

Case Report

Radiation-associated Synovial Sarcoma Arising in the Digestive Tract: A Case Report and Literature Review

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Abstract

Synovial sarcoma of the digestive tract is an extremely rare tumor. Only 12 cases were reported; none of these was in the gastroduodenal region. Radiation therapy is well known for its long-term carcinogenesis, especially of soft tissue sarcomas. Only four cases of radiation-associated synovial sarcoma have been reported. We report a case of primary gastroduodenal synovial sarcoma in a 54-year-old woman who was treated for Hodgkin's lymphoma at age 35, using external radiation to the mantle field and the paraortic strip (including abdominal paraaortic nodes). She presented with epigastric pain and sensation of fullness, associated with loss of appetite and weight. An upper endoscopy showed a distal gastric mass extending to the post-pulpal duodenum; a tissue biopsy of the mass showed monophasic synovial sarcoma with positive epithelial membrane antigen (EMA). The diagnosis was confirmed when reverse transcriptase-polymerase chain reaction (RT-PCR) demonstrated the presence of a SYT-SSX fusion transcript. She underwent total duodenectomy and partial gastrectomy and gastrojejunostomy. After surgery she regained her appetite and started gaining weight. She has been symptom-free for 7 months after the surgery.

Key words: Duodenum, synovial sarcoma, radiation, cytogenetics.

Introduction

Synovial sarcoma is a stromal tumor that usually arises in adolescents and young adults from preformed synovial structures near the joints of

the extremities. Ten percent of the cases arise from soft tissues around the head, neck, thoracic or abdominal wall, and retroperitoneum. It has been reported as a primary tumor in the heart, lungs, kidneys, prostate, and other sporadic sites in the human body.¹ Only 12 reported cases were in the digestive tract, and none of these was in the gastro-duodenal region.²⁻³

The most distinctive feature of synovial sarcoma is (X;18) translocation, which results in a SYT-SSX

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fusion gene. Among the immune-histopathological markers, epithelial membrane antigen (EMA) is the most specific for synovial sarcoma.⁴⁻¹⁰ Synovial sarcoma seems to have a bad prognosis, with a 5-year survival rate of 60%. It usually metastasizes to the lungs, lymph nodes, and bone marrow. It is also known to recur or metastasize after long remission periods.⁴

Radiation therapy is well-known for its long-term carcinogenesis, especially of soft tissue sarcomas, which occur in 0.1% of patients receiving radiotherapy. Radiation-associated sarcomas include fibrosarcoma, angiosarcoma, fibrous histiocytoma, osteosarcoma, and malignant peripheral nerve sheaths sarcomas.⁵ We report a case of radiation-associated gastro-duodenal synovial sarcoma in a 54-year-old woman who was treated at age 35 for stage 1 Hodgkin's lymphoma. Four cases of radiation-associated synovial sarcoma were previously reported.⁶⁻⁸ Three of these were in women⁶⁻⁷ and only one in a man.⁸ Moreover, the male case diagnosis was not confirmed by the presence of the epithelial membrane antigen (EMA) in immune-histopathological staining or t(X;18) in reverse transcriptase-polymerase chain reaction (RT-PCR). Further, the amount of radiation therapy the male patient had received was not documented. Including our patient, there are four documented cases of radiation-associated synovial sarcomas in female patients and possibly only one in a male patient. We propose that gender might have an effect on the risk of developing radiation-associated synovial sarcoma, bearing in mind that women have two X chromosomes.

Case Report

A 54-year-old woman known for hypertension and peptic ulcer disease with a family history significant for Hodgkin's lymphoma in a maternal aunt, cancer of the larynx in a maternal aunt, and cancer of the larynx in a maternal uncle. In September 1987, at age 35, she was diagnosed with stage 1B nodular sclerosing Hodgkin's lymphoma, which presented as a thymic mass causing recurrent chest pain. She underwent a mediastinostomy with thymectomy, followed by a 4000 cGy external radiation to the mantle field (October 27 to November 23, 1987) and 3600 cGy to the paraaortic strip (including abdominal paraaortic nodes) in the period (December 10, 1987 to January 21, 1988). After that she remained

