

Synovial Sarcoma of the Liver – A Case Report

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Abstract

Citation: Janevska V, Filipovski V, Banev S, Janevski V, Jovcevski A, Spasevska L, Jovanovic R, Kostadinova-Kunovska S, Dukova B. Synovial Sarcoma of the Liver – A Case Report. *Maced J Med Sci.* 2011 Jun 15; 4(2):185-191. doi:10.3889/MJMS.1957-5773.2011.0168.

Key words: Synovial Sarcoma; Liver; SYT-SSX; Immunohistochemistry; FISH.

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Received: 24-Mar-2010; Revised: 25-Mar-2011; Accepted: 26-Mar-2011; Online first: 27-Apr-2011

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Competing Interests: The author have declared that no competing interests exist.

We report a case of synovial sarcoma of liver in a 44 year old man, presented as a tumor mass in left hepatic lobe. The patient was admitted at the hospital with clinical symptoms of acute abdomen and severe pain in the right upper quadrant.

Imaging examinations showed a tumor mass in the left hepatic lobe and free liquid in the abdominal cavity, due to the rupture of the tumor. A resection of 2 segments of the left hepatic lobe, where the tumor was located, was performed. Morphological, immunohistochemical and FISH studies confirmed the diagnosis of monophasic synovial sarcoma. Additional clinical and imaging examinations, made after the surgery, did not confirm tumor mass in any other localization. The patient refused any therapy other than surgery, at that time.

A relapsing tumor mass was found 6 months later and another surgical intervention was done. The patient received five monotherapy cycles of Doxorubicin, 75 mg/m², after the second surgical intervention. He is still alive 11 months after the first operation receiving the same therapy and having second relapsing inoperable tumor mass filling the retroperitoneal space and a great fraction of the abdominal cavity.

Introduction

Synovial sarcoma is a common soft tissue sarcoma arising in deep soft tissue around the joints, affecting children and young adults, accounting for 2,5-10% of all primary soft-tissue sarcomas [1].

Extremities are the most common affected sites, followed by head, neck and trunk [1-3].

Rare localizations, such as skin, heart, larynx, pleura, lung, esophagus, colon, vulva, ovary, prostate, kidney, liver, scull, peripheral nerve, central nervous

system, thyroid gland and mediastinum have been described also [2, 4-9].

Monophasic synovial sarcoma may present a difficult diagnostic problem due to its similar histological appearance to other spindle cell neoplasm especially when the tumor localization is unexpected [1, 3]. Molecular and cytogenetic studies may be very helpful in diagnosing such lesions and may confirm the diagnosis of synovial sarcoma. The t(X;18)(p11.2;q11.2) translocation and the chimeric gene SYT-SSX are considered to be specific for synovial sarcoma [10-13].

To the best of our knowledge only two cases of primary synovial sarcoma arising in the liver have been described [4, 5].

We present a case of hepatic spindle cell sarcoma with SYT gene interruption, consistent with synovial sarcoma.

Case report

A 44 year old man was admitted at the hospital with clinical symptoms of acute abdomen and severe pain in the right upper quadrant. Computerized tomography showed a highly vascular tumor mass in the left hepatic lobe, measuring 14 x 11cm. The tumor mass was heterogeneous and multilobulated, with hypodense areas (Figure 1).

Table 1: Immunohistochemical stains used for the Avidin-Biotin immunoperoxidase technique.

Antibody	Vendor	Dilution	Results/tumor cells Semi quantitative
CD 31	Dako	1:50	-
CD 34	Dako	1:50	-
Factor VIII	Dako	1:100	-
Vimentin	Dako	1:100	+++
Desmin	Dako	1:50	-
EMA	Dako	1:200	+
Cytokeratin 8	Dako	1:50	-
Cytokeratin 19	Dako	1:50	-
CKHMW	Dako	1:50	-
CKWS	Dako	1:500	+
Chromogranin	Dako	1:100	-
Synaptophysin	Dako	1:100	-
NSE	Dako	1:100	-
S-100	Dako	1:400	-
Melan A	Dako	1:50	-
HMB45	Dako	1:50	-
Alpha Feto Protein	Dako	1:100	-
CD99	Dako	1:75	+++
Bcl2	Dako	1:50	+++
CD 45 RA	Dako	1:50	-
CD117	Dako	1:400	-

Ledend:

- No tumor cells show positive staining;
+ Groups or clusters of positive tumor cells;
+++ 90-100% tumor cells showing positive staining.

