Bilateral gynaecomastia as the sole presenting feature of a Y chromosome abnormality complicated by a gonadal tumour in an otherwise phenotypically normal male

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Abstract

We report the case of a 33-year-old male presenting with bilateral gynaecomastia whose karyotype was mosaic with 60% of the cells showing an isochromosome for the short arm of the Y chromosome and 40% showing 45,X complement. Further investigation revealed evidence of a stage one seminoma of the right testis and complete azoospermia. He was treated with bilateral orchidectomy and adjuvant radiotherapy and made an uneventful recovery. The case highlights the importance of cytogenetic investigation and appropriate testicular imaging in patients who present with gynaecomastia.

Introduction

Gynaecomastia is not uncommon in males and palpable breast tissue was reported in 36% of military recruits (Nuttall 1979) and in up to 65% of hospitalised patients (Niewoehner & Nuttall 1984). In most instances gynaecomastia is idiopathic in origin and no serious underlying pathology is found. Karyotyping is not a routine investigation in patients with gynaecomastia with the exception of patients who present with clinical features suggestive of Klinefelter syndrome. We here report a patient who presented with bilateral painless gynaecomastia in whom cytogenetic investigation unveiled a chromosome abnormality associated with high risk of gonadal malignancy with the subsequent diagnosis of a right testicular seminoma.

Case report

A 33-year-old engineer was referred with an 18 month history of bilateral painless gynaecomastia. There was no galactorrhea, his libido was normal and he could sustain normal erections. His frequency of shaving had not altered and there was no change in his voice. He thought that his gynaecomastia had been regressing over the few weeks prior to being seen in the outpatient department. There were no neurological symptoms, he was on no medication and generally he felt very fit and well.

Examination confirmed moderate bilateral gynaecomastia with bilateral firm discoid tissue underneath the nipples. His height was 163 cm and his weight 68.2 kg. The external genitalia appeared normal and the rest of the physical examination was unremarkable. Initial investigations in the referring hospital (Table 1) showed normal gonadotrophins, oestradiol and thyroid function tests, but the progesterone level was raised at 3.2 nmol/l (normal for males <3 nmol/l) and his testosterone was slightly low at 8.6 nmol/l (reference range 8.8-34 nmol/l). An MRI scan of the pituitary gland, undertaken because of biochemical evidence of hypogonadotrophic hypogonadism, was normal. Following referral the only amendment to the above was the finding of a possibly slightly larger and firmer right testis. Our investigations confirmed the above results and in addition 17-OH-progesterone, chorionic gonadotrophin (hCG) and prolactin levels were within normal limits. Cytogenetic investigation was requested in view of the possible testicular abnormality. This revealed a mosaic karyotype with 40% of the lymphocytes showing a chromosome count of 45 with a single X chromosome.
and no Y chromosome and 60% of the cells showing a chromosome count of 46 with one normal X chromosome and an abnormal Y chromosome. The G-banding characteristics of the Y chromosome were consistent with it being a dicentric isochromosome resulting in duplication of the short arm of the Y chromosome and deletion of most of the long arm (Fig. 1). This interpretation was confirmed with fluorescent in situ hybridisation studies with a Y centromere specific probe, which showed two discrete areas of labelling separated by a short segment consisting of long arm material (Fig. 2).

Ultrasound examination of the testes showed a 15 mm hyperechoic lesion typical of a malignant tumour, probably a seminoma, in the right testis. Semen analysis revealed complete azoospermia, and therefore the patient was referred for bilateral orchidectomy in view of the high risk of malignancy in the apparently normal left testis. Histological examination confirmed the diagnosis of a right testicular seminoma and the lack of spermatogenesis in both testes. Both testes showed scattered large atypical germ cells within tubules but no in situ germ cell tumour was seen. He made an uneventful recovery and was referred for prophylactic radiotherapy.

**Discussion**

The aetiology of gynaecomastia is extensive and testicular tumours are an important cause requiring prompt exclusion. Our patient had very subtle clinical findings, if any, pointing to the diagnosis of a testicular tumour and his

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**Table 1** Hormone levels in the patient.

