

Spindle-cell carcinoma of the prostate

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ABSTRACT

Sarcoma of the prostate and sarcomatoid carcinoma of the prostate are rare conditions, both characterized by a poor prognosis. Sarcomatoid carcinoma of the prostate typically arises from the evolution of an underlying adenocarcinoma, occasionally featuring heterologous elements, bulky disease being possible but rare. In contrast, sarcoma of the prostate derives from non-epithelial mesenchymal components of the prostatic stroma, shows rapid growth, and frequently presents as massive pelvic tumors obstructing the urinary tract at the time of diagnosis. We report the case of a 55-year-old patient with a two-month history of symptoms of urinary obstruction. The patient presented with an extremely enlarged heterogeneous prostate, although his prostate-specific antigen level was low. The lack of a history of prostatic neoplasia led us to suspect sarcoma, and a transrectal prostate biopsy was carried out. An immunohistochemical study of the biopsy specimen did not confirm the clinical suspicion. However, in view of the clinical features, we believe that sarcoma of the prostate was the most likely diagnosis. The patient received neoadjuvant chemotherapy followed by radiation therapy. At this writing, surgical resection had yet to be scheduled.

Keywords: Prostate; Sarcoma; Carcinoma.

CASE REPORT

We report a case of a 55-year-old male patient who sought treatment in the Surgery Department Hospital. His primary complaint was acute urinary retention. He had a two-month history of symptoms of urinary obstruction. Physical examination revealed hard, lobulated enlargement of the prostate. Computed tomography (CT) scans of the abdomen and pelvis (Figures 1 and 2) showed an extremely enlarged heterogeneous prostate (estimated

volume, 300 cc) without evidence of adjacent tissue invasion. At diagnosis, his serum prostate-specific antigen (PSA) level was 0.7 ng.mL⁻¹ (reference range, 0-4 ng.mL⁻¹). Despite urinary catheterization, the patient developed renal failure. Another CT scan performed on post-admission day 10 showed rapid tumor growth, the volume of the prostate having increased to 700 cc.

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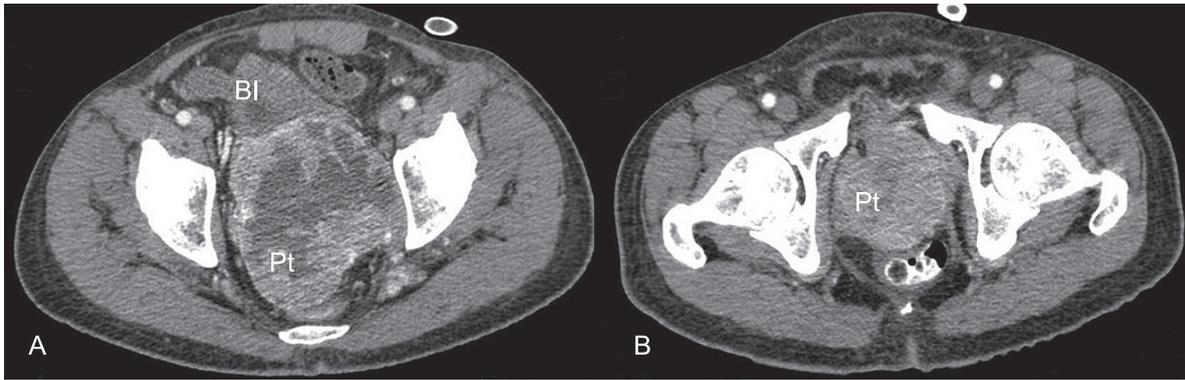


Figure 1 – Axial computed tomography of the pelvis showing a massive tumor, with well-defined borders, in the topography of the prostate. In **A**, note the compression of the rectum and the bladder by the tumor. Pt: prostate; Bl: bladder.



Figure 2 – Multidetector computed tomography of the abdomen and pelvis. Reformatted sagittal image showing a massive tumor occupying virtually all of the pelvic space. Note the heterogeneous distribution of the contrast medium.

