Angiosarcoma of the seminal vesicle: a case report of long-term survival following multimodality therapy

Kenneth Chang,[1] Terence T. Sio,[1] Vishal S. Chandan,[2] Matthew J. Iott,[1] Christopher L. Hallemeier[1]

[1]Department of Radiation Oncology, [2]Department of Anatomical Pathology, Mayo Clinic, Rochester, MN, USA

Abstract

Angiosarcoma of the seminal vesicle is an extremely rare malignancy, with few published case reports in the literature. We present a case of primary angiosarcoma of the seminal vesicle in a 45-year-old male who was treated with multimodality therapy, consisting of neoadjuvant chemotherapy and chemoradiation followed by surgical resection and intraoperative radiation therapy. He has been free of cancer recurrence for more than six years after completion of therapy. To our knowledge, this represents the longest reported survival of a patient with this rare tumor, and one of the few cases reported using a multimodality therapy approach.

Case Report

A previously healthy 45-year-old male developed sharp left lower quadrant and groin pain. He was evaluated by his primary physician and his symptoms were thought to be related to diverticulitis. He was treated conservatively with an antibiotic, though there was no resolution of his symptoms.

A computed tomography (CT) scan of the pelvis revealed a 5.6×5.1 cm heterogeneously enhancing mass involving the left lobe of the seminal vesicle and minimally the right lobe across the midline. The mass was invading the left bladder base and ureterovesicular junction (UVJ), and a few cm of left distal ureter (Figure 1A). This was accompanied by left-sided hydronephrosis. The mass also invaded the left obturator internus muscle, and potentially the base of prostate gland as well as into the perirectal space abutting the rectum. There was no pelvic lymphadenopathy. A transrectal biopsy of the mass was performed which was reviewed at several different institutions, though it was considered indeterminate. A second transrectal biopsy of the periprostatic/seminal vesicle soft tissue mass was performed, which was reviewed at our institution and found to be a grade 4 (of 4) epithelioid angiosarcoma. Immunohistochemical stains showed the tumor cells reacted strongly and diffusely with antibodies to CD31 and vimentin, but did not react to antibodies to keratin (Cam 5.2, 7, 20 and wide spectrum), prostate specific antigen, actin, desmin, melanin A, S-100, CD117 (C-kit), synaptophysin, and chromogranin, supporting the diagnosis.

The patient was referred to our institution for further evaluation and management. Digital rectal examination revealed a normal anal sphincter tone and a large, firm, fixed mass in the left lateral rectal area without apparent rectal mucosal involvement. Magnetic resonance imaging (MRI) was performed, which showed an infiltrating soft tissue mass in the left lower pelvis involving the left seminal vesicle, the base of the prostate and the left bladder wall (Figure 1B-D). The mass extended laterally resulting in effacement of the left obturator internus muscle. A fatty soft tissue plane separated the mass from the adjacent left anterior rectal wall. A chest CT showed a few small indeterminate pulmonary nodules and a small calcified granuloma within the left lower lobe. A colonoscopy showed no evidence of rectal invasion. Given the presence of locally advanced tumor and the high risk for micrometastatic disease, the multidisciplinary team consisting of urology, medical oncology, and radiation oncology physicians recommended multimodality therapy consisting of neoadjuvant chemotherapy and radiotherapy followed by potential surgical resection.

The patient received two cycles of neoadjuvant IMAP chemotherapy, consisting of ifosfamide (2500 mg/m^2 IV days 1-2), Adriamycin (40 mg/m^2 IV day 2), mitomycin (4 mg/m^2 IV day 2), cisplatin (60 mg/m^2 IV day 2), and mesna (1500 mg/m^2 IV and 2500 mg/m^2 per days 1-2.) Repeat imaging following IMAP showed that the soft tissue mass in the left pelvis slightly decreased in size from 5.6×5.1 cm to 4.3×4.0 cm. The patient then received external beam radiation therapy (Figure 1E) consisting of 50 Gray in 25 fractions delivered daily over 5 weeks with 2 cycles of concomitant MAP chemotherapy, consisting of mitomycin (8 mg/m^2 IV), adriamycin (40 mg/m^2 IV) and cisplatin (60 mg/m^2 IV).

Following a six-week recovery from preoperative chemoradiation, repeat imaging studies showed no significant change in the pelvic mass and no evidence of distant metastatic disease. He then proceeded to surgical resection with a radical prostatectomy, partial cystectomy, distal ureterectomy, bilateral pelvic lymph node dissection, and ureteroneocystostomy. Frozen section margins at the bladder and left pelvic sidewall were positive. Additional resection was performed and the margins were negative. An intraoperative electron radiation therapy boost (9 Gy) was given to the left pelvic sidewall as there was a concern for residual microscopic disease. Review of the surgical pathology demonstrated grade 4 (of 4) epithelioid angiosarcoma forming a 3.5×2.6×1.8 cm mass in soft tissue in the region of the left seminal vesicle (Figure 2). The tumor involved the left seminal vesicle, infiltrated adjacent skeletal muscle, and extensively involved regional nerves and ganglia, but tumor did not extend into prostatic parenchyma. The final surgical margins were negative for tumor. Multiple left and right pelvic lymph nodes (external iliac, internal iliac, common iliac and obturator regions) were negative for tumor involvement.

