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Angiosarcoma of the Bladder: Review of the Literature and Discussion About a Clinical Case

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ABSTRACT

Our reported case is a 72 year-old man who presented with hematuria. A transurethral resection of the bladder tumor (TURB-T) has been performed. Histopathological diagnosis was an epithelioid angiosarcoma. CT scan revealed a bladder thickening. The treatment consisted in a complete pelvectomy with urinary and digestive diversion. Following the operation, the patient developed liver and pulmonary metastasis. He died 5 months after the initial diagnosis.

Introduction

Angiosarcoma is a vascular malignant tumor developed from blood vessels wall connective tissue. It is a rare neoplasia with bad prognosis and affects any organ. Bladder angiosarcoma is rare and is the subject of very few publications. Information about diagnosis, treatment, evolution and prognosis of this type of tumor are very limited. In this paper we report a 72-year-old patient case, harboring bladder angiosarcoma revealed by macroscopic hematuria.

Case presentation

The patient was 72-year-old man. He was admitted in emergency for a first episode of macroscopic hematuria complicated with acute urinary retention. His medical history was high blood pressure, a weaned smoking addiction, and benign prostatic hyperplasia (BPH). As a formal cinema industry worker, he had undergone chemical products exposure. At the first clinical examination, he presented with no pain, a supple abdomen without palpable mass. The biological checkup was normal. A bladder blood clot was seen on ultrasound. A cystoscopy was performed in emergency revealing a voluminous mass with a wide implantation located in the left side of the bladder. A TURB-T was performed. Pathological analysis reported an epithelioid bladder angiosarcoma (ISUP 2012 classification). The tumor was located in the submucosae bulging the normal urothelium.

On architectural analysis, tumor cells were undifferentiated; they contained abundant cytoplasm and large, irregular nuclei with many mitosis. Necrosis rate was superior to 50%. There was no vascular embolus (Fig. 1). Immunohistochemical (IHC) staining was positive for CD31 (Fig. 2), FLI-1, ERG (Fig. 2) and vimentin, but negative for CD34 and cytokeratin. Proliferation index with Ki67 staining was of 90%.

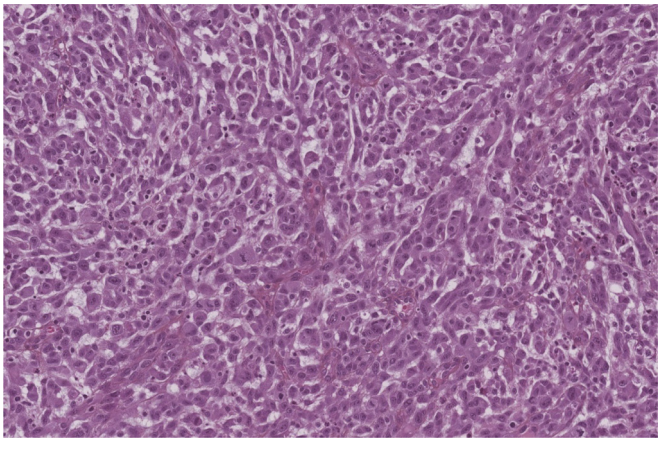

Figure 1. Malignant epithelioid cells, HES stain.

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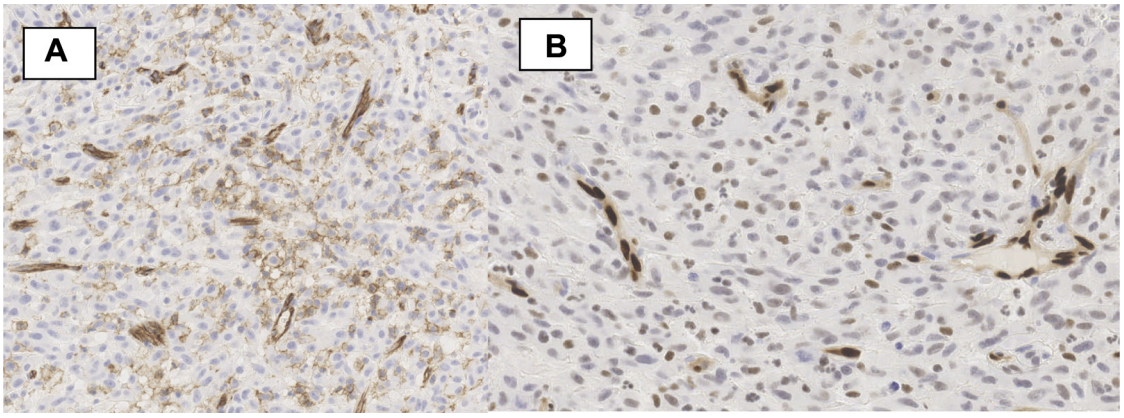