<table>
<thead>
<tr>
<th>Investigation</th>
<th>Referring hospital</th>
<th>Our hospital</th>
<th>Reference range in males</th>
</tr>
</thead>
<tbody>
<tr>
<td>FSH</td>
<td>6.1 U/l</td>
<td>7.0 U/l</td>
<td>0.9-15.0 U/l</td>
</tr>
<tr>
<td>LH</td>
<td>7.0 U/l</td>
<td>6.4 U/l</td>
<td>1.3-12.9 U/l</td>
</tr>
<tr>
<td>Progesterone</td>
<td>3.5 nmol/l</td>
<td>3.2 nmol/l</td>
<td>&lt;3.0 nmol/l</td>
</tr>
<tr>
<td>Testosterone</td>
<td>8.6 nmol/l</td>
<td>10.6 nmol/l</td>
<td>10.0-40.0 nmol/l</td>
</tr>
<tr>
<td>Oestradiol</td>
<td>93 pmol/l</td>
<td>87 pmol/l</td>
<td>&lt;130 nmol/l</td>
</tr>
<tr>
<td>17-OH-progesterone</td>
<td>—</td>
<td>6 nmol/l</td>
<td>&lt;20 nmol/l</td>
</tr>
<tr>
<td>hCG</td>
<td>—</td>
<td>&lt;1 IU/l</td>
<td>0-5 IU/l</td>
</tr>
<tr>
<td>Prolactin</td>
<td>—</td>
<td>154 mU/l</td>
<td>50-560 mU/l</td>
</tr>
</tbody>
</table>

FSH = follicle-stimulating hormone; LH = luteinising hormone.

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**Figure 1** G-banded karyotype of a metaphase from a lymphocyte culture showing the dicentric isochromosome of the short arm of the Y.
gynaecomastia was regressing. The results of the cytogenetic studies prompted us to review the clinical findings and arrange appropriate imaging of the testes. In addition, his abnormal karyotype highlighted the increased risk of malignancy in the 'normal' testis which was subsequently removed.

Isodicentric Y chromosomes are relatively common structural abnormalities of the Y chromosome. Individuals with this genetic abnormality may be classified into four phenotypic groups with increasing degree of virility: infantile females; individuals with ambiguous genitalia; males with hypospadias; and azoospermic males (Daniel 1984). Subjects with a 45,X cell line and a cell line with a structurally abnormal Y chromosome are at increased risk of developing gonadal tumours, which are invariably gonadoblastomas but may be associated with dysgerminoma or occasionally other malignant cell line elements. The prevalence of gonadal tumours in cases with a cell line including a dicentric Y chromosome has been estimated at about 26% (Verp & Simpson 1987) and the development of gynaecomastia in these patients is an indication of malignant change. The clinical prognosis in such cases depends primarily on which malignant cell elements are present. Our review of the literature revealed two cases with similar chromosomal abnormalities presenting with gynaecomastia in addition to one or more other presenting features (Interlandi et al. 1981, Ponzio et al. 1981). To the best of our knowledge our patient is the first reported with an isochromosome of the Y in whom gynaecomastia was the sole presenting feature.

Gynaecomastia is thought to be determined by the net oestrogen/androgen ratio that effectively acts on breast tissue (Glass 1994). It is worth mentioning that our patient's biochemical investigations did not reveal any obvious disturbance in this ratio or raised gonadotrophin or hCG levels. The raised progesterone is probably secondary to oversecretion by tumour cells and may be, at least partially, responsible for the development of gynaecomastia in our patient probably secondary to its known anti-androgenic properties.

In conclusion, this case report discusses a patient with an uncommon chromosomal abnormality presenting with gynaecomastia and highlights the importance of cytogenetic studies in these patients. Unless an obvious cause of gynaecomastia is detectable or pubertal gynaecomastia suspected, male patients presenting with de novo gynaecomastia should undergo ultrasound examination of the testes, as emphasised previously (Conway et al. 1988), and cytogenetic investigation should also be considered.

References