Malign Soliter Fibröz Tümör Sitolojik Bulguları ve Ayırıcı Tanısı: Olgu Sunumu

Cytological Findings and Differential Diagnosis of Malignant Solitary Fibrous Tumors: A Case report.

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ÖZ

Soliter fibröz tümörler (SFT) nadir mezenkimal neoplazmdır. En sık torasik kavite ve plevrada görülmektedir. Yaklaşık %90'ı benigndir. Tanı için ince iğne aspirasyon sitolojisinin artan kullanımı ile sitolojik yaymalarda bu tümörlerle daha sık karşılaşmaktayız. Bu yazıda malign SFT olgusunun sayılı vakada tanımlanmış sitolojik bulgularını ayırıcı tanısı eşliğinde sunmaktayız. 66 yaşında erkek hasta dispne ve sağ üst kadranda dolgunluk hissi şikayetleri ile hastanemize başvurdu. Endoskopik ultrasonografi rehberliğinde 22 gauge iğne kullanılarak karaciğerin alt yüzeyinde bulunan heterojen lezyondan ince iğne aspirasyonu biyopsisi yapıldı. Preparatlarda, dar sitoplazmalı iğsi/oval şekilli hücreler ve az sayıda inflamatuar hücre içeren kollajenize stromal fragmanların belirgin bir paterne sahip olmadan gelişigüzel dizildiği görüldü. Doku kesitlerine yapılan immünohistokimyasal çalışmalarda, vimentin ve CD34 yaygın pozitif, Bcl-2 soluk pozitif, SMA, desmin, S100, CD117, DOG1ve pansitokeratin negatif sonuç elde edildi. Bu bulgularla olguya mezenkimal tümör, SFT ile uyumlu tanısı verildi. Olgumuzda sadece sitolojik bulgular değerlendiriliyor olsaydı tanı mezenkimal neoplazi ile sınırlı kalabilirdi. İmmünohistokimyasal boyama tekniğinin uygulanabiliyor olması spesifik tanıya gidilmesini sağlamıştır. Literatüde sınırlı sayıda malign SFT olgusu bulunması nedeniyle literatüre katkı sağlanacağı düşünülmektedir.

Anahtar Kelimeler: *Soliter fibröz tümör, malign, sitopatoloji.*

ABSTRACT

Solitary fibrous tumors (SFTs) are rare mesenchymal neoplasms. SFTs are usually located in the thoracic cavity and pleura. Nearly 90% of SFTs are benign. With the increasing use of fine needle aspiration (FNA) cytology in diagnosis, we encounter with cytological smears of these tumors more frequently. Herein, we report a rare case of malignant SFT with relevant cytological findings and differential diagnosis in the light of literature data. 66-year-old male patient was admitted to our center with dyspnea and feeling of abdominal fullness in right upper quadrant. We performed FNA biopsy from the heterogeneous lesion located in the liver using of endoscopic ultrasonography. Slides showed spindle/oval-shaped cells with a scanty cytoplasm and a patternless arrangement in the collagenized stromal fragments. Immunohistochemical studies demonstrated vimentin and CD34 diffuse positivity, pale Bcl-2 staining, SMA, desmin, S100, CD117, DOG1 and pancytokeratin negativity. The patient was diagnosed with SFT of mesenchymal origin. If cytological findings were evaluated alone in our case, the diagnosis could be limited to mesenchymal neoplasia. The application of the immunohistochemical staining technique led to a specific diagnosis. Due to the limited number of data regarding cytological findings of malignant SFTs, our case report contributes to the ongoing body of literature.

Keywords: *Solitary fibrous tumor, malignant, cytopathology.*

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INTRODUCTION

Solitary fibrous tumors (SFTs) are rare mesenchymal neoplasms. These tumors were first described in 1931 by Klemperer and Rabin as distinct mesothelial tumors arising from the pleura (1). Although SFTs are usually located in the thoracic cavity and pleura, they have been reported in numerous other extrathoracic sites including orbit, meninges or intra-abdominal space, liver, and pancreas (2-5). They mostly present as asymptomatic masses and manifest with non-specific symptoms such as abdominal fulness, palpable masses, or paraneoplastic syndrome. In addition, SFTs are histopathologically diverse with a variable mixture of fibroblast-like cells and connective tissue in varying proportions with a patternless pattern (6). Nearly 85 to 90% of SFTs are benign and criteria of malignancy are not standardized. According to the World Health Organization (WHO) Classification of Soft Tissue Tumors, malignant SFTs are characterized by hypercellularity, at least focal moderate to marked cellular atypia, tumor necrosis, ≥4 mitoses/10 high-power fields, and infiltrative margins (2,7).

With the increasing use of fine needle aspiration (FNA) cytology in diagnosis, which is a less invasive technique than biopsy, we encounter with cytological smears of these tumors more frequently. Herein, we report a rare case of malignant SFT with relevant cytological findings and differential diagnosis in the light of literature data.

