Unusual presentation of more common disease/injury

An unusual cause of gynaecomastia

Sridhar Subbiah,¹ Rama Walia,¹ Santhosh Kumar,² Uma Nahar,³ Anil Bhansali¹¹Department of Endocrinology, PGIMER, Chandigarh, India;²Department of Urology, PGIMER, Chandigarh, India;³Department of Pathology, PGIMER, Chandigarh, India**Correspondence to** Professor Anil Bhansali, anilbhansali_endocrine@rediffmail.com**Summary**

Gynaecomastia in adolescents and young adults is a common endocrine disorder with usually benign aetiology. However, gynaecomastia in middle-aged men is uncommon and warrants intensive search to unravel its aetiology. The authors report a 42-year-old male who presented with gynaecomastia due to feminising adrenocortical carcinoma.

BACKGROUND

Gynaecomastia in middle-aged men warrants appropriate investigation to unravel its aetiology. We describe a case of adrenocortical carcinoma (ACC) presented as gynaecomastia, which is a very rare cause of gynaecomastia.

CASE PRESENTATION

A 42-year-old man was referred to endocrinology outpatient department for investigation of gynaecomastia. He had early satiety and epigastric discomfort of 2 months duration. He had no history suggestive of exogenous use of androgens or oestrogens. On examination, he was centrally obese (waist circumference of 113 cm) with body mass index of 27.4 kg/m² (height of 175 cm and weight of 84 kg). He had plethora, ecchymotic skin lesion, and wide violaceous striae over the abdomen and thigh. He also

had gynaecomastia with diameter of palpable tissue being 10 cm on both sides (figure 1). Testicular volume was 20 ml each and these were soft in consistency. On abdomen examination, a bimanually palpable mass was felt in the right hypochondrium and lumbar region, extending 8 cm from the right costal margin.

INVESTIGATIONS

On investigation, haemoglobin was 14.1 gm/dl, complete blood count, liver and renal function tests were normal. Serum creatinine was 70 µmol/l (N, 44 – 84 µmol/l) while potassium was 4.8 mmol/l (N, 3.5 – 5.0 mmol/l). Fasting blood glucose was 117 mg/dl and post 75 gm glucose load level was 197 mg/dl. Hormonal profile showed serum luteinising hormone ≤ 0.01 (N, 1.7 – 8.6 mIU/ml), follicular stimulating hormone < 0.1 (N, 1.5 – 12.4 mIU/ml), prolactin

Figure 1 Bilateral gynaecomastia.

Figure 2 CT showing a large heterogenous right adrenal mass. Note the filling defect in IVC seen on the right CT images.

Figure 3 Microphotograph showing large tumour cells in sheeting arrangement with necrosis. Inset shows cellular pleomorphism with high mitotic activity.

19.2 (N, 4.0 – 15.2 ng/ml), total testosterone 4.33 (N, 9.9 – 27.8 nmol/l), dehydroepiandrosterone sulfate 273.90 µg/dl (N, 10 – 619 µg/dl) and high oestradiol levels 436.6 pg/ml (N, 7.63 – 42.6 pg/ml). 08:00 and 23:00 h cortisol were 1453 and 1338 nmol/l respectively with adrenocorticotrophic hormone of <1.00 pg/ml. 08:00 h serum cortisol was non-suppressible after overnight, low dose and high dose dexamethasone suppression test (1254, 1213 and 1196 nmol/l respectively). The 24-h urinary metanephrine was 116 µg (N, 0 – 360 µg).

Ultrasound scan showed a large suprarenal mass. To delineate this further, CT abdomen showed a large well-defined heterogenous enhancing mass (measuring 13.7 × 12 × 11.4 cm) in the right suprarenal region with

calcification and necrosis (figure 2). The liver measured 22 cm with focal lesion, suggestive of metastasis. Incidentally thrombus was found in pulmonary artery during CT chest and the patient was subsequently subjected to CT pulmonary angiogram. Otherwise patient had no symptoms of pulmonary thromboembolism in the recent past. CT pulmonary vessels showed hypodense filling defect suggestive of thrombus in the medial basal segment of right upper and lower lobe. Chest x-ray showed normal lung fields and no cardiomegaly. His two-dimensional echocardiogram showed a normal-sized heart with good wall motion (ejection fraction 60%) and contractility. Based on the above investigations patient was considered to have stage IV disease.