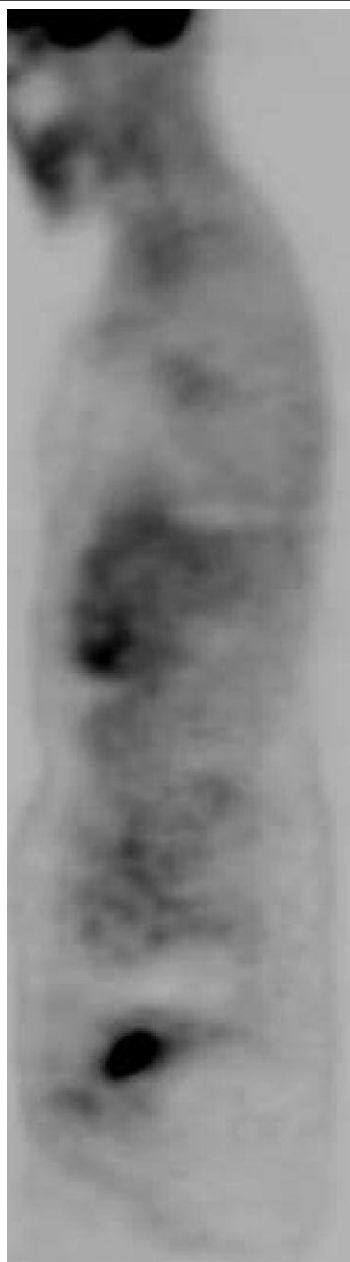


Figure 1. PET scan showing increased activity at the gastro-duodenal region.

disease-free and was followed with interval chest X-rays and computed tomography (CT) scans. In November 2005, she was diagnosed with stage 1 mucinous ductal carcinoma of the left breast. She was treated with lumpectomy and 3400 cGy external radiation using standard mammo-site technique to the left breast over 5 days (December 19-23, 2005). Subsequently, she was started on anastrozole. In October 2006, she presented with gnawing epigastric pain for 3 weeks, accompanied by a sensation of fullness. Her pain was nonradiating and occurred 30 minutes to 2 hours after meals with no associated nausea, vomiting, hematemesis, or melena. She lost her appetite and 20 pounds in 2 months prior to this presentation. Her

physical examination revealed a moderately built female in no apparent distress. There was no evidence

of pallor or lymphadenopathy. Cardiorespiratory examination was normal, and her abdominal examination showed epigastric tenderness and no palpable masses or evidence of organomegaly.

A CT scan of the chest showed radiation changes in lung apices and evidence of sternotomy. A CT of the abdomen and pelvis showed no evidence of duodenal or hepatic masses. PET-CT scan showed increased metabolic activity at the gastroduodenal junction (Figures 1, 2).

An upper endoscopy showed a distal gastric mass

extending to the postpulpal duodenum. The mass measured 3 x 3.5 cm (Figure 3). A tissue biopsy of the mass showed monophasic synovial sarcoma with negative CD 117, CD34, desmin, S 100 and smooth muscle actin. EMA was positive. The diagnosis was confirmed when RT-PCR demonstrated the presence of a SYT-SSX fusion transcript resulting from t(X;18) translocation.

Subsequently, the patient underwent total duodenectomy and partial gastrectomy. The mass was resected with a free margin. Grossly, the specimen consisted of the duodenum and distal part of stomach, with an off-white, firm, smooth, partially circumscribed mass measuring 3.5 x 3 x 1.5 cm at the gastroduodenal junction. Part of the lesion showed ulceration (Figure 4).

Hematoxylin and eosin stain showed an ulcerated, cellular mesenchymal neoplasm. The tumor involved the luminal aspect extending into the muscularis propria. The neoplastic cells were small spindle cells forming solid sheets with focally myxoid stroma. Perivascular arrangement was also noted. Mitotic activity was not high, but tumor necrosis was present (Figure 5).

After surgery the patient recovered reasonably. She regained her appetite and started gaining weight. After a second opinion the decision was made to follow up the patient with interval CT scans of the chest, abdomen, and pelvis without further intervention, unless she developed recurrence or metastasis. She is currently disease-free 7 months after her surgical resection of the tumor. She remains on anastrozole for her previously treated breast cancer.