CASE REPORT

A 66-year-old male patient was admitted to the gastroenterology outpatient clinic in our center with dyspnea and feeling of abdominal fullness in right upper quadrant. Computed tomography (CT) showed a 25x14x12 cm solid mass lesion originating from the right hemithorax into the abdomen and displacing the liver, right kidney, and right surrenal gland anteriorly with visible cystic and necrotic regions. The liver, intra-hepatic biliary tract, pancreas, and para-aortic zone were normal. Thoracic CT revealed a 16x15x14 cm mass nearly covering the complete right hemothorax, displacing the heart and mediastinal structures toward left, obliterating the right brachiocephalic vein with narrowing of the vena cava superior. The images obtained in 2013 demonstrated that these lesions were relatively smaller with a significant growing rate over time. The patient had hepatitis B surface antigen (HbsAg) positivity (+).

A written informed consent was obtained from the patient and we performed FNA biopsy from the heterogeneous lesion located in the inferior surface of the liver (25x20 cm in size) using 22-gauge needle under the guidance of endoscopic ultrasonography (EUS) (Figure 1a).

Smears were air dried and fixed in 95% ethanol. The remaining specimens were fixed in tissue solution. Smears were stained with the May-Grunwald-Giemsa (MGG) and Papanicolaou (PAP) stain. Liquid-based cytological preparations and cell blocks were prepared using the specimens fixed in the tissue solution. Cytological smears using the aspiration material showed moderate cellularity in a background rich in red blood cells. There were a few number of oval nuclei which were individually dispersed and devoid of cytoplasms with a thin chromatin fibers and indeterminate nucleoli. In addition, there were cell groups with spindle/oval-shaped cytoplasms with similar nuclear properties. Connective tissue fragments compatible with collagen within the groups were evident (Figures 1b,1c,1d).

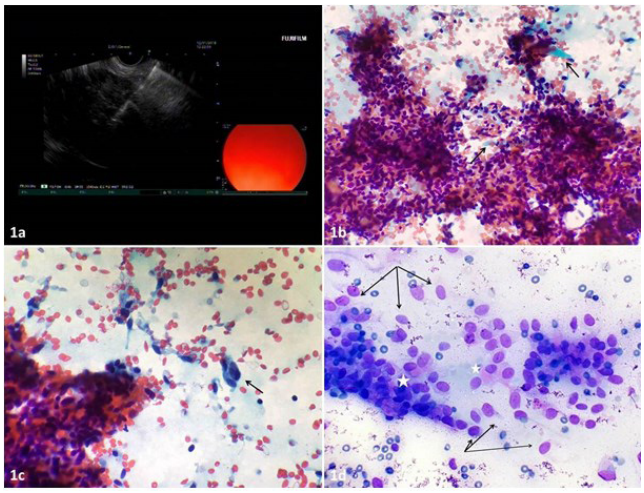

Figure 1. (1a) An EUS image of a heterogeneous lesion (25x20 cm in size) located in the inferior surface of liver. Smear slides of a SFT. (1b) PAP staining showing cells individually dispersed and devoid of cytoplasms in a background rich in red blood cells. Spindle-shaped cells with a patternless arrangement in the collagenized stromal fragments. Collagen connective tissue fragments in blue color (arrow). (1c) individual cells with cytologic atypia (arrow) (Papx200). (1d) Cellular smear individual basis and in a cluster. A few number of oval nuclei individually dispersed and devoid of cytoplasm with a thin chromatin fibers (arrow) and indeterminate nucleoli containing collagenized areas (stars) and pink in appearance with cluster of cells (MGGx200). EUS, endoscopic ultrasonography, SFT, solitary fibrous tumor; PAP, Papanicolaou. MGG, May Grunwald Giemsa.

Slides derived from the cell block showed spindle/oval-shaped cells with a scanty cytoplasm and a patternless arrangement in the collagenized stromal fragments with a few number of inflammatory cells. There were cellular atypia and increased cellularity, although no atypical mitosis or necrosis was seen (Figure 2a). Immunohistochemical (IHC) studies using tissue samples demonstrated vimentin diffuse positivity, CD34 diffuse positivity (Figure 2b), positive pale Bcl-2 staining, smooth muscle actin (SMA) negativity, desmin negativity, S100 negativity, CD117 negativity, DOG1

negativity, factor-8 negativity, pan-cytokeratin negativity, and epithelial membrane antigen (EMA) negativity. The Ki-67 proliferation index was 5%. Histochemical examination revealed that the Masson's trichrome (MT) was staining the connective tissue in the collagen. No Congo-red stained amyloid was detected in polarized light.

Based on these findings, the patient was diagnosed with a SFT of mesenchymal origin. The biopsy from the thoracic lesion revealed malignant SFT (Figure 2c,2d).