Post-operatively he had left thigh numbness that subsequently resolved. He developed a vesicourethral anastomotic leak which required prolonged (3 months) Foley catheter use; however, this completely resolved. He developed an abscess that was drained and resolved. The patient was then seen in regular follow up with serial imaging studies over the subsequent six years following surgery and he has not developed evidence of cancer recurrence.

Correspondence: Christopher L. Hallemeier, Department of Radiation Oncology, Mayo Clinic, 200 First St SW, Rochester, MN 55905, USA.
Tel. +1.507.266.5232 - Fax: +1.507.284.0079.
E-mail: hallemeier.christopher@mayo.edu

Key words: angiosarcoma, seminal vesicle, prostate, neoadjuvant, surgery, chemoradiation, trimodality therapy.

Contributions: KC, literature review, preparation of manuscript, approval of final version of manuscript; TTS, data collection, literature review, preparation of manuscript, approval of final version of manuscript; VSC, MJI, CLH, data collection, preparation of manuscript, approval of final version of manuscript.

Conflict of interests: the authors declare no potential conflict of interests.

Received for publication: 28 November 2013.
Revision received: 8 December 2013.
Accepted for publication: 9 December 2013.

Rare Tumors 2014; 6:5202
doi:10.4081/rt.2014.5202

Discussion and Conclusions

Soft tissue sarcomas (STS) comprise 1-2% of all cancers and can appear in any type of connective tissue throughout the body.[1] Angiosarcomas are a rare subtype of STS, and arise in endothelium of blood vessels and represent 2% of STS cases.[2] Reported risk factors for development of angiosarcoma include prior exposure to ionizing radiation or toxic chemicals, longstanding lymphedema (Stewart-Treves syndrome), and venous stasis, although most patients diagnosed with angiosarcoma have no identifiable risk factors.[2,3] Angiosarcomas are most commonly found in the scalp, face, neck, extremities, or breast.[3] In contrast, angiosarcoma of the genitourinary system is exceedingly rare.

Very few cases of angiosarcoma of the prostate or seminal vesicle have been reported in the literature (Table 1).[4-14] For angiosarcomas of the seminal vesicle, presenting symptoms may include testicular discomfort and

Table 1. Clinical summaries of primary seminal vesicle and prostate angiosarcoma patients in literature, with one patient per row.

Authors	Year	Age	Management	Outcome
Angiosarcoma of the seminal vesicle				
This study	2014	45	CT, RT, SR	*NED*, 6 years AT
Chiou[11]	1985	63	SR	Died, 1 month AT
Panageas[14]	1990	53	SR, RT	NED AT
Lamont[12]	1991	52	SR, RT, CT	Died, ~3 months AT
Matthew[13]	2006	55	SR, CT	*NED*, 2 years AT
Angiosarcoma of the prostate				
Matthias[9]	1889	70	PC	Died, 6 months
Botesco[5]	1902	2	PC	Died, 1 day
Mogi[10]	1911	38	PC	Died, 4 months
Salleras & Vilar[5]	1924	32	PC	Died, AD
Smith[10] (2 patients)	1986	60 42	SR SR, CT	Died, 6 months AD *NED*, 24 months AT
Chan[4]	1990	35	PC	Died, 5 weeks AD
Oliva[5]	2001	36	SR, CT	*NED*, 36 months
Chandan[5]	2003	77	SR	Died, 4 days AT
Lee[8]	2006	19	CT, SR	*NED*, 16 months AT
Guo[6]	2009	65	SR	Died, 2 months
Khaliq[7]	2012	73	SR, CT	Died, 2 weeks AT

AD, After diagnosis; AT, After treatment; CR, Chemoradiation; CT, Chemotherapy; NED, No evidence of disease; PC, Palliative care; RT, Radiotherapy; SR, Surgical resection.