The patient was submitted to transrectal prostate biopsy. Examination of the biopsy specimen revealed undifferentiated malignant neoplasia. The results of an immunohistochemical panel (Table 1) were consistent with malignant neoplasia, the pleomorphic and spindle cell characteristics of which were suggestive of high-grade sarcoma or sarcomatoid carcinoma.

Considering both diagnostic possibilities, the poor prognosis of both conditions, and the lack of any evidence-based treatment protocols, neoadjuvant chemotherapy and radiation therapy were initiated, with the objective of preparing the patient for subsequent surgical resection.

DISCUSSION

In the case reported here, the patient presented symptoms of urinary obstruction, an extremely enlarged prostate, and a low serum PSA level. In such cases, it is not uncommon for the patient to be misdiagnosed with prostatic hyperplasia. Despite the rarity of the condition, it is always advisable to include adenocarcinoma in the differential diagnosis of benign prostatic hyperplasia.

As in the case reported here, prostate biopsy specimens do not easily permit the differentiation between stromal tumors with spindle-cell morphology and poorly differentiated adenocarcinomas with a sarcomatoid component.¹ A lack of awareness of this differential often delays the diagnosis, thereby compromising the treatment success and consequently worsening the prognosis.²⁻⁵

In the last two decades, numerous cases of rare carcinoma variants and stromal prostate cancer have been reported.^{2,3} We conducted a PubMed search using the search terms “prostate” and “sarcoma” and limited to studies published in English within the last 20 years and involving adults. We found twenty-five publications involving <3 patients,⁶⁻³¹ two involving 3-10 patients,^{2,4} and four involving >10 patients.^{1,3,32-34} The studies involving ≥5 patients or more were considered representative and are summarized in Table 2. A second search, with the same limiters, was conducted using the search terms “prostate” and “sarcomatoid carcinoma”. Twenty-seven papers were retrieved, only three of which involved ≥5 patients.^{10,11,35}

Sarcoma of the prostate in adults is a rare disease that derives from non-epithelial mesenchymal components of the prostatic stroma.

Table 1 – Immunohistochemical panel of the prostate biopsy specimen

Antibody	Clone	Interpretation
SMA	1A4	Positive
Vimentine		Positive
HMB45	HMB-45	Negative
AE1-AE3	AE1-AE3	Negative
Desmine	D33	Negative
S-100	Polyclonal	Negative
34 beta E12	34 beta E12	Negative
EMA	E29	Positive
Calponine	Calp1	Negative
CD34	QBEnd-10	Negative
Ki-67	MIB01	Positive in 25% of cells
PSA	Calp1	Negative

SMA = smooth muscle actin, EMA = epithelial membrane antigen, PSA = prostatic specific antigen.

Sarcomas account for <5% of all genitourinary tumors and for only 0.01-0.02% of all prostate tumors.^{2,4}

Sarcomas can be classified by histological subtype, cell differentiation, and tumor size.³ In cases of sarcoma of the prostate, the most common histological subtype is rhabdomyosarcoma followed by leiomyosarcoma, the latter being the most common subtype in adults.^{34,36}

Sarcoma of the prostate grows rapidly, presenting as extensive pelvic tumors, leading to urinary tract obstruction, and typically has a poor prognosis.²⁻⁵ In the case reported here, the clinical presentation consisted of symptoms of urinary obstruction and an initial CT scan of the topography of the prostate showed a massive heterogeneous mass that grew rapidly, despite the fact that the patient had a normal serum PSA level.