TREATMENT

The patient underwent right open adrenalectomy. Intraoperative finding revealed 20 × 13 cm mass with level one tumour thrombus arising from the right adrenal vein extending into the inferior vena cava (IVC). In view of tumour thrombus, segmental thrombectomy was performed along with right adrenalectomy. The histopathological examination of the right adrenal gland showed marked nuclear pleomorphism with hyperchromatic nucleus with high nuclear-cytoplasmic ratio. There was a large area of necrosis with capsular invasion (figure 3). The modified weiss score was 6/7.

OUTCOME AND FOLLOW-UP

The patient was treated with intravenous hydrocortisone in the immediate postoperative period which was subsequently changed to oral hydrocortisone. The postoperative course was uneventful. There was a significant rise in serum testosterone (4.33–7.69 nmol/l) and decrease in oestradiol levels (436.6–38.57 pg/ml) on postoperative day 7. He was discharged after 2 weeks. Subsequently received mitotane, local radiation and EDP (etoposide, doxorubicin and cisplatin) chemotherapy regimen during the follow-up visit.

DISCUSSION

We describe a middle-aged man having ACC who presented with gynaecomastia. Gynaecomastia is a common endocrine problem and usually caused by medications including spironolactone, ketoconazole, verapamil, H₂ blockers (cimetidine), use and abuse of androgen. A forthcoming drug history easily establishes the diagnosis. However, in the absence of drug exposure, an intensive search should be made to define the aetiology of gynaecomastia, and this becomes more relevant particularly in middle-aged and older men. The other causes in this age group include chronic liver disease, chronic renal failure and uncommon disorders like Leydig cell tumour of the testis and rarely ACC.

ACC in the middle-aged and older subjects are usually non-functional and if functional they present with features of Cushing's syndrome.^{1 2} Very rarely gynaecomastia may be the presenting or accompanying feature of ACC. Prevalence of gynaecomastia in ACC is not known as only anecdotal case reports are described.^{3 4} Gynaecomastia in ACC has been attributed to increase in tumour tissue aromatase activity⁵ resulting in increased oestradiol production. Another possible mechanism is efficient conversion of weaker androgens produced by the adrenal tumour into oestrone by peripheral adipose tissue. In the index case direct production of oestrogen by the tumour tissue appears to predominate as circulating oestradiol levels are

very high with a significant alteration in E₂/T ratio (3:1, normal 1:200). The low levels of gonadotropins and testosterone can be explained by inhibition of hypothalamo-pituitary-testicular axis by circulating levels of cortisol and oestrogen.

The tumour extension into IVC is well described in renal cell carcinoma and very sparingly it has been reported in patients with ACC. Involvement of inferior vena cava is a risk factor for surgical treatment of ACC.⁶ ACC can affect the IVC by either compression or direct invasion or by intraluminal extension in the form of thrombus.⁷ Massive involvement of the IVC is generally considered a limiting factor for resection of ACC.⁸ Since our patient had level one thrombus arising from the right adrenal vein, segmental thrombectomy was performed along with right adrenalectomy. The outcome of ACC depends upon stage of the disease and proliferation index. The 5-year disease-free survival in stage IV disease is 15–20% even with the use of mitotane and or chemotherapy.

Learning points

- ▶ Gynaecomastia in middle-aged and older men, in the absence of drug history requires intensive search for its aetiology.
- ▶ ACC is a rare cause of gynaecomastia.
- ▶ High oestradiol levels in ACC suggest increased oestrogen secretion by the tumour tissue.

Competing interests None.

Patient consent Obtained.

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