A presence of free liquid in the abdominal cavity, due to the rupture of the tumor, was demonstrated by ultrasound. The preoperative differential diagnosis was hepatocellular carcinoma or angiosarcoma.

A resection of 2 segments of the left hepatic lobe, where the tumor was located, was performed. The tumor was attached to the diaphragm and gastric wall and ruptured toward the left triangular ligament.

Additional clinical and imaging examinations, performed after the surgery, did not confirm tumor mass in any other localization. The patient refused any therapy other than surgery, at that time.

A relapsing tumor mass consisting of two tumor nodules, measuring 3 and 2 cm in the greatest dimension, was found 6 months later at the site of operation and another surgical intervention was done. The two tumor nodules were located along the resection line of the first operation. They were intrahepatic at the time of the second operation and only a tumorectomy was performed. The patient received five monotherapy cycles of Doxorubicin, 75 mg/m², after the second surgical intervention.

No other tumor mass was confirmed, neither clinically nor by imaging techniques during the control examinations, using 64 slice computed whole body tomography.

He was absent 2 months due to his attempt to get medical care abroad. When he came for a medical control two months later, he had a large tumor mass growing in the abdominal cavity, displacing the abdominal organs, penetrating through the visceral peritoneum and extending into the retroperitoneal space, also. He continued to receive the same therapy and he died 13 months later having second relapsing inoperable tumor mass that filled the retroperitoneum and a large proportion of the abdominal cavity. No autopsy was performed.

Material and Methods

Twenty one tissue specimens of the hepatic tumor were sampled; formalin fixed and cut in 5 micron thin sections for routine light microscopy. Immunohistochemical stains were made by the Avidin-Biotin immunoperoxidase technique using CD31, CD34, Factor VIII, Vimentin, Desmin, EMA, Cytokeratin 8, Cytokeratin 19, CKHMW, CKWS, Chromogranin, Synaptophysin, NSE, S-100, Melan-A, HMB-45, AFP, CD99, Bcl2, CD45-RA, and CD117 antibodies (Table 1). Fluorescent in situ hybridization (FISH) was used to detect the interruption of SYT gene. The interruption of SYT gene was detected at the Institute of Pathology, Faculty of Medicine, University of Ljubljana, where we sent paraffin blocks.

Results

1st Operation: The resected hepatic tissue measured 14 x 9 x 6 cm in its greatest dimensions. The tumor node, located eccentrically in the hepatic tissue, meas-

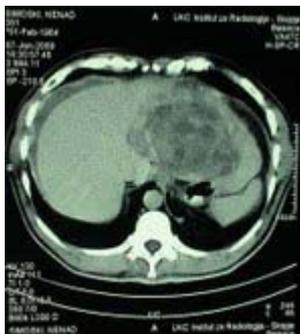


Figure 1: Computerized tomography - a tumor mass in the left hepatic lobe, 52x58mm (72 x 72 DPI).

ured 10 cm in the greatest dimension and was ruptured in a 2.5 cm long line. It looked like a well circumscribed cyst filled with coagulated mass mixed with tumor tissue (Figure 1 and 2).



Figure 2: A hepatic segment with a cystic tumor filled with coagulated mass, 711x533mm (72 x 72 DPI).

Microscopically, the tumor was composed of highly cellular areas of neoplastic spindle cells accompanied by a rich vascular network. Polygonal and round cells were also found. There was hemangiopericytoma-like arrangement of the cells in many areas, but fascicular or storiform patterns were also found. The cytoplasmic borders were indistinct, nuclei were oval, vesicular with prominent nucleoli, or hyperchromatic. The mitotic figures were frequent, average about 25 per 10 high-power magnification fields in the most cellular areas (Figures 3,

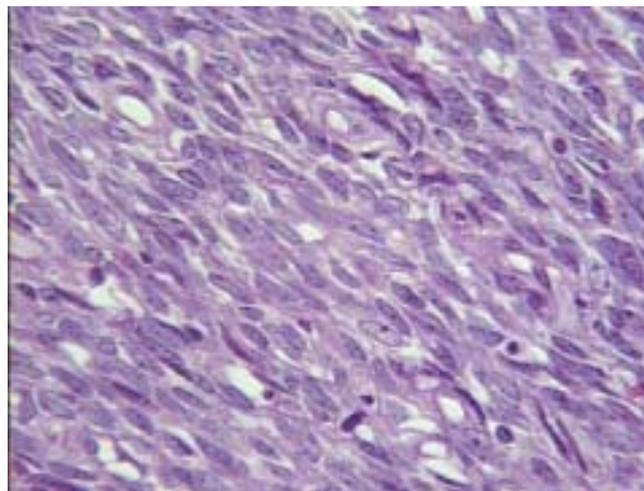


Figure 3: Fascicular architecture of tumor cells (Hematoxylin-eosin, original magnification 20x10), 254x193mm (72 x 72 DPI).

