CASE REPORT

Good response of an aggressive rare variant of signet ring cell carcinoma of prostate with hormonal therapy

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SUMMARY

Primary signet ring cell carcinoma (SRCC) of the prostate is a rare entity, characterised by its aggressive nature and dismal prognosis. We report a case of an advanced SRCC of the prostate presenting as a large pelvic mass with obstructive uropathy and rectal involvement managed by complete androgen blockade. At 24 months follow-up, the patient has no evidence of progression or metastasis. Aggressive management with multimodality approach combining surgery, radiation and hormonal ablation can result in long disease-free survival in some patients, despite the aggressive nature of this disease.

BACKGROUND

Signet cells are characterised by large intracytoplasmic vacuoles that push the nucleus into the periphery, making it crescentic in shape. Signet ring cell carcinoma (SRCC) is commonly seen in organs with mucin-secreting epithelium such as the stomach or colon but can be rarely seen in non-mucin-secreting organs such as the pancreas, breast or prostate.¹ Primary SRCC of the prostate is rare and usually presents as an advanced disease. The treatment recommendations are not well defined and the prognosis is grim. We report a case of primary SRCC presenting with haematuria and a large pelvic mass causing obstructive uropathy. Serum prostatic-specific antigen (sPSA) level was at 1990 ng/mL. The diagnosis was confirmed by transrectal ultrasound-guided biopsy. He was managed with complete androgen blockade. After 24 months of follow-up, sPSA was undetectable with resolution of obstructive uropathy and complete reduction of pelvic mass.

CASE PRESENTATION

A man aged 65 years presented to our institute with a history of bothersome obstructive lower urinary tract symptoms and painless gross haematuria of 2 months duration. On rectal examination, a large mass was felt anterior to the rectum, its upper margin could not be reached and the prostate could not be felt separately. The overlying rectal mucosa was indurated and lumen of the rectum was compromised. Laboratory work-up was remarkable for serum creatinine of 4 mg/dL and sPSA of 1990 ng/mL. Ultrasonography revealed bilateral moderate hydronephrosis. He was planned for bilateral double J stenting, which failed as bilateral ureteric orifices could not be visualised and there was active

bleeding from prostatic fossa. Ultrasound-guided bilateral percutaneous nephrostomies were placed to relieve obstruction and TRUS-guided 12-core prostate biopsy was performed. Histopathological examination revealed SRCC with a Gleason score of 5+5 in all cores with no normal or hyperplastic prostatic glands (figure 1). Immunohistochemistry staining was performed to determine organ of origin and tumour cells showed diffuse and strong positivity for PSA and weak reactivity for alpha-methylacyl-CoA-racemase and were negative for CK 20. Intracytoplasmic vacuoles were negative for mucin, suggesting prostatic adenocarcinoma. A non-contrast CT showed large pelvic mass and a bone scan showed no evidence of bony metastasis (figure 2A). Upper and lower gastrointestinal (GI) endoscopy did not show any evidence of primary gastrointestinal tumour and his CA 19-9 and carcinoembryonic antigen (CEA) levels were within normal limits.

INVESTIGATIONS

Serum PSA was 1990 ng/mL. Renal function: serum creatinine was 4 mg/dL.

TRUS-guided biopsy: signet ring cell adenocarcinoma of the prostate.

Bone scan: no evidence of metastases.

Upper and lower GI endoscopy: no evidence of primary gastrointestinal tumour.

Serum CEA: normal.

DIFFERENTIAL DIAGNOSIS

- ▶ Primary signet ring cell adenocarcinoma of the prostate
- ▶ Metastatic SRCC of the prostate from the gastrointestinal tract

TREATMENT

He underwent surgical castration and oral antiandrogen therapy was started to achieve complete androgen blockade.