Discussion

Synovial sarcoma of the digestive tract is a rare tumor. After searching the literature, we found only 12 reported cases, none of which was in the gastroduodenal junction. Ten of these cases were reported in the esophagus, one was in the stomach,³ and one in the jejunum.²

The main differential diagnosis for synovial sarcoma of the digestive tract is benign and malignant gastro-intestinal stromal tumor (GIST), the most common mesenchymal malignancy of the digestive tract.² Sixty to seventy percent of GISTs are positive for CD34, and 95% are positive for CD117 (Both of these markers were negative in our case). GISTs are

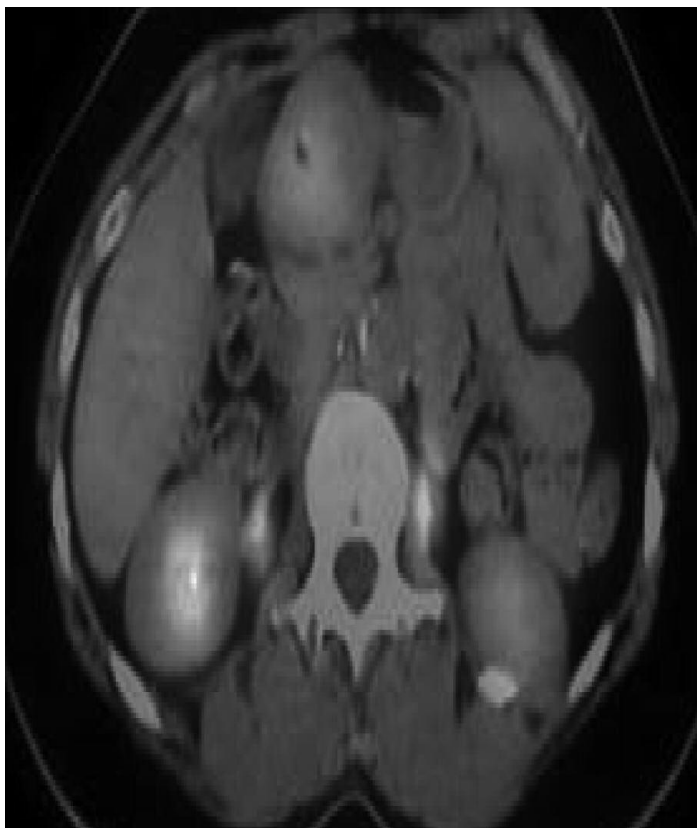


Figure 2. PET scan showing increased activity at the gastro-duodenal region.



Figure 3. Upper endoscopy showing a 3-cm x 3.5-cm nonobstructive mass in the gastro-duodenal region.

more common in men and occur mostly in the stomach. Synovial sarcoma of the gastrointestinal tract could be more frequent than the reported cases. Some of the cases could have been misdiagnosed as GIST. In our case, the initial diagnosis was also thought to be GIST before further analysis.

Radiation therapy is well known for its long-term carcinogenesis, especially of soft tissue sarcomas. Radiation-associated tumors are defined as tumors arising in a previously irradiated field after a latency period of 2 or more years. They are histologically different from the irradiated tumor. Radiation-associated sarcomas are more aggressive than idiopathic sarcomas.⁹ The amount of radiation received by patients with radiation-associated sarcoma has been reported in the range of 1600-12,440 cGy in a total of 146 patients.⁹ Our patient had received a total of 3,400 cGy to the paraortic strip. The latency period ranged from 2 to 40 years. The latency duration tends to be shorter with higher doses of irradiation defined as 3,000-3,600.⁹ Four cases of radiation-associated synovial sarcoma were reported⁶⁻⁸ (Table 1). One occurred in a 34-year-old woman, 27 years after radiation therapy for congenital hemihypertrophy. The second case occurred in a supraclavicular lymph node of a 42-year-old woman, 17 years after radiation for breast cancer. The third case occurred in a 36-year-old woman, 8 years after radiation therapy for Hodgkin's lymphoma. And the fourth case occurred in a 28-year-old man's neck 14 years after radiation to his face and neck for acne. Our patient's development of synovial sarcoma in the gastro-duodenal region appears to be related to her history of irradiation. She has a strong personal and family history of cancer; but her case fits all the criteria to diagnose radiation-associated neoplasm with latency period of more than 2 years, with proof that the secondary neoplasm is histologically different from the primary one, and the development of the neoplasm in the previously irradiated field (She received radiation to the paraaortic strip, which involves the retroduodenal area). Further, the amount of radiation therapy she had received was in the range of radiation known to induce malignant transformation. Moreover, our patient did not receive chemotherapy.