Figure 2. A: CD31 membranous staining of infiltrating tumor cells. We can observe also the normal vessel wall staining. B: Moderate ERG nuclear staining of tumor cells. We can also observe a stronger staining of normal endothelial capillary cells.

Despite a complete resection, a CT scan performed 3 weeks after TURB-T revealed massive local recurrence with a 42 * 37 mm mass (Fig. 3). No secondary lesion was diagnosed at this time.

For the treatment, the institutional sarcoma board has decided an initial external radiation therapy followed by surgery if the mass did not increase. After beginning the radiation therapy, the patient degraded. He presented a sepsis. The CT-scan showed an air bubble inside the bladder near the mass evocating tumor necrosis (Fig. 3).

Despite broad-spectrum intra-venous antibiotics, the patient declined indicating a surgical extirpation. A total pelvectomy with urinary and digestive diversion was performed 3 months after initial presentation.

After surgery, the patient presented an atrial fibrillation. One week after surgery, a CT-scan revealed liver and lung metastasis with peritoneal carcinomatosis.

The patient died 5 months after initial diagnosis.

Discussion

Non-urothelial bladder tumors represent less than 5% of bladder tumors. Bladder angiosarcoma was described for the first time in 1907 by Jungano.[1] Since that date, thirty-two cases had been reported in literature. Some cases are reported after radiation therapy for prostate or gynecologic cancer. Angiosarcoma following radiation therapy was previously described. Hematuria is always the first symptom (macroscopic or microscopic). Associated symptoms are dysuria, pain, obstruction, vaginal bleeding and weight loss. Men are more affected than women with a ratio of 1/5. Liver and lung are usual metastatic sites.

Pathological diagnosis can be difficult.[2] According to Matoso and Epstein, Angiosarcoma is confirmed if at least one endothelial marker including Factor VIII (F VIII), CD31, CD34 or ERG is positive on IHC.[3]

In our case, epithelioid bladder angiosarcoma diagnosis is founded on CD31, FLI-1 and ERG positive staining. CD34 and Cytokeratin are negative. A second expert opinion concluded in angiosarcoma or undifferentiated sarcomatoid carcinoma. An uropathologist board discussion decided that further molecular analysis would not have any value. In the literature, 27 cases are positive for at least one endothelial marker, including ERG (n = 5), F VIII (n = 12), CD31 (n = 20) and CD34 (n = 12). Five cases report no immunohistochemical analysis. No molecular analysis is reported (Table 1).

There is still no consensus on optimal treatment for bladder angiosarcoma. In our case, radiation therapy and radical pelvectomy was performed. Our patient had rapid disease progression after surgery; therefore he did not fit for adjuvant therapy. No significant superiority of any of those strategies has been reported.