4, and 5). A pushing border and pseudo capsule were present adjacent to the hepatic tissue. The tissue samples of the hemorrhagic mass from the cystic lumen were identified as tumor tissue with hemorrhage and necrosis.

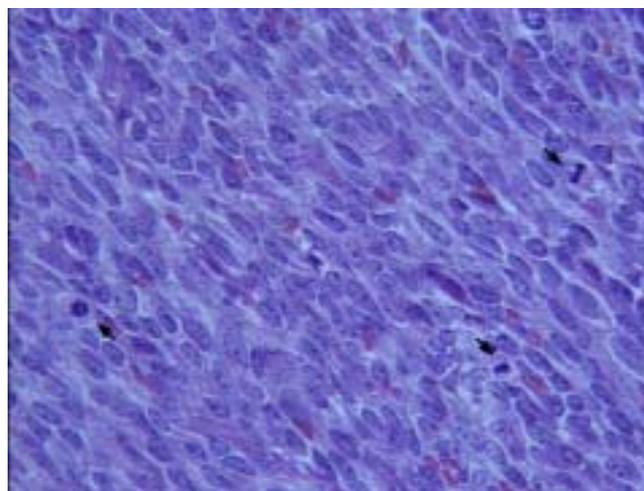


Figure 4: Spindle-shaped cells with oval nuclei containing nucleoli and mitotic figures-arrows (Hematoxylin-eosin, original magnification 40x10), 254x193mm (72 x 72 DPI).

Immunohistochemically, neoplastic cells showed diffuse strong positivity for vimentin, CD99 and Bcl2, and focal positivity for epithelial membrane antigen and cytokeratin wide spectrum. They were negative for all of the other listed immunohistochemical stains (Figure 6, Table 1).

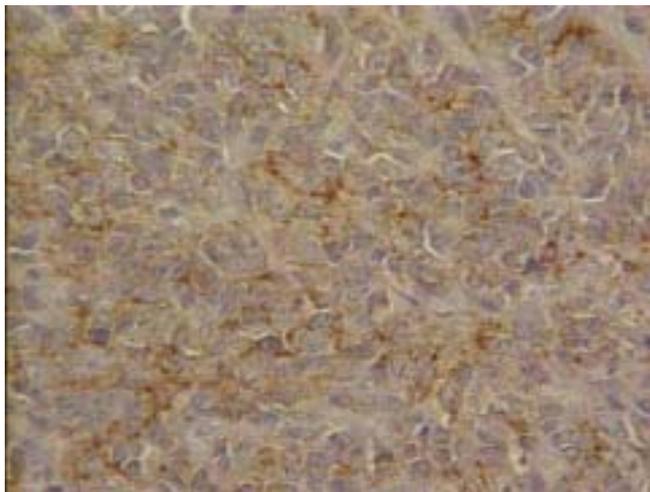


Figure 5: The tumor cells showed focal immunoreactivity for EMA (Immunohistochemical reaction for epithelial membrane antigen, original magnification 40x10), 254x193mm (72 x 72 DPI).

FISH showed interruption of SYT gene and confirmed the diagnosis of a monophasic synovial sarcoma.

2nd Operation: The operative material consisted of two grayish colored tumor nodules with glistening surface and firm consistency. They measured 3x2x1 cm and 2x1.7x 1 cm in the greatest dimensions. The tissue was compact with areas of hemorrhage.

