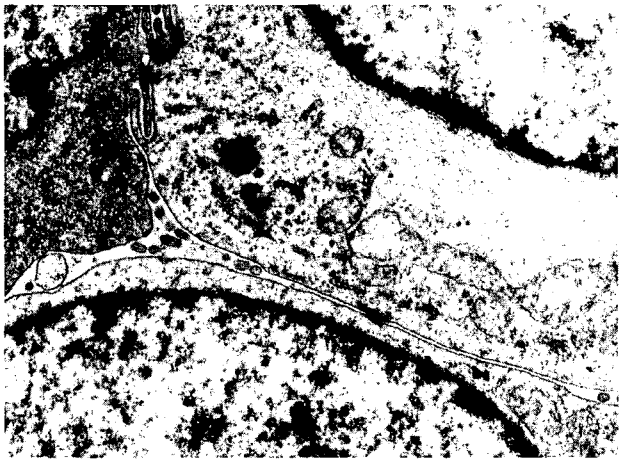

Fig. 5. Electron microscopic findings : Desmosomes and microvilli are present.

sarcoma, particulary in the presence of cytokeratin expression.[2] The common features between PNET/Ewing's sarcoma and our case were: small uniform cells, rosettes formation, high nuclear/cytoplasmic ratio, nuclear molding with an evenly distributed fine chromatin, and small nucleoli. But cytoplasmic vacuolization, crush artifact, and nuclear streaming, as seen in PNET/Ewing's sarcoma, were absent in our case.

Rhabdomyosarcoma occurs in pediatric age group. The cytomorphologic feature is the presence of cytoplasmic projections that could be confused with cytoplasmic tags

of PNET and neurobastoma.[7] And the tumor cells show variation in size and shape, and are composed of small round malignant cells and large bizarre cells with abundant cytoplasm. The cells have prominent nucleoli and dense chromatin and reveal positivity on desmin and actin. Cytoplasmic microvacuole and stripped tumor cell nuclei are occasionally seen. Layfield et al.[8] reported that strap or tadpole cells are closely correlated with rhabdomyosarcoma. Compared to rhabdomyosarcoma, our case showed more monotonous small round cells having fine granular chromatin and small nucleoli. And cytoplasmic vacuole or strap cell were not seen in our case.

Neuroblastoma is the most common solid nonlymphoreticular tumor in pediatric age group. The smears are hypercellular and consist of numerous individually scattered small cells or some cohesive groups showing nuclear molding. Differentiating neuroblasts characterized by a larger size and a moderate amount of cytoplasm can occasionally be present. Multinucleated ganglion cells and Homer-Wright rosettes are frequently present.[1,7-8] Layfield et al.[8] reported that rosettes strongly support neuroblastoma. The most helpful diagnostic cytologic feature which enables the recognition of neuroblastic cells is the presence of neuropil seen in smears. Our case showed vague gland-like structure, mimicking Homer-Wright rosettes and perivascular psedorosettes. Neuropil and ganglion cells were not found in our case.

Smear of non-Hodgkin's lymphoma shows noncohesive population of small round cells lying in a background containing many lymphoglandular bodies.[1,4,8] And lymphoma cells reveal characteristic immunohistochemical findings.

Our case showed very similar cytomorphologic feature with other small round cell tumors. However, the positivity for CD99 and EMA and presence of desmosome and microvilli support the diagnosis of poorly differrentiated synovial sarcoma.

In conclusion, poorly differentiated synovial sarcoma has substantially overlapping cytomorphologic features and immunohistochemical results with other small round cell tumor. Their distinction solely by morphologic background can be extremely difficult. But immediate microscopic evaluation of the smears would prompt additional passes to obtain material for the ancillary studies. We think that cytology coupled with clinical data and ancillary studies are helpful to specific correct diagnosis.

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