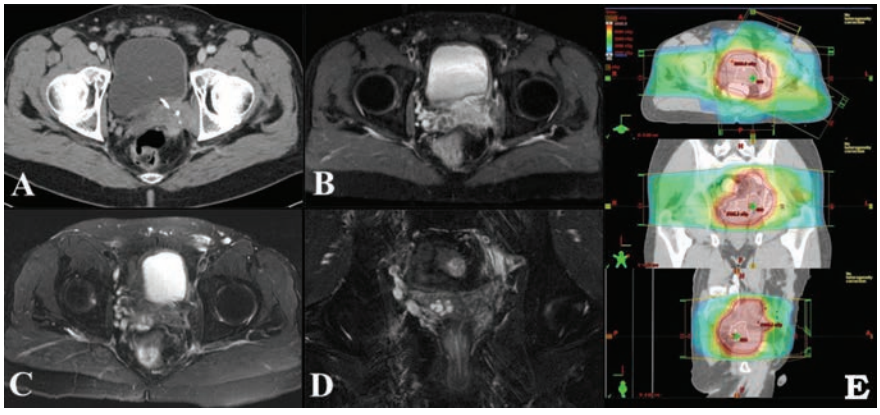

Figure 1. Imaging studies at the time of initial presentation show a mass emanating from the left seminal vesicle and invading the left posterior bladder wall and the left obturator internus muscle. The mass demonstrates contrast enhancement on axial computed tomography (A) and magnetic resonance imaging (B). The mass is hypointense on T2 weighted axial (C) and coronal (D) magnetic resonance imaging. E) Pre-operative external beam radiotherapy plan with a prescribed dose of 50 Gray delivered in 25 fractions. The gross tumor volume (GTV) is delineated in white outline and the planning target volume (PTV) is delineated in black outline. The GTV, representing the tumor as visualized on CT and MRI, was expanded by 1.5 cm to generate the clinical tumor volume (CTV). The CTV was expanded by 0.7 cm to generate the PTV.

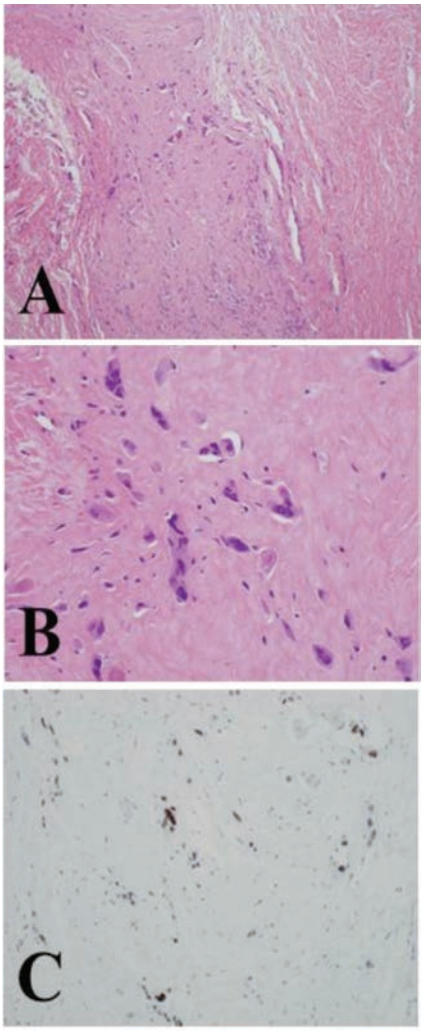

Figure 2. Microscopic examination showed a poorly differentiated malignant tumor involving the left seminal vesicle soft tissue (A). The tumor showed large pleomorphic cells with prominent nucleoli (B). Few mitotic figures were also present. Immunostains were performed and the tumor cells were positive for FLI-1 (C) and CD31; and negative for Cam 5.2, cytokeratin 7, cytokeratin 20, actin, desmin, S100, CD117, synaptophysin, chromogranin and prostate specific antigen (PSA). These results supported the diagnosis of an angiosarcoma.

perineal pain which may radiate to the lower back.[11,13,14] Prostatic angiosarcoma can present with symptoms similar to prostatic adenocarcinoma, including dysuria, hematuria, or pelvic pain.[7] Biopsy is required for definitive diagnosis. The defining histologic features of angiosarcoma are an abnormal appearance of the endothelial lining and cellular dedifferentiation.[15] Generally, positive immunohistochemical staining for the normal endothelial hallmarks, Factor VIII related antigen, vimentin, CD31, CD34, Ulex europaeus agglutinin 1, and VEGF, confirm the diagnosis.[15] In our patient immunostaining was positive for CD31 and vimentin consistent with a diagnosis of angiosarcoma.

As angiosarcoma of the prostate or seminal vesicle is rare, no definitive treatment schemes have been established. Surgical resection is usually performed for lesions that are amenable to such an approach. However, clinical outcomes following surgical resection alone are generally poor. All 4 patients treated with this approach and reported in the literature[5,6,10,11] developed distant metastases and death within one year (Table 1). In other reports, chemotherapy and/or radiotherapy have been used as an adjunct to surgery, with some patients experiencing freedom from disease recurrence, supporting the use of a multimodality treatment approach. Our patient had locally advanced angiosarcoma arising from the left seminal vesicle. He was felt to be at high risk for local and distant failure with surgical resection alone, thus we utilized multimodality therapy consisting of chemotherapy, chemoradiation, and surgical resection with IORT. He is alive and without evidence of disease recurrence for six years following completion of treatment, and we believe that this is the longest disease-free survival reported to date.

Recent phase II trials have demonstrated safety and modest efficacy of single agent paclitaxel or bevacizumab for unresectable angiosarcoma.[16,17] Several case reports have demonstrated marked response of angiosarcoma to radiotherapy combined with paclitaxel or bevacizumab, with acceptable treatment-related toxicity.[18-20] For patients with localized angiosarcoma of the prostate or seminal vesicle, multimodality treatment incorporating these regimens should be considered.

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