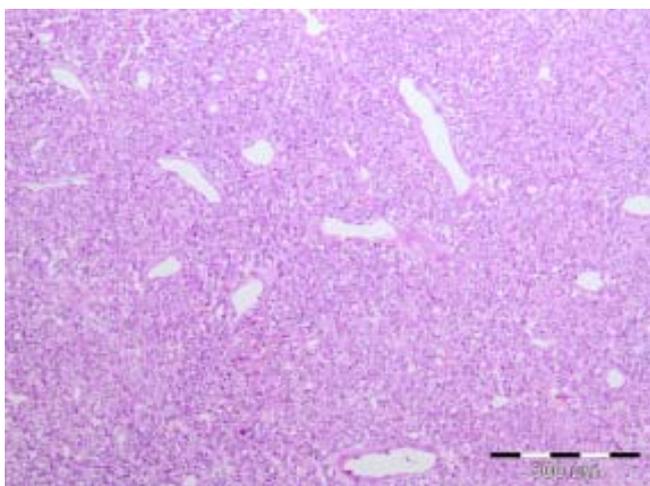


Figure 6: Hemangiopericytoma-like pattern (Hematoxylin-eosin, original magnification 4x10), 903x677mm (72 x 72 DPI).

Microscopically, both tumors had identical histological pattern. A neoplastic proliferation of spindle cells arranged in fascicles and sheets was found. The hemangiopericytic arrangement was rare, but slit-like

spaces were present. The cytological characteristics were identical to the cells described in the previously resected tumor (Figure 6).

Discussion

Synovial sarcoma is a soft tissue neoplasm most often occurring in para-articular regions, usually near the large joints. It rarely occurs within the joint cavity itself and most commonly it is intimately related to tendons, tendon sheets and bursas. Synovial sarcoma may arise in areas with no obvious synovial or periarticular structures and rare cases are described in almost all parts of the body, including abdominal cavity [16].

Histologically synovial sarcomas are subdivided into three groups: biphasic, monophasic and poorly differentiated [1, 3].

The biphasic synovial sarcoma is composed of two components or two types of cells: mesenchymal spindle cells and epithelial cells, in varying proportions. The spindle cells are uniform with ovoid pale-staining nuclei and inconspicuous nucleoli. The epithelial cells have abundant cytoplasm and ovoid nuclei and they usually form glands. The glands may contain papillary structures and mucin. The epithelial cells may also be arranged in solid sheets, cords, nets and they may show squamous metaplasia. Epithelial component may predominate in some cases and may mimic adenocarcinoma.

The monophasic synovial sarcoma is a neoplasm in which the spindle cell component predominates or it occurs alone without the epithelial component. The tumor cells are uniform with oval nuclei and indistinct nucleoli and they are arranged in highly cellular interlacing fascicles and sheets. Areas of hemangiopericytoma-like vascular pattern and stromal collagen or mucin in various amounts may be found.

Poorly differentiated synovial sarcoma is highly cellular neoplasm composed of relatively uniform cells having epithelioid, rhabdoid or small round cell appearance. Geographic type of necrosis and high mitotic activity are present [1, 3].

Synovial sarcoma is a distinctive soft tissue sarcoma with well described immunohistochemical and cytogenetic characteristics [10-12]. The most of synovial sarcomas, about 90%, express cytokeratins in the epithelial component and in some clusters of spindle cells. Vimentin is expressed in spindle cell component. Epi-

thelial membrane antigen is also often present in the epithelial cells. Bcl-2 protein is diffusely positive in all synovial sarcomas and some of them may express CD99 and S-100 protein [3].

The t(X;18)(p11;q11) is present in most of synovial sarcomas. Several studies had shown that genes SSXT from chromosome 18 and SSX1, SSX2 and SSX4 from the X chromosome are affected by t(X;18)

Fluorescence in situ hybridization is used to detect the interruption of SYT gene and rapid diagnosis of synovial sarcoma [3, 10-13].

Monophasic synovial sarcoma may present a difficult diagnostic problem due to its similar histological appearance to other spindle cell neoplasms especially when the tumor arises in unusual sites, but immunohistochemical and cytogenetic characteristics may reach the diagnosis.

Primary sarcomas of the liver are rare and small number of angiosarcoma, malignant fibrous histiocytoma, leiomyosarcoma, fibrosarcoma, malignant solitary fibrous tumor and malignant hemangiopericytoma are described [4, 14].

Srivastava et al previously reported a monophasic synovial sarcoma of the liver and described well-circumscribed diffusely hemorrhagic, tan-gray nodules with foci of necrosis composed of highly cellular areas of spindle shaped cells arranged in fascicular or storiform growth pattern. The author, also, described hemangiopericytoma-like vascular pattern, in the same tumor [4].

Holla et al reported another case of primary liver synovial sarcoma with very similar macroscopic and microscopic findings to that Srivastava already had described. The tumor was well-demarcated, soft with foci of hemorrhage and necrosis. It was a highly cellular neoplasm composed of uniform spindle cells with no epithelial component and with areas resembling hemangiopericytoma [5].