Three patients⁶⁻⁷ diagnosed with radiation-associated synovial sarcoma, along with our current case, are women. All of them demonstrated the pres-

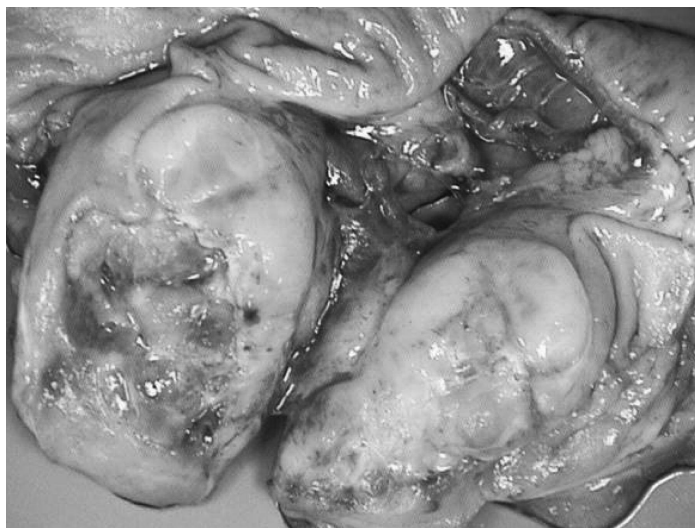


Figure 4. Gross photograph of off-white, firm, smooth, partially circumscribed synovial sarcoma mass.

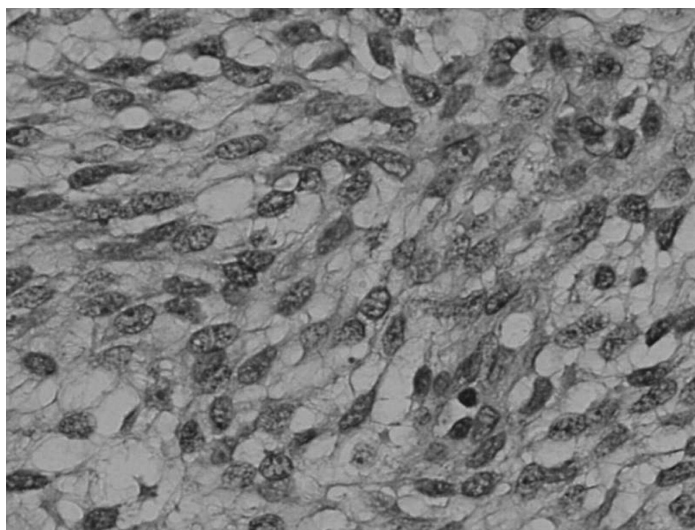


Figure 5. Microscopic photograph showing spindle neoplastic cells forming solid sheets.

ence of the SYT-SSX fusion gene. In the only reported case in a man,⁸ diagnosis was not confirmed by RT-PCR and the amount of radiation received by that patient was not documented. Since the involved chromosomes in translocation t(X;18) are chromosome 18 and chromosome X, and by nature women have two X chromosomes in every single cell, females might be at a higher risk for developing radiation-associated X chromosome related translocations such as the one producing the SYT-SSX fusion gene, causing synovial sarcoma.

Table 1. Summary of reported cases of radiation-associated synovial sarcoma.

Author	Gender and Age	Synovial Sarcoma Location	Indication for Radiotherapy	Years after RT	Radiation Therapy Dose	RT-PCR	Immune-histopathology
Egger et al ⁶	Female, 42	Infraclavicular	Right breast cancer	17	5,000 cGy Right breast 5,200 cGy axillary lymph nodes 4,700 cGy parasternal lymph nodes	t(X;18)	EMA + CD99 + CD117 + CD34 - Desmin - S100 -
Egger et al ⁶	Female, 34	Left hand	Hemihypertrophy	27	NA	t(X;18)	EMA + CD99 + CD117 + CD34 - Desmin - S100 -
Van de Rijn et al ⁷	Female, 36	Infraclavicular	Hodgkin's lymphoma	8	3,300 cGy paraortic and splenic pedicle 4,400 cGy mantle field	t(X;18)	EMA + CD99 - CD34 - S100 +
Mischler et al ⁸	Male, 28	Neck	Acne	14	NA	NA	NA
Current case	Female, 54	Gastro-duodenal	Hodgkin's lymphoma	19	4,000 cGy mantle field 3,600 cGy paraortic strip	t(X;18)	EMA + CD99 - CD117 - CD34 - S100 - Desmin -

Note: NA: not available; RT: radiation therapy; RT-PCR: reverse transcriptase-polymerase chain reaction; EMA: epithelial membrane protein.

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