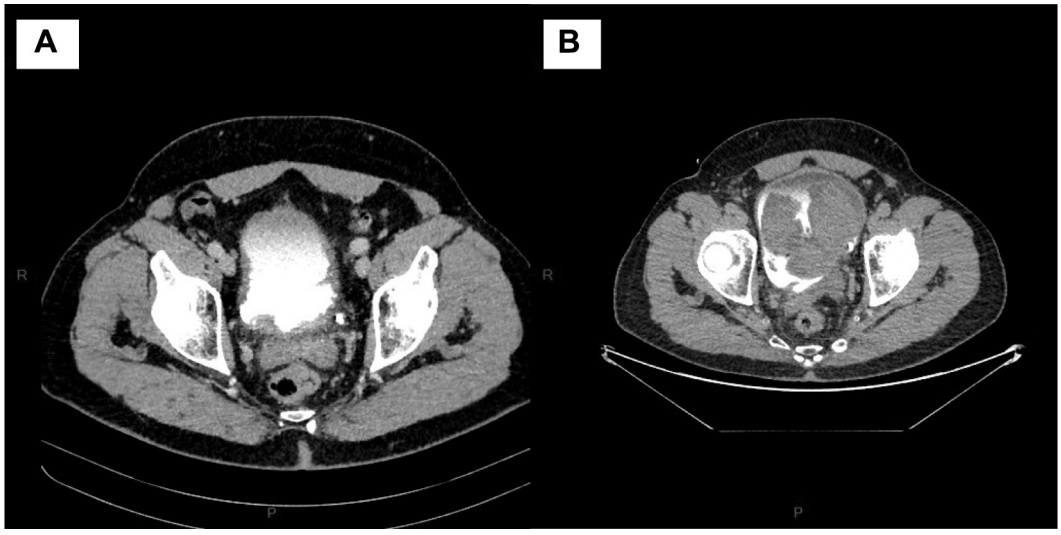

Figure 3. CT images show the rapid local progression of the tumor bladder. A: Day of diagnosis. B: 2 months after diagnosis.

Table 1
Diagnosis, treatment and outcome of bladder angiosarcoma.

Reference	Age/sex	Presenting symptoms	Immunophenotype	Treatment	Outcome
Jungano, 1907[1]	54/M	Hematuria and obstruction	N/A	Resection of tumor	N/A
Casal et al., 1970	85/F	Hematuria, dysuria and weight loss	N/A	Partial cystectomy	Died 3 days after diagnosis from myocardial infarction, no autopsy
Schwartz et al., 1983	46/M	Hematuria and enlarging cutaneous nodules	N/A	10 courses of cis-platinum, doxorubicin and cyclophosphamide	Died 23 months after diagnosis, angiosarcoma in lung, brain and scrotum
Stroup and Chang, 1987	68/M	Hematuria	Factor VIII+ Keratin−	Partial cystectomy	Died 8 month after diagnosis from myocardial infarction; autopsy showed lung and liver metastases
Morgan et al., 1989	72/F	Vaginal bleeding and hematuria	Factor VIII+	N/A	N/A
Aragona et al., 1991	78/M	Dysuria and hematuria	Factor VIII+ ULEX+ Keratin−	Diverticulectomy	Died 2 months after diagnosis from myocardial infarction, no autopsy
Ravi, 1993	55/M	Hematuria	N/A	Partial cystectomy and adjuvant radiation therapy (5500 cGy)	Alive 8 months after diagnosis
Navon et al., 1997	78/M	Hematuria	Factor VIII+ CD34+ ULEX+	Radical cytoprostatectomy	Alive 30 months after diagnosis
Engel et al., 1998[4]	47/M	Hematuria, flank pain and suprapubic pain	N/A	Radical cystoprostatectomy, 5 cycles of chemotherapy and pelvic irradiation.	Alive and well 32 month after diagnosis
Schindler et al., 1999	47/M	Dysuria, hematuria and suprapubic pain	Vimentin+ CD31+ CD34− Keratin− Factor VIII−	Radical cystoprostateectomy	N/A
Seethala et al., 2006	66/M	Hematuria	CD31+ CD34+ Keratin−	Radical Cystoprostatectomy and 5 cycles of Gemcitabine and Docetaxel	Alive 19 months after diagnosis
Kulaga et al., 2006	83/F	Microhematuria	Vimentin+ CD31+ Factor VIII− CD34−	TURB (transurethral bladder resection)	Died 3 months after diagnosis, no autopsy
Pazona et al., 2007[5]	47/M	Hematuria, suprapubic pain	CD31+	Radical cystoprostatectomy, 5 cycles ofchemotherapy and pelvic irradiation	Died 6 years after diagnosis, from myocardial infarction. Autopsy: no evidence of recurrent.
Williams et al., 2008	71/M	Hematuria	Factor VII+ CD31+ CD34+	Radical cystoprostatectomy	Died 3 months after diagnosis
Tavora et al., 2008	73/F	Hematuria		Radical cystectomy	Died 2 months after diagnosis
	77/M	Hematuria	CD31+ and CD34+ for 3 cases	N/A	Died 5 months after diagnosis
	71/M	Hematuria		N/A	Died 4 months after diagnosis
	63/F	Hematuria	Keratin− for all	N/A	Died 3 months after diagnosis
Warne et al., 2011	32/F	Hematuria and left side flank pain	CD31+ Factor VIII+ ULEX+ Keratin+	TURB + 6 cycles of ifosfamide, epirubicin + single fraction radiotherapy	Died 19 months after diagnosis, lung metastases. No autopsy
Abbasov et al., 2011	51/M	Hematuria	Keratin+ Factor VIII+ Vimentin+ CD31+ CD34−	Radical cystoprostatectomy	Died 5 weeks after diagnosis
Beyazal et al., 2014	20/M	Hematuria and disseminated pelvic pain	CD34+	Partial cystectomy	Alive 1 year after diagnosis
Bahouth et al., 2015	89/M	Hematuria	CD31+ CD34+ Factor VIII+ Keratin−	Palliative radiotherapy	Died 3 months after diagnosis
Matoso et al., 2015[3]	73/F	Hematuria	CD31+ Factor VIII+	TURB followed by partial cystectomy	Died 6 months after diagnosis
	77/M	Hematuria	CD31+ CD34+ Factor VIII−	TURB	Died 14 months after diagnosis
	71/M	Hematuria	CD31+ Factor VIII+	TURB followed by partial cystectomy	Died 7 months after diagnosis
	85/M	Hematuria	CD31+ CD34+ Factor VIII+	TURB	Died 6 months after diagnosis

