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WORD COUNT	2723	TIME SUBMITTED	13-FEB-2023 04:02PM
		PAPER ID	96548088

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Name of Journal: *World Journal of Clinical Cases*

Manuscript NO: 81517

Manuscript Type: CASE REPORT

Based literature review of primary seminoma of the prostate : a rare and easily misdiagnosed disease: A case report

Diagnosis and treatment of prostate seminoma

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Abstract

BACKGROUND

Primary seminoma of the prostate (PSP) is a rare extragonadal germ cell tumour type that is easily misdiagnosed, owing to lack of specific clinical features. It is therefore necessary for clinicians to work toward improving the accuracy of PSP diagnosis.

CASE SUMMARY

A 59-year-old male patient presenting with acute urinary retention was admitted to hospital. A misdiagnosis of benign prostatic hyperplasia led to an improper prostatectomy. Histopathology revealed PSP invading the bladder neck and bilateral seminal vesicle. Further radiotherapy treatment for the local lesion was performed, and the patient went on to have a disease-free survival time of 96 mo. This case was analysed alongside 13 other cases of PSP pulled from a literature review. Only four of the cases (28.6%) were initially confirmed by prostate biopsy. In these cases, imaging examinations showed enlarged prostates (range 6-11 cm) involving the bladder neck (13/14). Of the 14 total cases, 11 (78.6%) presented typical pure seminoma cell features, staining strongly positive for PLAP, CD117, and OCT4. The median age at diagnosis was 51 (range 27-59) years, and patients had median progression-free survival times of 48 (range 6-156) months when treated by cisplatin-based chemotherapy combined with surgery or radiotherapy. The remaining three were cases of mixed embryonal tumours with focal seminoma, which had clinical features similar to those of pure PSP, except they also had elevated serum AFP, β-hCG, and LDH.

CONCLUSION

PSP should be considered in patients younger than 60 years with enlarged prostates invading the bladder neck. Further prostate biopsies may aid in proper PSP diagnosis. Cisplatin-based chemotherapy is still the main therapy for the primary treatment of PSP.

Key Words: Prostatic neoplasms, Seminoma, Germ Cell and Embryonic Neoplasms, Diagnosis, Case report

Cao ZL, Lian BJ, Chen WY, Fang XD, Jin HY, Zhang K, Qi XP. A case report based literature review of primary seminoma of the prostate : a rare and easily misdiagnosed disease. *World J Clin Cases* 2023; In press

Core Tip: Primary seminoma of the prostate (PSP) is a rare extragonadal germ cell tumour type that is easily misdiagnosed, owing to lack of specific clinical features. To the best of our knowledge, there have been only 13 cases of PSP reported in the literature, and lack of systemic research on the condition. Through this case and literature review we found that PSP should be considered in patients younger than 60 years with enlarged prostates invading the bladder neck. This symptom occurs in 92.9% of PSP patients, and has high sensitivity but low specificity. However, additional prostate biopsies may aid diagnosis, and histopathological studies are the most effective diagnostic technique. The prognoses of PSP patients are often good. While cisplatin-based chemotherapy seems to be the first-line treatment, surgery or radiotherapy may also be important options, depending on each patient's response to chemotherapy and the location of the residual tumour.

INTRODUCTION

Germ cell tumours (GCTs) are growths of cells that form from reproductive cells. Most GCTs occur in the testicles or the ovaries; however some GCTs, named extragonadal germ cell tumours (EGCTs), occur in other areas of the body through mechanisms that remain unclear[1]. EGCTs are rare, and most of them occur in the midline of the body, such as mediastinal tumours, thymus tumours, retroperitoneal tumours, and pineal tumours[1]. Seminoma is the most common of the GCTs, and one of the rare malignant tumours that can be cured by chemotherapy[2]. Primary seminoma of the prostate (PSP) without any primary testicular lesions is extremely rare. To our knowledge, only 13

cases have been previously reported[3-15]. The clinical symptoms of EGCTs are non-specific and vary according to tumour location. In the prostate, EGCTs may cause urinary symptoms. The clinical manifestations of this may include progressive dysuria, haematuria, and an enlarged prostate invading the bladder[4-12]. The diagnosis of PSP is difficult based on these non-specific clinical features alone, and the standard of treatment remains controversial[3-12]. We report the case of a patient with primary seminoma arising from the prostate. We also systematically reviewed the previous literature on PSP and summarized potential optimized diagnostic and clinical management options.

