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\textsuperscript{-1} (reference range, 0-4 ng.mL\textsuperscript{-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.
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. A lack of awareness of this differential often delays the diagnosis, thereby compromising the treatment success and consequently worsening the prognosis.

In the last two decades, numerous cases of rare carcinoma variants and stromal prostate cancer have been reported. 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, two involving 3-10 patients, and four involving >10 patients. 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.

Sarcoma of the prostate in adults is a rare disease that derives from non-epithelial mesenchymal components of the prostatic stroma.
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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.36 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

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.

| 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.

Table 1 – Immunohistochemical panel of the prostate biopsy specimen
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. Progressive tumor enlargement can lead to bladder outlet obstruction and often requires multiple resections of the prostate in order to relieve the symptoms. In that study, 25% of patients died from the disease, one lost to follow-up, and one lost to follow-up. 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. In fact, no clinical or pathological data have proven useful in stratifying cases of sarcomatoid carcinoma by prognosis.1,36

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%             | NA                            |
|               | Rhabdomyosarcoma           | 4  |                | NA      | NA  | NA   | 75%             | NA                            |
|               | 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                            |
|               | Rhabdomyosarcoma           | 9  |                | NA      | NA  | NA   | NA              | NA                            |
|               | Other                      | 4  |                | 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              | 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.
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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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