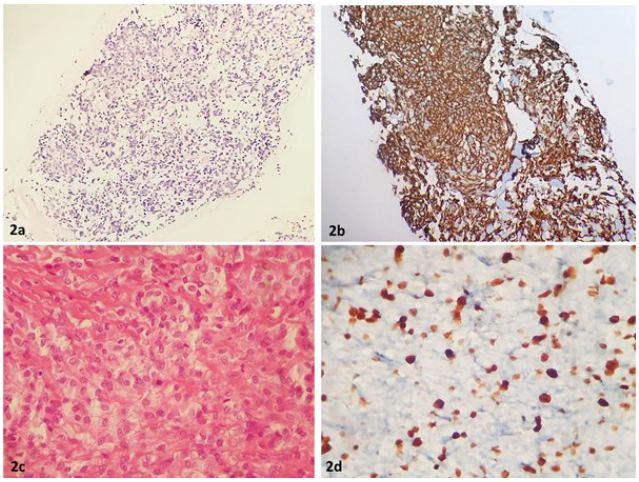

Figure 2. (2a) Slides derived from cell block showing focal cytologic atypia without mitosis or necrosis with a patternless arrangement. Collagenized inclusion body shown between the neoplastic cell groups with an amorphous nature in light pink color (H&Ex100). (2b) CD34 showing diffuse, strong, positive staining (CD34x100). (2c) Slides derived from intra-thoracic lesion showing a tumoral mass. The tumor is cellular with cellular atypia and mitosis in collagenized stromal fragments (Hex400). (2d) Ki-67 staining (Ki67x400).

DISCUSSION

There is a very limited number of data on cytopathological findings of malignant solitary fibrous tumor in fine needle aspiration (3,4,6-10). In recent years, FNA biopsy has been increasingly used in the diagnosis of masses of unknown origin. As this technique is associated with less complications and is easy-to-use with a high diagnostic value, cytological smears have become a reliable and alternative resource in the practice of pathology. For soft tissue masses, the FNA biopsy is used for two purposes: primary diagnosis in new cases before treatment and evaluation of recurrence or metastasis in previously diagnosed patients (7). The FNA biopsy allows not only preparing cytological smears, but also preparing the cell blocks and IHC, histochemical, and molecular testing, thereby, increasing the rate of primary diagnosis.

On the other hand, there is a limited number of data regarding the cytological findings of SFTs in the literature including: The background is rich in red blood cells. In such a background, the presence of spindle-shaped cells should be alerting for a SFT. The cellularity depends on each patient. In benign cases, the cellularity is less. The presence of intracellular collagen is a helpful manifestation for the diagnosis of the lesion. Smears usually show a cluster of cells with a bland oval/spindle-shape devoid of cytoplasm with bare nuclei or scanty cytoplasm. In benign cases, monotonous cells are prominent and no nucleoli dominance is expected. However, in malignant cases, mild-to-moderate nuclear atypia with nucleoli are seen. In malignant SFTs, smears are hypercellular with cohesive and crowded tissue fragments, haphazard cell arrangements and many single cells. The presence of mitosis and necrosis are very rare even in malignant cases; however, the presence of mitosis, but not necrosis, supports the diagnosis of malignancy. In benign cases, necrosis has been reported (6-10).

In our case, focal cytologic atypia was present (Figure 2b). In the imaging studies, no necrotic zones detected in a cell blocks were seen. The hypercellularity, cohesive and crowded tissue fragments with many single cells and mild nuclear atypia were all suggestive of malignancy in our case.
In the differential diagnosis of SFT, fibrosarcoma, solitary myofibroma, metastatic malignant mesothelioma, neurofibroma and peripheral nerve sheath tumors, synovial sarcomas, gastrointestinal stromal tumors, dermatofibrosarcoma protuberans, and smooth muscle tumors should be considered (4,10). It is very difficult to discriminate SFTs from other spindle-shaped neoplasms by cytological examination alone without IHC and imaging studies, although it is far from impossible. The implantation of IHC markers to the cell block derived from the FNA biopsy makes the differential diagnosis easier.

The most useful markers for SFT are STAT6 and CD34. STAT 6 is a highly sensitive immune marker for SFT that shows nuclear staining (11). Since it has not been studied in our center, it could not be applied to our case. CD34 is a marker of hematopoietic stem cells and hematopoietic progenitor cells, and is positive in primitive mesenchymal cells, SFTs, gastrointestinal stromal tumors, and dermatofibrosarcoma protuberans. In addition to CD34 and Bcl-2 positivity, CD117 and DOG1 negativity is used in the differential diagnosis of gastrointestinal stromal tumors, S100 negativity of peripheral nerve sheath tumors, keratin negativity of mesothelioma, and SMA and desmin negativity of smooth muscle tumors. On radiological examination, dermatofibrosarcoma is located more superficially than SFTs (8,9). The main problem lies on the cytological specimens for the

differential diagnosis of benign and malignant SFTs (5,7). In most cases, malignancy cannot be decided for solitary fibrous tumor with fine needle aspiration findings. It will be more appropriate to decide on malignancy in biopsy tissue.

CONCLUSION

The diagnosis of SFTs should be based on cytological, IHC, and radiological findings. Due to the limited number of data regarding cytological findings of malignant SFTs, our case report contributes to the ongoing body of literature.

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