We describe similar tumor, well-circumscribed, diffusely hemorrhagic, and highly necrotic with the same microscopic pattern. It showed vimentin, CD99 and Bcl-2 diffuse positivity and epithelial membrane antigen and cytokeratin wide spectrum focal positivity, consistent with synovial sarcoma. The diagnosis was confirmed by demonstrating interruption of SYT gene by FISH.

Srivastava et al described 5 tumor nodes in the hepatic tissue [4], and Holla et al described solitary

tumor mass measuring 21x14x5 cm, more similar to ours that was solitary tumor mass measuring 14x9x6 cm [5]. The first relapse of the disease in our case was composed of two separate nodes similar to that Srivastava et al had described [4]. Both previously described tumors were well circumscribed, necrotic and highly hemorrhagic as our case was. Both authors described the tumors as highly cellular neoplasms composed of spindle shaped cells arranged in a fascicular and storiform growth pattern with areas of hemangiopericytoma-like vascular pattern [4, 5]. We found identical microscopic feature in our case, but we also found areas of polygonal and round cells.

Fisher et al reported 11 cases of synovial sarcomas arising in the abdomen, pelvic cavity or retroperitoneum, five of them monophasic [16]. The author describes eight retroperitoneal tumors, one that arose near the duodenum, one attached to a retroperitoneal base and three pelvic tumors. In our case the tumor was located in the liver. The exploration of the abdominal cavity done by the surgeon and the total body scan confirmed the tumors location restricted only to the liver.

Immunohistochemically the tumor cells showed diffuse strong positivity for vimentin and Bcl-2 and focal weak staining with muscle-specific and smooth muscle actin and were negative for pan keratin, cytokeratin 7, cytokeratin 20, epithelial membrane antigen, desmin, S-100 protein, HMB-45, MART-1, CD 34, chromogranin, synaptophysin, CD 99 and carcinoembryonic antigen in the case of Srivastava et al [4].

Foci of spindle cells were positively stained with antisera to cytokeratin, but were negatively stained using antisera to CD99, CD 34, and CD 117 in the case of Holla et al [5].

In our case neoplastic cells showed diffuse strong positivity for vimentin, CD99 and Bcl-2 and focal positivity for epithelial membrane antigen and cytokeratin wide spectrum. They were negative for all other listed immunohistochemical stains

The difference between the two previously described tumors and our case was the positive staining for CD99 in our case that may be seen in monophasic synovial sarcomas of other localization [3]. Another difference appeared in staining with muscle-specific and smooth muscle actin antisera which showed weak positivity in the case of Srivastava et al and was negative in our case.

Some cases of monophasic spindle cell synovial sarcoma may be negative for cytokeratin and epithelial membrane antigen, so the demonstration of the cytogenetic abnormality is necessary to confirm the diagnosis of synovial sarcoma [3, 15].

It is now well known that 2 closely related but distinct X-chromosomal genes (SSX1 and SSX2) are rearranged in different subsets of synovial sarcomas. The cytogenetic detection of the t(X;18)(p11.2;q11.2) translocation is highly sensitive and specific marker for synovial sarcoma.

According to the total body scan and the surgeon's intra-abdominal visual and manual investigation, the location of the neoplasm was restricted to the liver. That fact excluded intra-abdominal synovial sarcoma [16] and C kit negativity excluded metastatic deposition of GIST. Spindle cell neoplasms with muscle origin were excluded by desmin negativity of tumor cells and angiogenic origin was excluded by morphological feature and CD 31, CD34 and Factor VIII negativity. We excluded malignant peripheral nerve sheath tumor by S-100 negativity. Still the doubt about Ewing's sarcoma existed and it was supported by CD99 positive staining of the tumor cells.

In our case we needed a confirmation of the diagnosis by detection of cytogenetic abnormality. Such kind of studies are not available in our laboratory, so we sent paraffin blocks to Institute of Pathology, Faculty of Medicine, University of Ljubljana, where our colleagues detected interruption of SYT gene by FISH and confirmed the diagnosis of a monophasic synovial sarcoma.

Immunohistochemical and cytogenetic studies are necessary to make a definitive diagnosis of synovial sarcoma especially when it arises in unusual sites, like it happened in our case.

Acknowledgement

We express a deep gratitude to Professor V. Ferlan-Marlot, Professor B. Luzar and Professor M. Brachko from the Institute of Pathology in Ljubljana for FISH analysis and contribution to the diagnosis of the case.

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