In the largest known study of sarcoma of the prostate, involving 21 patients, Sexton et al.² found that 16 (76%) had obstructive symptoms, 10 (48%) had pelvic or perineal pain, and 7 (33%) had irritative urinary symptoms. They also found that 5 (24%) had a history of urinary retention.² In patients with sarcoma of the prostate, the serum PSA level is almost always normal, because of the non-epithelial origin of the sarcoma.^{2,5} At diagnosis, the majority of such patients have symptoms of urinary obstruction, which, together with the normal PSA level, often result in a misdiagnosis of prostatic hyperplasia,

which can lead to transurethral resection of the prostate, thus delaying the diagnosis of sarcoma.^{5,11}

The largest series on sarcoma of the prostate retrieves data from 21 patients retrospectively reviewed along 3 decades. In the Sexton et al. study, the one-, three-, and five-year survival rates were 81%, 43%, and 38%, respectively.² Long-term survival was mainly related to tumor-free surgical margins and the absence of metastatic disease at diagnosis.² Neither tumor size nor grade (cell differentiation) have been shown to affect the prognosis, and there are conflicting data regarding the impact that the histological subtype has on the outcome.^{2,3} However, delayed diagnosis and advanced stage at the time of diagnosis have been shown to worsen the prognosis.^{4,37}

Although there is as yet no consensus regarding the best treatment for sarcoma of the prostate, there is increasing evidence that a combined multimodal approach increases survival.² Radical cystoprostatectomy is the recommended surgical procedure. Most studies suggest that the success rates are higher for the surgical approach than for other types of treatment used in isolation.^{2,37} Complete resection with tumor-free margins provides the best prognosis—five-year survival of 67%, compared with 0% when the surgical margins are invaded by tumor.¹ These findings are similar to those obtained by Dotan et al.,³² who studied cases of sarcoma of the genitourinary tract. The authors demonstrated a disease-specific five-year survival rate of 65% when complete resection was performed, compared with 21% for partial resection.³² Despite the lack of published evidence regarding adjuvant and neoadjuvant therapy, as well as that of prospective trials evaluating the impact of those therapies, it seems logical and understandable that a multimodal approach would improve outcomes.³²

Sarcomatoid carcinoma of the prostate is even rarer than is sarcoma of the prostate and combines high-grade epithelial and sarcomatoid histological components. Although controversial, the epithelial and sarcomatoid components are currently thought to originate from a single cell.³⁸ It is possible that sarcomatoid carcinoma represents the evolution of an underlying adenocarcinoma into a lesion with associated sarcomatoid features and, in some cases, heterologous elements, resembling osteosarcoma, chondrosarcoma, and rhabdomyosarcoma³⁶. Fewer than 100 cases have been reported, and there have been only three studies involving more than 10 patients.^{35,36,39} The

Table 2 – Data from the last 20 years on sarcoma of the prostate: studies involving ≥5 patients

Year, author	Histology	N	Mean age, years	Surgery	RT	ChT	5-year survival	Follow up
1992, Russo et al. ³⁴	Total	10		6	5*	1+ 5*	NA	NA
	Rhabdomyosarcoma	5		5*	5*	5*	NA	NA
	Leiomyosarcoma	5		1	NA	NA	NA	NA
1995, Cheville et al. ³³	Leiomyosarcoma	23	61	Varied: usually multi-modal	NA	NA	17%	30% died from the tumor in 3-72 months
2000, Sexton et al. ²	Total	21	49	8	1	12	38%	8 patients survived to 81.5 months
	Leiomyosarcoma	12		NA	NA	NA	16%	75% died from the disease. One lost to follow-up
	Rhabdomyosarcoma	4		NA	NA	NA	75%	No patients died, one lost to follow-up
	Malignant fibrous histiocytoma	1		NA	NA	NA	0%	NA
	Unclassified sarcoma	4		NA	NA	NA	100%	NA
2006, Dotan et al. ³²	Total	21	36	NA	NA	NA	29%	NA
	Leiomyosarcoma	8	NA	NA	NA	NA	NA	NA
	Rhabdomyosarcoma	9	NA	NA	NA	NA	NA	NA
	Other	4	NA	NA	NA	NA	NA	NA
2008, Ren et al. ⁵	Total	7	45	6	1 [†]	1 [†]	NA	NA
	Leiomyosarcoma	5	56	NA	NA	NA		NA
	Rhabdomyosarcoma	2	21	NA	NA	NA	NA	NA
2009, Janet et al. ³	Total	5	NA	NA	NA	NA	NA	NA
	Rhabdomyosarcoma	2	19	0	1	2	50%	18.5 months
	Leiomyosarcoma	1	35	0	1	0	100%	6 months
	High grade	2	49	2	1	1	100%	15.5 months

