Lobular carcinoma-in-situ within a fibroadenoma of the breast

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Summary

We present a case of an in-situ lobular carcinoma within an otherwise benign fibroadenoma in a 45-year-old woman.

Keywords: fibroadenoma; carcinoma-in-situ

Fibroadenoma are one of the most common benign tumours of the breast. We present a case of an in-situ lobular carcinoma within an otherwise benign fibroadenoma.

Case report

A 45-year-old woman presented with a painless mass in her right breast which she had discovered one week earlier. She was pre-menopausal and had no history or any known risk factors for breast cancer. A firm, well-defined, mobile mass, 1.5 × 1 cm in diameter was found in the upper inner quadrant of the right breast. No enlarged axillary or supraclavicular lymph nodes were palpable. Mammography revealed a well-circumscribed density corresponding to the palpable mass. Fine-needle aspiration yielded benign cells. A diagnosis of fibroadenoma was made. Three months later when the mass had grown to 2.5 × 2 cm, the patient requested surgery. Local excision of the mass was therefore done. Histological examination of the mass revealed a fibroadenoma with a focus of lobular carcinoma-in-situ that was completely confined within the fibroadenoma (figures 1 and 2).² After discussing treatment options with the patient, a policy of continued surveillance was decided upon. The patient remains asymptomatic 25 months later.

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Figure 2 At higher magnification, the affected glands are distended and filled by a uniform cell population (Haematoxylin & Eosin × 100)

Discussion

Carcinoma within a breast fibroadenoma is very rare, having a reported incidence of 0.1–0.3%.^{1,2} As in our case, patients with these lesions typically are older than patients with fibroadenoma, having a mean age of 42 years. Although this is similar to the peak age reported for a lobular carcinoma-in-situ, it is considerably older than the 20–25 year average age of patients with fibroadenomas.³

Pre-operative diagnosis of these lesions is difficult because their presenting features are similar to those of benign fibroadenoma. Mammography may reveal an abnormality, but rarely indicates malignancy.³ As in our case, the diagnosis usually is a histological surprise.

Fibroadenomas have been found to contain both in-situ and invasive malignancies.^{1–4} In 66% of the reported cases of carcinomas occurring in a fibroadenoma, the malignancy has been an in-situ lesion; in 34% of cases, the cancer is invasive.³ In 65% of patients with an in-situ lesion in a fibroadenoma, the lesion is lobular carcinoma-in-situ.³ About two-thirds of the carcinomas arising within a fibroadenoma have lobular morphology; the rest are ductal or mixed ductal and lobular.^{2–4}

The biological behaviour of a carcinoma occurring in a fibroadenoma is no different from that of breast carcinoma unrelated to fibroadenoma.^{2,5} Although the treatment of invasive cancer within a fibroadenoma is similar to that of carcinoma of the breast, the treatment of in-situ cancer is less well defined. Thirty-three per cent of patients with lobular carcinoma-in-situ in a fibroadenoma develop an invasive carcinoma, intraductal or lobular,

Figure 1 Lobular carcinoma-in-situ within fibroadenoma (Haematoxylin & Eosin × 40)

in the same or contralateral breast.² This corresponds to the 17–36% incidence of carcinoma developing in patients with lobular carcinoma-in-situ without fibroadenoma.^{6–8} In two large series of patients, the observed and expected ratios of invasive cancer in patients whose lobular carcinomas-in-situ had been treated by excisional biopsy alone were 6.9:1 and 9:1, respectively.^{7, 8}

Excision followed by surveillance or mastectomy are the two options that have been used to treat lobular carcinoma-in-situ in a fibroadenoma. Ozzello *et al*² found that of 16 patients treated by local excision, only two developed a recurrence, one after 3 years and the other after 5 years. In another report, one out of five patients with lobular carcinoma-in-situ developed a recurrence after local excision.⁴ In a literature review, Pick *et al*³ found that of 28 patients with lobular carcinoma-in-situ in a fibroadenoma, 10 had been treated with local excision, two of whom developed recurrences. Eighteen patients had been treated initially with mastectomy (eight simple, seven modified radical, and three radical) with no recurrences. The two patients with recurrences after local excision were then successfully treated by mastectomy. Twenty-seven of the 28 patients were alive, with only one showing evidence of disease. The single death was from an unrelated cause. Follow-up ranged from 0.2 to 26 years.

Forty per cent of patients with lobular carcinoma-in-situ who develop subsequent breast cancer are found to have another lobular carcinoma-in-situ, and 50% of all subsequent

Lobular carcinoma-in-situ in a fibroadenoma

- these lesions occur in older patients than do simple fibroadenomas (mean ages 42 years and 25 years, respectively)
- there is a 42–50% incidence of concurrent cancer in surrounding breast tissue
- lobular carcinoma-in-situ is the most common noninvasive cancer in fibroadenoma, whereas ductal carcinoma-in-situ is in the most common nonfibroadenomatous breast cancer
- the biological behaviour of these tumours is similar to that of lobular carcinoma-in-situ in a breast without fibroadenoma

cancers, both invasive and in-situ, occur in the contralateral breast.⁸ A policy of close observation is advocated for these cases. This policy can also be adopted for lobular carcinoma-in-situ in fibroadenomas. Forty-two to 50% of all cases of carcinoma in a fibroadenoma cancer occur in the adjacent breast tissue.^{2, 3, 9}

A wide margin of excision should be obtained in a clinically detected fibroadenoma in middle-aged patients.³ Lobular carcinoma-in-situ predisposes to subsequent invasive cancer. Moreover, this risk is cumulative, lifelong, and increases with time. In selected patients, especially those with a familial history of breast cancer, bilateral total mastectomy may be the appropriate treatment. The patient's choice of a particular modality of treatment should ultimately determine management.