OUTCOME AND FOLLOW-UP

After 6 months of therapy, sPSA came down to 19 ng/mL, serum creatinine normalised and nephrostogram and renal dynamic scans on both sides showed non-obstructive drainage. Thus, the nephrostomies were removed. At 1 year, sPSA further reduced to 1.87 ng/mL and imaging revealed a 30% reduction in pelvic mass. At 24-month follow-up, his sPSA was 1.2 with complete resolution of pelvic mass on MRI (figure 2D). He is

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Figure 1 Low-power microphotograph shows a tumour arranged in sheets morphologically similar to signet cell adenocarcinoma (A, $\times 200$, H&E). High-power microphotograph shows the tumour cells with prominent cytoplasmic vacuoles pushing the nucleus aside (arrow) (B, $\times 400$, H&E). The tumour cells show strong and diffuse cytoplasmic immunopositivity for prostatic-specific antigen (C, $\times 400$) and weak and focal cytoplasmic immunopositivity for alpha-methylacyl-CoA-racemase (D, $\times 400$) while immunonegative for CK7 (E, $\times 400$) and CK20 (F, $\times 400$). The cytoplasmic vacuoles are negative for mucin (G, $\times 400$, Alcian blue periodic acid-Schiff).

Figure 2 CT and MRI. (A) Bilateral hydronephrosis. (B) Frozen pelvis. (C) Significant resolution of pelvic mass after 3 months. (D) Complete resolution of pelvic mass after 1 year.

currently doing well with tolerable lower urinary tract symptoms on combined antiandrogen and α blocker therapy.

DISCUSSION

Primary SRCC of the prostate is a rare disease with only about 60 cases published in the English literature. The mean age at diagnosis is 68 years, the mean sPSA at diagnosis is 95.3 ng/mL and 75% of cases present with locally advanced or metastatic disease.² Our patient was a man aged 65 years and had locally

advanced disease (T4N0M0). His serum PSA was 1990 ng/mL indicating large burden of disease in the form of large pelvic mass causing obstructive uropathy. Such large mass aptly depicts the characteristic diffusely infiltrating growth pattern of SRCC.

The diagnosis of primary prostatic SRCC depends on demonstration of signet cells that stain positive for PSA and negative for periodic acid-Schiff, alcian blue and mucicarmine along with negative gastrointestinal work-up. All of these criteria were met

in our patient and additionally, CEA and CA 19-9 were negative, suggesting primary prostatic SRCC.

The treatment of choice is not defined due to scarcity of the available literature and various combinations of surgery, radiation and hormone therapy have been used. It is generally considered that SRCC of the prostate responds poorly to hormonal therapy and multimodality approach is usually preferred.² The best outcomes are achieved with surgery and adjuvant therapy.³ These patients have low-stage resectable disease. However, our patient had a large fixed unresectable mass and surgery was not possible. Thus, we opted for complete androgen blockade. Akagashi *et al*⁴ also reported good response with complete androgen blockade in stage IV disease leading to 20 months of recurrence-free survival. Thus, hormonal therapy is effective and should be considered where surgical resection is not possible, with or without addition of local radiation.

SRCC is considered poorly differentiated and aggressive form of adenocarcinoma. The reported mean survival is 29 months with a 5-year survival ranging from 0% to 11.7%. The prognosis of patients with advanced disease is even worse. There are only occasional reports of long-term survival in patients with advanced disease. One such case was reported by Akagashi *et al* where hormonal therapy alone was used and the follow-up was 20 months and another was reported by Lilleby *et al*⁵ where neoadjuvant hormone with radiation was employed and the patient was followed for 12 months. Another recently published series of nine patients by Warner *et al*⁶ have shown varying survival rates ranging from 5 months to 9 years depending on the stage and treatment received. Our patient is doing well and has no evidence of disease progression or metastasis at 24-month follow-up.

Learning points

- In patients with histologically proven signet ring cell carcinoma (SRCC) of the prostate, upper and lower gastrointestinal endoscopy should be performed to rule out any primary malignancy.
- Even though SRCC of the prostate normally has a grim prognosis and normally managed with multimodality approach, hormone therapy can produce a favourable result.
- In SRCC, immunohistochemistry should be done to determine the organ of origin.

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