(*continued on next page*)

Table 1 (*continued*)

Reference	Age/sex	Presenting symptoms	Immunophenotype	Treatment	Outcome
	39/M	Hematuria	CD31+	TURB followed by partial cystectomy	Died 13 months after diagnosis
	64/M	Hematuria	CD31+ ERG+	TURB followed by partial cystectomy	Alive 12 months after diagnosis
	43/M	Hematuria	CD31+ Factor VIII+ ERG+ CD34–	TURB	Alive 6 months after diagnosis
	73/M	Hematuria	CD31+ ERG+	TURB	Died 3 months after diagnosis
	64/M	Hematuria	CD34+ ERG+	TURB	Alive 3 months after diagnosis
Ojerholm et al., 2015	61/M	Hematuria	N/A	Radical cystoprostatectomy	Alive 4 months after diagnosis
Current case	72/M	Hematuria and urinary retention	ERG+ Vimentin+ CD31+ CD34– Keratin–	Radiotherapy and radical pelvectomy	Died 5 months after diagnosis

Traditionally, sarcomas are treated by chemotherapy, surgery and radiotherapy.[2] The triple association has shown promising results in high-grade sarcomas of the head and neck.[2] Due to the rarity of angiosarcoma, it is unlikely to reach high level of evidence guidelines. The reported experience suggests that surgery and radiotherapy should be used initially. The role of chemotherapy should be defined.

Suggested treatment option includes chemotherapy, radiotherapy and radical surgery, with some sort of combination. Adjuvant radiotherapy and combined surgical and chemotherapeutic approach are reported with short-term survival.[4] Chemotherapy regimens, reported are doxorubicin and ifosfamide.[2,4] These drugs are reported as active in sarcoma treatment. In unextirpable or metastatic disease, chemotherapy and/or radiotherapy could be an option.

Bladder angiosarcoma has a poor prognosis. In our reported case, the patient died 5 months after diagnosis. In the literature, ten patients survived more than 1 year and 3 more than 2 years. Mean age at diagnosis is 63.5 (range 20–89). Mean overall survival is 10.6 months (range 3 days to 6 years). Pazona[5] and Engel[4] report long-term survival after multimodal treatments. Pazona[5] reports a 6 years survival with no evidence of disease on autopsy after radical cystectomy with adjuvant chemotherapy followed by pelvic irradiation. Engel[4] reports on another combined cystectomy, chemotherapy and external beam radiation with no evidence of recurrence after 32 months of follow-up.

Conclusion

We report one of the very few cases of bladder angiosarcoma. It remains an aggressive tumor with poor prognosis. Optimal treatment for bladder angiosarcoma remains unclear, a multimodal aggressive approach combining radical surgery, radiotherapy and chemotherapy might be the key strategy.

Conflict of interest

Authors declare no conflict of interest.

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