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Hypoxaemia – think of the liver! Every internist should be aware of the hepatopulmonary syndrome

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Summary

Hepatopulmonary syndrome is characterised by arterial hypoxaemia, liver disease, and intrapulmonary vascular dilatation. A case is reported in which severe hypoxaemia, detected by chance, led to the diagnosis of liver disease and hepatopulmonary syndrome.

Keywords: hypoxaemia; hepatopulmonary syndrome

When confronted with a severely hypoxic patient, it is unusual for the clinician to make a list of differential diagnoses beyond cardiorespiratory diseases. Hepatopulmonary syndrome (HPS) is characterised by a triad of arterial hypoxaemia, liver disease, and intrapulmonary vascular dilatation.¹ Though the association of chronic liver disease, cyanosis, and digital clubbing was first described over 100 years ago, and the term 'hepatopulmonary syndrome' was suggested in 1977,² this entity has generated interest only recently.³ Literature outlining major recent developments in HPS has appeared mainly in specialist journals, whereas it is likely that internists and emergency room physicians (as in this case) would be the first ones facing the diagnostic dilemma of hypoxaemia of obscure aetiology. I report a case in which severe hypoxaemia, detected by chance, led to the diagnosis of liver disease and HPS.

Case report

A 57-year-old man, not known to have liver disease, felt dizzy while waiting for transportation home after a routine orthopaedic clinic visit. In the emergency room, pulse oximetry recording at room air was alarmingly low at 78% and a simultaneous PaO₂ of 6.26 kPa (normal 11–13 kPa) confirmed the hypoxaemia. With 100% oxygen delivered by a face mask, his oxygen saturation improved to 88%. On inquiry, he reported mildly progressive exertional dyspnoea for 24 months, dizziness for 18 months, weakness and fatigue for 12 months, and minimal lower extremity swelling for the past 2 weeks. He denied any other cardiorespiratory symptoms. He reported a 30-year history of alcohol abuse that had ended 18 months earlier. He was an active smoker with a 60-pack-year history. Examination revealed a middle-aged Caucasian male in no apparent distress. His other vital signs were stable. Positive findings were mild jaundice, digital clubbing, numerous spider naevi on the chest, and

trace ankle oedema. Pulmonary and cardiac examinations were unremarkable. There was no obvious ascites on abdominal examination and the hepatic span was 8 cm. Spleen was not palpable. Laboratory studies showed a haematocrit of 46% (normal 42–52%), haemoglobin of 161 g/l (140–180 g/l) and a mean corpuscular volume of 107.9 fl (86–98 fl). Whole blood count was $10.9 \times 10^9/l$ ($4.3\text{--}10.3 \times 10^9/l$) and the platelet count was $97 \times 10^9/l$ ($130\text{--}400 \times 10^9/l$). Total bilirubin was 53.01 $\mu\text{mol/l}$ ($5.1\text{--}17 \mu\text{mol/l}$) with a direct fraction of 20.52 $\mu\text{mol/l}$ ($1.7\text{--}5.1 \mu\text{mol/l}$). Alkaline phosphatase was 148 IU/l ($30\text{--}120 \text{ IU/l}$), alanine aminotransferase 58 IU/l ($0\text{--}35 \text{ IU/l}$), and aspartate aminotransferase 135 IU/l ($0\text{--}35 \text{ IU/l}$). Serum albumin level was 29 g/l ($35\text{--}55 \text{ g/l}$), total protein 66 g/l ($55\text{--}80 \text{ g/l}$), and INR was 3.0. Serum glucose, electrolytes, creatinine and blood urea nitrogen levels were normal. Serological testing for viral hepatitis was negative. Antinuclear antibody was not detected. Electrocardiogram and chest radiograph were normal. A technetium-99m labelled macroaggregated albumin (^{99m}Tc-MAA) perfusion scan of the lung (figure) showed no perfusion defects suggestive of a pulmonary embolus. However, a significant amount of the radioisotope was taken up by the kidneys and brain indicating an arteriovenous shunt, and the shunt fraction was quantified at 38% (normal < 5%). A contrast echocardiogram using microbubbles generated by agitation of normal saline showed crossover of bubbles from the right ventricle to the left atrium after five ventricular beats, excluding an intracardiac shunt and confirming its intrapulmonary location. Pulmonary function tests showed normal spirometry and lung volumes. The diffusing capacity for carbon monoxide was reduced at 58% of the predicted value. Computed tomography (CT) of the lungs was normal except for minimal pleural thickening at the posterior aspect of the right lung base. A CT scan of the abdomen revealed a small nodular liver, with a preserved caudate lobe. The liver was surrounded by a mild to moderate amount of ascites. Mild enlargement of the spleen with varices in the splenic hilum were noted. These radiological findings were consistent with liver cirrhosis and portal hypertension. Endoscopy showed 2+ oesophageal varices and moderate portal hypertensive gastropathy. A diagnosis of alcohol-related liver disease (probably cirrhosis) and hepatopulmonary syndrome was made.

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