CASE PRESENTATION

Chief complaints

A 59-year-old man presenting with acute urinary retention was admitted to a local hospital in August 2014.

History of present illness

He had been diagnosed with benign prostatic hyperplasia (BPH) for the preceding three years, with a chief symptom of progressive obstructive voiding.

History of past illness

The patient's past medical history was unremarkable.

Personal and family history

The patient denied any family history of related conditions.

Physical examination

Physical examination showed the patient's prostate was enlarged to more than twice the normal size, and was slightly hard without any palpable nodules on a digital rectal examination.

Laboratory examinations

Microscopic haematuria was evident, but the patient's serum prostate specific antigen (PSA) level was within normal limits (1.412 ng/mL).

Imaging examinations

Ultrasound and computed tomography (CT) images revealed an enlarged prostate (7.0 × 6.5 × 5.5 cm) involving the bladder neck (Figure 1A).

Initial diagnosis and treatment

Due to a progression of his urinary symptoms despite medical treatment and lack of necessary equipment for transurethral resection of the prostate at the local hospital, the patient was initially submitted to traditional suprapubic prostatectomy. During the operation, it was confirmed that the lesion was more than just BPH, with a neoplasm that involved the prostate capsule, seminal vesicles, and bladder neck as well. Subsequently, the patient underwent prostatectomy, excision of the seminal vesicles, and rectal surgical repair (due to intraoperative rectal injury).

MULTIDISCIPLINARY EXPERT CONSULTATION

Histopathology revealed seminoma of the prostate, invading the bladder neck and bilateral seminal vesicles with a positive margin, but no involvement of the rectal wall. Postoperatively, careful examination of the scrotum, mediastinum, and retroperitoneum by ultrasound, and CT/magnetic resonance imaging (MRI) scanning revealed no neoplastic lesion. Serum germ cell tumour markers including alpha-fetoproteins (AFP), beta-human chorionic gonadotropin (β-hCG), and lactose dehydrogenase (LDH) had no abnormality.

All prostatectomy specimens were fixed in 10% neutral buffered formalin, embedded in paraffin, and routinely processed. After referral to a tertiary hospital, histology sections were cut at 4 μm intervals and stained with haematoxylin and eosin (H & E).

Immunohistochemical stains were prepared using the MaxVision™ method (MaxVision TM HRP-Polymer anti-Mouse IHC Kit, Maixin Biotech. Co. Ltd, Fuzhou, China). Immunostains were performed for the following antibodies: AFP (polyclonal, Abnova, Taipei, Taiwan), β-hCG (clone ZSH17), pan Cytokeratin (clone AE1/AE3), high molecular weight Cytokeratin (clone 34βE12), CD45RB/Leukocyte common antigen (LCA) (clone PD7/26+2B11), Vimentin (clone V9), S100 protein (clone 4c4.9), epithelial membrane antigen (EMA) (clone E29), Bcl-2 (clone 8C8), PSA (clone ER-PR8), prostatic serum acid phosphatase (PSAP) (clone PASE/4LJ), placental alkaline phosphatase (PLAP) (clone 8A9), CD117, c-kit (clone YR145) (β-hCG ~ CD117, c-kit, all provided by Maixin Biotech. Co. Ltd., Fuzhou, China), and periodic acid-Schiff stain (ab-150680, Abcam, Cambridge, UK). Microscopically, the prostatectomy specimen revealed a poorly circumscribed infiltrative tumour with poorly-defined margins invading the prostate capsule, bladder neck, and bilateral seminal vesicles. The neoplastic cells were arranged in ill-defined solid nests, had no glandular structure, abundant clear cytoplasm, distinct cell membranes, and large hyperchromatic and prominent nucleoli. Many lymphocytes and plasma cells infiltrated into the interstitial tissue (Figure 2). Compared to common prostate adenocarcinoma tumours, the atypical nests of the patient's poorly-differentiated tumour cells were more prominent, with various abnormal areas of necrosis. Immunohistochemical studies demonstrated that the tumour cells were diffuse and showed strong expression of PLAP (Figure 3), CD117, and periodic acid-Schiff, but were negative for cytokeratin AE1/AE3, 34βE12, PSA, PSAP, AFP, LCA, Bcl-2, vimentin, S100 protein, and EMA.

