CASE REPORT

Gynaecomastia: an unusual presenting symptom of bladder cancer

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Accepted 6 June 2015

SUMMARY

A 74-year-old man presented to the outpatient clinic with painful gynaecomastia. A detailed physical examination to sort out possible causes of the gynaecomastia, including intracranial tumour, liver cirrhosis, hyperthyroidism, and adrenal and testicular tumour, was negative. No offending agent was found in his medication list. A CT scan of the head and ultrasound of the scrotum did not show any mass lesion. His serum β -human chorionic gonadotropin (β -hCG) and oestradiol levels were elevated. A CT scan of the abdomen and pelvis revealed bladder wall thickening with soft tissue mass. A cystoscopic biopsy confirmed transitional cell carcinoma with muscle invasion. The patient was started on chemotherapy but responded poorly. This case report describes the β -hCG and oestradiol-secreting transitional cell carcinoma of the bladder presenting as gynaecomastia in an older man.

BACKGROUND

Gynaecomastia is a glandular proliferation of breast tissue. It occurs due to hormonal imbalance of androgen and oestrogen in males. Primary or secondary hypogonadism, testicular tumour, hyperthyroidism, liver cirrhosis, chronic kidney disease, drugs and puberty are the common causes of gynaecomastia. Ectopic production of β -human chorionic gonadotropin (β -hCG) and oestradiol by transitional cell carcinoma of the bladder causing gynaecomastia is very rare. Bladder cancer may often be asymptomatic and difficult to diagnose. The most common symptoms are painless haematuria, urinary frequency and urgency, and dysuria. Obstructive symptoms are usually because of late presentation with advanced disease. The extent of invasion of the tumour is the most important factor for progression and overall survival. The choice of treatment is also dependent on this particular factor.

CASE PRESENTATION

A 74-year-old man presented to the outpatient clinic with right nipple pain and mild enlargement of the breasts. His symptoms started nearly 25 days prior to presentation. He was previously diagnosed with hypertension, coronary artery disease and hyperlipidaemia. He did not have headache, vision change, testicular swelling or pain, weight loss, or other symptoms during that time. He was a chronic smoker for the past 42 years. On physical examination, there was mild enlargement of both breasts with palpable disk-like soft tissue underneath both nipples. They were slightly tender to touch. There was no nipple

discharge or overlying skin change. The abdomen was soft and non-tender without any palpable mass. Both the testicles and the scrotal sac appeared normal. A careful review of the patient's medication list was performed for possible adverse reaction to medication; it did not reveal any notable findings. His home medications were metoprolol succinate, amlodipine, aspirin and atorvastatin. An ultrasound of the breast was performed, which reported slightly dense fatty tissue. Several blood tests conducted at the same time revealed a β -hCG level of 95 mIU/mL (normal reference range: <5 mIU/mL) and oestradiol level of 90.4 pg/mL (normal reference range: 10–50 pg/mL). The serum prolactin, serum luteinising hormone (LH), total and free testosterone, thyroid stimulating hormone and free thyroxine (T_4) levels were normal. A CT scan of the head did not show any intracranial lesion. A testicular ultrasound did not reveal any testicular mass. Nearly 6 weeks after his clinic visit, the patient presented to the emergency department of the hospital with dark urine, and ill-defined lower abdominal and back pain. A urine analysis revealed microscopic haematuria. A CT scan of the abdomen and pelvis revealed marked thickening and irregularity of the bladder wall, with soft tissue mass adjacent to the anterior and posterior wall of the bladder (figures 1 and 2), consistent with bladder neoplasm. There was also bilateral hydronephrosis and hydroureter, more prominent on the left. A CT scan of the chest did not show any suspicious lesion suggestive of metastasis or mediastinal germ cell tumour. There was no hepatic lesion either. A transurethral resection of the bladder tumour (TURBT) was performed. A stent was placed on both the ureters (figure 1). The histopathological examination showed high-grade transitional cell carcinoma (figure 3) with muscularis propria, lymphovascular

Figure 1 CT scan of the abdomen and pelvis showing bladder wall thickening (yellow arrow) and bilateral hydroureter with stents placement (green arrow).