RT: radiation therapy; ChT: chemotherapy; NA: not available. *Multimodal therapy (surgery + ChT + RT); [†]ChT + RT.

largest of those involved 42 patients.³⁶ In that study, there was a history of prostate adenocarcinoma in 66% of the patients for whom clinical data were available and many patients were diagnosed with sarcomatoid carcinoma many years after having been diagnosed with acinar adenocarcinoma. Half of the patients showed a high Gleason score at diagnosis.³⁶ Although some reports have raised the possibility that prior radiation or hormone therapy influences the development of sarcomatoid carcinoma, there is no consistent evidence of a correlation between treatment modality and disease progression.³⁶ In fact, no clinical or pathological data have proven useful in stratifying cases of sarcomatoid carcinoma by prognosis.^{1,36}

Sarcomatoid carcinoma of the prostate is an aggressive tumor with a poor prognosis. Similar to those of sarcoma of the prostate, the clinical manifestations of sarcomatoid carcinoma include filling and voiding defects.³⁸ Progressive tumor enlargement can lead to bladder outlet obstruction and often requires multiple resections of the prostate in order to relieve the symptoms.¹ For sarcomatoid carcinoma, there is no serum tumor marker, and patients with the condition present with PSA levels that are lower than would be expected, given the considerable size of the tumor. The low PSA levels might be due to the mesenchymal component.³⁸ On palpation, the prostate is typically enlarged, nodular, and hard. Transrectal needle biopsy is usually

diagnostic, and the differential diagnosis should include other conditions that combine malignant spindle-cell elements with epithelial components. In some cases, only sarcomatoid elements are seen. In such cases, the differential diagnosis should include pure sarcoma and pseudosarcoma.³⁸ It should also be borne in mind that it is difficult to distinguish poorly differentiated adenocarcinoma with a sarcomatoid component from a primary mesenchymal tumor or benign prostatic hypertrophy.³⁸

Regardless of the prostate tumor histology, CT and magnetic resonance imaging (MRI) are useful for showing the local extent of the disease and can inform the surgical planning.^{5,37} One recent study showed that sarcoma typically presents as a large, hypervascularized cystic tumor with heterogeneous soft-tissue enhancement in radiological studies (MRI and CT). The main MRI feature is a marked increase in the choline:citrate ratio, to a level higher than that observed in normal prostate tissue.⁵

The rarity of both types of prostate tumors discussed here might justify the difficulty in obtaining larger patient samples. Consequently, reliable data regarding treatment options and prognosis are scarce.^{2,4,36} The histological heterogeneity of and lack of a standardized staging system for such tumors make it difficult to draw comparisons across studies.^{2,4,32,37} Apparently, outcomes are worse for sarcomatoid carcinoma than for sarcoma. Although surgical resection is an option for localized tumors, only a few cases are operable at the time of presentation. After a diagnosis of sarcomatoid carcinoma of the prostate, the risk of death during the first year is 20%.^{1,36}

Although the results of the immunohistochemical study of the case reported here did not allow us to differentiate between sarcomatoid carcinoma and high-grade sarcoma, we considered the latter diagnosis more suitable because of the clinical features (rapid growth of prostate, sudden onset of obstructive symptoms and very low PSA levels) and the lack of a history of prostate disease.

In the Surgery Department of the University of São Paulo University Hospital, 2,322 procedures involving the prostate, including biopsies and resections, were performed between 1990 and 2009. The present case was the only one identified as sarcoma of the prostate.

Sarcoma of the prostate is a major differential diagnosis in patients presenting with rapid prostate growth or extremely large prostate volume, accompanied by normal PSA values. A high level of suspicion is needed in order to avoid delaying the diagnosis and treatment.

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