In addition, clustered data were also identified from other patients with seminoma involving the prostate through PubMed (http://www.ncbi.nlm.nih.gov/pubmed/) and ISI Web of Knowledge (http://apps.isiknowledge.com/) with a cutoff date of August 2022, using the terms seminoma and prostate (or "extragonadal") (limitations "primary" and "English"). In addition to the current case, another 13 cases of PSP previously reported in the literature are summarized in Table 1 for comparative purposes[3-15]. Of these, only four cases were initially confirmed by prostate biopsy

(28.6%), and 10 cases were initially misdiagnosed (71.4%) as carcinoma/tumour, sarcoma, BPH, or abscess. The common clinical manifestations were dysuria (10/14), haematuria (6/14), frequent urination (3/14) and lumbago (3/14). Imaging examinations showed enlarged prostate (range 6-11 cm) involving the bladder neck (13/14, 92.8%). Of these, 11 (78.6%) presented with pure PSP, with a median age at diagnosis of 51 years (range, 27-59). Immunohistochemical examination showed that the typical seminoma cell components were all strongly positive for PLAP, CD117, OCT4, and had negative expression for epithelial markers. All 11 patients had complete remission. Among the eight who received chemotherapy, three were treated just by chemotherapy, three by chemotherapy combined with surgery, and two with chemotherapy followed by further radiotherapy for the iliac lymph node. Of the remaining three, one received surgery and radiotherapy, one received just radiotherapy, and the third lacked detailed treatment information. The available follow-up for the 11 patients with pure PSP indicated a good prognosis with a median progression free survival of 48 mo (range, 6-156 mo) (Table 1). The remaining three all had mixed endodermal sinus tumours (ESTs) with focal seminoma of the prostate. Their ages at diagnosis were 24, 47, and 47 years, and their chief clinical findings were of severe low urinary tract symptoms (dysuria, haematuria and lumbago) and signs of prostatic enlargement, with elevated serum AFP, β-hCG, and LDH. Cisplatin-based chemotherapy was the main chemotherapy used for treatment. One patient died after eight months of chemotherapy, whereas the other two were still living after 16 and 12 mo, respectively.

FINAL DIAGNOSIS

A diagnosis of PSP was made, which satisfied the diagnostic criteria of the absence of any demonstrable tumour in either testis, and a tumour confined to the prostate and bladder neck, without regional lymph node/distant metastasis involvement.

TREATMENT

Due to the positive margin and an apprehension surrounding chemotherapy, image guided radiation therapy (IGRT) was performed with a total prostate regional dose of 36 Gy over 18 fractions in a regional hospital, two months after the patient's surgical operation.

OUTCOME AND FOLLOW-UP

Complete remission of the patient's dysuria symptom was achieved, but frequency and urgency of urination persisted. In July 2015, the patient was referred to our hospital (a tertiary hospital). CT/MRI scanning showed no obvious mass at the surgical site (Figure 1B), and no evidence of para-aortic lymphadenopathy or distant metastasis. Cystoscopy showed a slightly coarse urothelium, especially at the posterior bladder neck and trigone. Histopathology by cystoscopy and biopsy revealed the bladder neck had inflammatory reactants, but there was no evidence of tumour recurrence. The patient has been followed up with every 6 to 12 mo since that time, and has had PSP disease-free survival for 96 mo so far, at the time of writing this report.

DISCUSSION

EGCTs are very rare but well-known neoplasms, arising principally from the mediastinum, retroperitoneum, thymus or pineal gland, of which seminoma accounts for more than 60%[1]. Based on current study, prostatic seminoma without testicular involvement presented a total 14 cases, including 13 reported previously, of which 11 cases had primary pure seminoma[3-12] and three cases had malignant embryonal tumour mixed seminoma[13-15].

