Unusual association of diseases/symptoms

A rare case of male breast ductal carcinoma in-situ associated with prolactinoma

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Summary

A case of ductal carcinoma in-situ (DCIS) associated with prolactinoma in a male patient is described. A 56-year-old gentleman presented with lethargy and loss of libido. His prolactin at presentation was 3680 mU/l and an MRI scan of the head revealed a pituitary tumour suggestive of prolactinoma. Following 18 months of treatment with cabergoline, the prolactin level reduced to 914 mU/l. However, 3 years later he presented with blood stained nipple discharge, the cytology of which was negative for cancer. Ultrasound scan of his right breast revealed a single dilated mammary duct. Microdochectomy was performed. The histology revealed incompletely excised DCIS. There is increasing evidence of prolactinoma associated with breast cancer with or without DCIS in females. A review of the literature reveals only one previous case report of this association in males. This is the first case of pure DCIS preceded by prolactinoma in a male patient.

BACKGROUND

Breast cancer in males is rare. Rarer still is ductal carcinoma in-situ (DCIS) and its aetiology in male patients. To our knowledge, the reported case is the first case of pure DCIS preceded by prolactinoma in a male patient. We believe the publication of the attached case report will add to the body of knowledge concerning this condition and will stimulate those conducting research in this field.

CASE PRESENTATION

A 56-year-old man presented with a 6-month history of brownish discharge from his right nipple that became bloody in the last 2 weeks before presentation. He had no history of breast pathology. However, he was diagnosed with a microprolactinoma 3 years prior to this episode having initially presented with lethargy and loss of libido to another hospital. His prolactin level at diagnosis was

Figure 1 Histology of the resected mastectomy specimen (H&E), magnified view $\times 100$, shows a ductal carcinoma in-situ with no evidence of invasion.

Table 1 Prolactinoma associated with breast cancer in female patients

Paper	Breast cancer					Pituitary tumour				
	Year	Age	Side	Detection	Size (cm)	Axillary metastases	Histology	FHx	Tx	Symptoms
Daniels <i>et al</i> ³	1971	33	L	Mammogram, lump	1.5	4/17	IDC	N	M, DXT	FAS
Buytaert and Viaene ⁴	1981	25	R	Lump	'Pea-sized'	7/22	IDC	N	M, C	FAS
Valette and Agnani ⁵	1984	28	L	Lump	2.5	2/6	ILC	N	BCS, C, DXT	Loss of libido, bone pain, visual disturbance, galactorrhoea, oligomenorrhoea
Theodorakis <i>et al</i> ⁶	1985	31	L	Bloody nipple discharge	2	0	IDC; LCIS ER+ve PR+ve	Y	M	Bilateral galactorrhoea
Strungs <i>et al</i> ⁷	1997	56	R	Mammogram	5	1/18	IDC; DCIS ER+ve	N	M, H	Amenorrhoea
Strungs <i>et al</i> ⁷	1997	34	R	Lump; peau d'orange	1.4	17/22	IDC; DCIS ER+ve	N	M, C, DXT	Primary amenorrhoea
Sato <i>et al</i> ⁸	2007	43	L	Nipple mass; discharge	1.6	5/14	IDC; ER+ve PR+ve	N	M, C, H	Amenorrhoea

Interval = Time between symptoms of hyperprolactinaemia and diagnosis of breast cancer.

B, bromocriptine; BCS, breast conservation surgery; C, chemotherapy; DCIS, ductal carcinoma in situ; DXT, radiotherapy; ER, oestrogen receptor; FAS, Forbes Albright syndrome (amenorrhoea-galactorrhoea); FHx, family history of breast cancer; H, hormonal therapy; IDC, invasive ductal carcinoma; L, left; LCIS, lobular carcinoma in situ; M, mastectomy; N, No; PR, progesterone receptor; PT, pituitary tumour visualised on imaging; R, right; S, pituitary surgery; Tx, treatment; Y, yes.

3680 mU/l (75–375 mU/l). MRI scan revealed only a mild projection of the pituitary on the left aspect of the gland. Following 18 months treatment with cabergoline 500 mg twice weekly, his prolactin level was reduced to 914 mU/l. He had undergone coronary artery angioplasty in 1989 and coronary artery bypass grafting in 2002. His family history included familial hypercholesterolaemia and ischaemic heart disease. He had no family history of breast cancer.

On clinical examination, an ill-defined palpable swelling of approximately 0.5 cm was identified lateral to the right nipple. Ultrasound scan of the breast at the time of presentation revealed a dilated mammary duct at the 9.0 radian. Cytology of the discharge fluid did not reveal any malignant cells.

The case was discussed at the breast multidisciplinary meeting (MDT) and it was advised to proceed with microdochectomy.

The patient underwent right breast microdochectomy and fibro-fatty tissue weighing 1.3 g and measuring 3.5 × 1.5 × 0.5 cm was removed. The histology revealed 35 mm of low-grade DCIS reaching the excision margins. There was no evidence of invasive cancer. The lesion was ER strongly positive.