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To cite: Ahmed M, Kanji A, Begum T. *BMJ Case Rep* Published online: [please include Day Month Year] doi:10.1136/bcr-2015-210649

Figure 2 Scan of the abdomen and pelvis showing bladder wall thickening (yellow arrow).

and perineural invasion. Immunohistochemistry was strongly positive for cytokeratin 20 and p53, but weakly positive for β -hCG. A careful review of the histopathological slide did not reveal any trophoblastic or choriocarcinomatous differentiation of urothelial carcinoma. The patient was referred to an oncologist for further management.

TREATMENT

After initial evaluation, the patient was started on combination chemotherapy with cisplatin and gemcitabine. He responded poorly, and returned to the hospital within 3 months with acute renal failure and bilateral hydronephrosis. The previously placed stents were removed and new stents placed to relieve ureteric obstruction. His general health continued to decline. He adopted hospice and went back home with hospice care. He expired nearly 11 weeks after being discharged from the hospital.

DISCUSSION

Bladder cancer is the sixth most common cancer, representing 4.5% of all new cancer cases in the USA. It was estimated that there were 74 690 new cases of bladder cancer and nearly 15 580 people died of this disease in 2014.¹ Cigarette smoking, and various environmental and occupational exposures, are the major risk factors for bladder cancer. Toxic substances get concentrated in the urine and pose the risk of malignant transformation of the urothelial lining exposed to their carcinogenic effects. In the USA, cigarette smoking is associated with

50–60% of bladder cancers diagnosed in men and 30% diagnosed in women.²

Oestrogen action is mediated by estrogen receptor (ER), a protein that binds to DNA and alters gene expression. Oestrogen passively enters the cell where it binds to and activates the ER. Oestrogen is present in both men and women. It is usually higher in women and promotes secondary sexual characteristics. In men, it regulates certain functions of the reproductive system important to the maturation of sperm.³ Bladder cancer typically does not present with a hyperoestrogen state. In men, hyperoestrogenaemia related to cancer is usually due to a paraneoplastic effect of testicular cancers of choriocarcinoma, teratomas and embryonal carcinomas. Nearly 3% of patients who were referred to a breast surgeon for evaluation of gynaecomastia were diagnosed with a testicular tumour.⁴ Testicular germ cell tumours are known to have high levels of hCG, which is a LH analogue. Our patient had a very unusual presentation of a hyperoestrogen state. Levels of oestradiol and β -hCG were both elevated. Oestradiol and β -hCG both cause gynaecomastia in men.⁴ The presence of high levels of β -hCG and oestradiol in bladder cancer has rarely been reported in the past. Those bladder tumours that were positively stained for β -hCG were usually of a higher grade, higher stage and had an inferior outcome. The immunohistological expression of β -hCG would likely predict superficial tumours that would recur and muscle-invasive tumours with inferior outcome.⁵ Total β -hCG and free β -sub unit of hCG are the most suitable assays for the management of bladder carcinoma patients, as the ectopic secretion of chorionic gonadotropin is mainly due to the free β -subunit.⁶ It was suggested that β -hCG exerts autocrine/paracrine stimulation of tumour growth.⁷

Although a previously published review revealed that β -hCG has no role as a tumour marker for transitional cell cancer, and therefore appears unlikely to play a part in the clinical management or treatment of urothelial tumours,⁸ it may act as a good biological marker to differentiate between superficial and deep tumours.⁹

Patients presenting with signs and symptoms suggestive of bladder cancer typically undergo cystoscopy and imaging of the upper urinary tract. In addition, urine cytology should be obtained. If a tumour is detected on cystoscopy, a TURBT is indicated. All visible tumours are resected with sampling of underlying muscularis propria to determine the presence of and/or extent of invasion. The treatment of bladder cancer varies depending on the invasiveness of the disease.

Figure 3 Biopsy of the soft tissue mass from the bladder revealing transitional cell cancer.

Learning points

- ▶ Transitional cell carcinoma of the bladder may secrete β -human chorionic gonadotropin (β -hCG) and oestradiol, causing gynaecomastia in male patients.
- ▶ Although β -hCG does not have much significance as a tumour marker for bladder cancer, its presence may indicate a higher grade tumour with muscle invasion and poor prognosis.

Competing interests None declared.

Patient consent Obtained.

Provenance and peer review Not commissioned; externally peer reviewed.

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