All PSPs in the patients had no specific symptoms, with progressive difficulty in urination being the most common symptom[4-12]. Seminoma grow slowly and manifest concealed, slow, progressive symptoms, so most tumours were bulky by the time they were discovered, in late presentation. An enlarged prostate (range: 6-11 cm) that is tender/slightly hard and extends into the bladder neck, may represent a significant clinical characteristic of PSP, especially for patients younger than 60 years[3-15]. Of the 11

cases of pure seminoma, the median age at diagnosis was 51 years (range: 27-59), whereas patients with mediastinal or retroperitoneal primary seminoma were diagnosed at a median age of 33 years (range: 18-65) or 41 years (range: 23-70), respectively[16]. An initial misdiagnosis of PSP occurred in 71.4% of patients. This study highlights the notion that a prostate biopsy is crucial for an accurate diagnosis and proper management strategy for PSP, with positive immunohistochemical staining for PLAP, OCT4 and CD117, or negative biochemical tests such as PSA, AFP, β-hCG, and LDH, similar to the case for testicular seminoma[3-18]. In the case we described a lack of prostate biopsy before prostatectomy in the local hospital was a significant shortcoming. Operative morbidity including rectal injury could have been avoided if a biopsy had been done, considering the patient's CT findings.

Cytogenetically, most EGCTs are similar to their testicular counterparts[18]. The diagnosis of primary extragonadal seminoma requires careful examination of the entire body, particularly in males, and the condition should be considered as being primarily in that aera until the testes have been thoroughly examined and excluded as a possible source[18]. It has been documented that metastases from occult testicular tumours may masquerade as primary EGCTs if the original tumour site has already regressed leaving only a scar, referred to in the literature as a "burned-out" primary[13,16,19-21]. Approximately 1/3 of patients with EGCTs present with metachronous testicular carcinoma *in situ*[22]. As in the current case, examination data often suggest normal testes, which implies that testicular biopsies should not be recommended[23]. Clinical gonadal ultrasound examination and biochemical marker (AFP, β-hCG, LDH) tests should be routinely performed, however, and urinary cytology examination should be considered[14,17,19-24].

Seminomas have been noted to be sensitive to both chemotherapy and radiotherapy. The relapse-free rates in patients with stage 1 testicular seminoma managed with surveillance, radiotherapy, 1× carboplatin, and 2× carboplatin were 91.8%, 97.6%, 95%, and 98.5%, respectively, after a 30-month follow-up, in one report[25]. Based on current data, the optimal treatment for PSP remains controversial due to the limited number of

cases. All 11 of the pure PSP cases we described here, including our case, achieved complete remission after treatment, with a specific progression free survival rate of 100%. Two other cases with iliac lymph node metastases had a specific progression free survival rate of over 10 years. Of these two cases, one received cisplatin-based chemotherapy followed by radiotherapy[5], while the other received nine cycles of cyclophosphamide after total pelvic exenteration[8]. Three other cases received only cisplatin-based chemotherapy and had no relapses[3,4,7]. These results suggest that cisplatin-based chemotherapy as a primary therapy for PSP has a good curative effect, consistent with the efficacy of primary chemotherapy for patients with extragonadal seminoma (an objective remission rate of 92% and a 5-year overall survival rate of 88%)[3-10]. Chemotherapy should therefore be considered as the first-line therapy for these cases. In this case, radiotherapy was performed after prostatectomy, which found no evidence of distant metastasis and a positive tumour margin. This course of therapy resulted in a complete remission lasting over six years. Another case with a suspicious iliac lymph node was also treated with radiotherapy alone, and achieved complete remission for at least a two-year follow-up period[11]. However, it should be noted that recurrence rates approach 50% in patients with mediastinal or bulky retroperitoneal seminoma who are treated only by radiotherapy[16,24]. Because there are few cases reported of patients treated only by radiotherapy, the results suggest that the use of radiotherapy alone in patients with PSP should be considered carefully, and the most appropriate option still seems to be chemotherapy for cases of PSP with extraprostatic invasion[3-11,16,24].

Regarding the issue of Klinefelter syndrome (KS), there are more than 50 cases of KS in patients with EGCTs of the nonseminomatous subtype reported[16,26-30]. In the present study, one-tenth of the cases with prostate pure seminoma also presented with KS. Bokemeyer *et al* reported that all 103 patients who presented with extragonadal seminomas in their study (51 mediastinal and 52 retroperitoneal seminomas), however, had no KS[31-33]. Further studies are needed to clarify the role of KS in this rare tumour type.

CONCLUSION

The clinical presence of an enlarged prostate invading the bladder neck, and laboratory examination of prostate biopsies, may help in the diagnosis of the extremely rare pure PSP form of cancer. Cisplatin-based chemotherapy seems to be the first-line treatment for this condition, and surgery or radiotherapy may also represent important treatment options, depending on each patient's response to chemotherapy and the location of the residual tumour.

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