Following discussion at MDT, completion right mastectomy was performed. The excised specimen which weighed 233 g and measured 13.8 cm, contained two foci of low grade, solid DCIS, completely excised and measuring 1.4 mm (figure 1). The remainder of the breast tissue revealed gynaecomastia with branching ducts and mild usual type hyperplasia. No invasive carcinoma was identified. Six months after surgery he remains well, is currently not on any treatment, and continues to undergo annual review.

DISCUSSION

Previously reported associations of prolactinoma and breast cancer in males consist of four case reports. In all cases, there was evidence of invasive ductal carcinoma. In addition, in two of the described cases there was evidence of early non-invasive disease (tables 1 and 2). To our knowledge, our report is the only evidence of prolactinoma associated with pure DCIS. In the majority of previously described cases, prolactinoma preceded breast cancer, suggesting that prolactin may have played a role in breast tumourigenesis. In two of the cases there was evidence of gynaecomastia. The other two cases were associated with palpable breast lesions.

There is strong evidence linking hyperprolactinaemia to duct ectasia. Human breast cancer cells express prolactin receptors and prolactin has been associated with induction of breast carcinogenesis in animal models.² Hyperprolactinaemia has been correlated with poor prognosis in all stages of breast cancer.¹⁴ Transient increase of plasma prolactin level can result from breast manipulation, anaesthesia or stress. In line with this evidence, following mastectomy, our patient's serum prolactin increased to 1100 mU/l.

As summarised in tables 1 and 2, careful review of the literature revealed a clear association of prolactinoma and invasive breast cancer with or without presence of DCIS in 10 patients (four male and six female). Of the four male patients, three had bilateral disease. In our case, the time

Table 2 Prolactinoma associated with breast cancer in male patients

Paper	Breast cancer				Pituitary tumour									
	Author	Year	Age	Side	Detection	Size (cm)	Axillary metastases	Histology	FHx	Tx	Symptoms	PT	Tx	Interval
	Olsson <i>et al</i> ⁹	1984	48	R +veL	Gynaecomastia (11 years)	L 5 R 5	N N	DCIS; early invasion DCIS; early invasion	Y	M, DXT M, DXT	Bitemporal hemianopia and polyuria	Y	S, DXT	26 36
		1993	68	L	Induration of breast	3	'Almost all'	IDC ER+ve	N	M, C	Nil	Y	B	0
	Volm <i>et al</i> ¹¹	1997	70	R +veL	Lumps and previous bilateral gynaecomastia	L 2.5 R 1.9	0/7 1/15	IDC; ER+ve PR+ve IDC; ER+ve PR+ve	N M, H	M, H M, H	Infertility; incomplete 2 ^o sexual development and galactorrhoea	Y	S, DXT	>30
		2001	45	R +veL	Gynaecomastia and right nipple bloody discharge	L 1 R 1	0 0	DCIS; ER+ve PR+ve IDC; ER+ve PR+ve	? M	M M	Weight gain	Y	B	0 0

Interval = Time between symptoms of hyperprolactinaemia and diagnosis of breast cancer.

B, bromocriptine; BCS, breast conservation surgery; C, chemotherapy; Ca, Cabergoline; DCIS, ductal carcinoma in situ; DXT, radiotherapy; ER, oestrogen receptor; FHx, family history of breast cancer; H, hormonal therapy; IDC, invasive ductal carcinoma; IL, lobular carcinoma in situ; L, left; LCIS, lobular carcinoma in situ; M, mastectomy; N, No; PR, progesterone receptor; PT, pituitary tumour visualised on imaging; R, right; S, pituitary surgery; Tx, treatment; Y, yes; ?, potential presence/absence of a family history.

interval between the diagnosis of prolactinoma and DCIS was relatively short (3 years). However, in the majority of reported cases there was a significant time interval (4–32 years in females and 0–36 years in males) between the diagnosis of prolactinoma and breast cancer. The diagnosis of cancer was, in the majority of cases, made at an invasive stage. Both these facts would suggest that careful, periodic examination and investigation of the breasts in cases of prolactinoma may aid identification of early breast cancer. In the four male cases thus far reported, it is of note that breast cancer associated with prolactinoma was located in the areolar/subareolar region. In our case also, it is of note that the initial finding of DCIS was made within the microdochectomy specimen. The reasons for this are unclear.

In this reported case, prolonged exposure to hyperprolactinaemia resulted in abnormal nipple discharge and duct ectasia. It is therefore conceivable that hyperprolactinaemia may have contributed to the development of DCIS. We therefore advocate careful and periodic examination and investigation of male and female patients with prolactinoma for the presence of breast cancer. In female patients this may be performed with clinical examination, mammography and/or ultrasound examination. In male patients, clinical examination, ultrasound and/or MRI may need to be considered. Yearly clinical assessment and imaging as for groups at high risk of breast cancer¹⁵ may facilitate early diagnosis and treatment of breast cancer in patients with prolactinoma.

Learning points

- The aetiology of male breast cancer is poorly understood.
- There is increasing evidence of breast cancer associated with prolactinoma in male and female patients.
- Regular clinical ± radiological assessment for breast cancer may be warranted in male ± female patients.

Competing interests None.

Patient consent Obtained.

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