



## Original article

# 'Occult' breast cancer

MS Lloyd, AG Nash

*Breast Unit, The Royal Marsden Hospital, Sutton, Surrey, UK*

The aim of this paper is to explore current trends in the diagnosis, investigation and treatment of patients presenting with axillary lymph node metastases without a primary in the breast being found and, more rarely, those cases with metastatic breast cancer where the primary remains unknown – the so-called, 'occult' breast cancer. A retrospective study of 25 reported cases were selected from our database at the Royal Marsden and 6 patients were found to have true 'occult' breast cancer. These 6 patients are all still alive with no primary ever having been found in the breast. A literature review was then undertaken exploring the changing trends in this diagnostic enigma. MRI scanning, it is reported, may reveal the primary. Occult cancers in which imaging totally fails to show the primary will become increasingly rare. The prognosis of these, however, may be surprisingly better than one would expect from the nature of their presentation.

*Key words:* Occult breast cancer – Axillary lymph node metastases

The word 'occult' strikes a sense of fear, curiosity and malevolence into the hearts of most people. Adding 'cancer' to this already sinister idea produces a deadly combination of word play. Label a patient with breast disease as having 'occult' breast 'cancer' and no wonder many women fear for their lives. They seem to think they have been cursed with an unknown entity which sounds like a voodoo myth and they fear that the prognosis is hopeless.

On rare occasions, a breast cancer will present with enlarged axillary lymph nodes as the first sign of disease. In these patients where the primary has not been found, there is now a diagnostic and therapeutic dilemma and this is called 'occult' breast cancer. How should such a patient be investigated and treated and what is the outcome?

Very little has been written on this topic that has been shown to be grounded on solid scientific evidence. The purpose of this paper is to re-open the debate on this topic and dispel any myths.

## Patients and Methods

A retrospective review has been made of all the T<sub>0</sub>N<sub>1</sub>M<sub>0</sub> carcinomas at this large cancer centre which sees up to 750 new cancers each year. Between the years 1979 and 1999, 27 cases were selected from our audit database who had presented as so-called 'occult' primaries. The case notes for these 25 patients were taken from medical records, or reviewed on Kodak microfiche film, in order to see whether they fulfilled the necessary criteria of

---

**Correspondence to:** Mr AG Nash, Breast Unit, The Royal Marsden Hospital, Sutton, Surrey, UK

Table 1 Data as seen from our database

Diag.	Age (yr)	FH <sub>x</sub>	USS	Orig. mam.	FNA Ax	T	N	M	Axillary node status	ER	Date of chemo.	Date of DXT	Surgery	Rec.	Died
15/11/79	70	No		M3	C5	0	1a	0	Node -ve	+ve	22/5/90		3/12/79 Mast	2/90 Ca Vulva	29/06/90
04/06/80	53	No		M1	C5	0	1b	0	Node +ve	-ve	5/4/84		16/5/80 Ax Diss	12/2/82 Loc/Node	
25/07/85	56	No		M3	C5	0	1b	0	Node +ve	-ve	10/85-12/85	9/85 Br, Ax, Suprac	8/8/85 Ax Diss		
<b>*20/08/85</b>	<b>52</b>	<b>No</b>		<b>M2</b>	<b>C2</b>	<b>0</b>	<b>1b</b>	<b>0</b>	<b>Node +ve</b>	<b>-ve</b>		<b>10/85 Br, Ax, Supra</b>	<b>21/8/85 Ax samp</b>		
06/03/97	56	No	U2	M3	C5	0	1a	0	Node -ve	+ve		5/97 Br	10/3/97 Loc biopsy		
16/09/86	74	No		M3	C5	0	1b	0	Node +ve	-ve		11/86 Br, Ax/ Supra	9/10/86 WLE + Ax diss	1/8/89 Loc Node, Bn	15/03/94
07/06/88	80	No		M3	C5	0	2	0	Node +ve	-ve		5/89 Br, Ax, Mediasti	29/6/88 Ax Diss	7/3/89 Loc, node, Bn	03/11/91
24/01/89	78	No		M3	C5	0	2	0	Node -ve	-ve		2/89 Br	10/2/89 WLE	8/7/97 Loc, Node	
31/10/89	55	No	U5	M3	C2	0	1b	0	Node +ve	+ve	1/90-6/90	1/90 Br	7/12/89 WLE + Ax Diss		
15/08/91	81	No		M2	C5	0	1b	0	Node -ve						
<b>*14/01/92</b>	<b>38</b>	<b>No</b>	<b>U4</b>	<b>M2</b>	<b>C2</b>	<b>0</b>	<b>1b</b>	<b>0</b>	<b>Node -ve</b>	<b>+ve</b>	<b>2/92-5/92</b>	<b>9/92 Br, Ax, supra</b>	<b>29/6/92 Ax Diss</b>		
30/06/92	50	No		M2	C2	0	1b	0	Node -ve	-ve	8/92-2/93	9/92 Br, supra	30/7/92 Ax Surg		
05/11/92	64	Yes	U5	M2	C2	0	1b	0	Node -ve	-ve	11/92-4/93	3/93 Br, 9/93 Br, 9/94 Br, Ax, Supra	4/2/93 Ax Diss	21/4/94 Loc nodes	16/09/94
01/06/93	63	No	U2	M2	C2	0	1b	0	Node +ve	+ve	8/93-1/94	10/93 Br	28/6/93 Loc biop	11/2/97 Bn, Liver	04/12/98
30/07/93	43	No	U2	M2	C2	0	1b	0	Node -ve	-ve	9/93-2/94	9/93 Br	26/7/93 WLE		
04/08/94	50	Yes	U5	M2	C2	0	1b	0	Node +ve	+ve	8/94-12/94	9/94 Br	9/8/93 WLE + Ax Diss		
<b>*18/06/96</b>	<b>78</b>	<b>No</b>		<b>M2</b>	<b>C5</b>	<b>0</b>	<b>0</b>	<b>0</b>	<b>Node +ve</b>	<b>+ve</b>			11/8/94 WLE + Ax Diss		
03/03/97	58	No		M3	C5	0	1b	0	Node -ve	+ve	7/97-11/97	7/97 Br, Supra	<b>8/7/96 Ax Diss</b>		
11/11/97	59	No		M2	C5	0		0	Node -ve	+ve	12/97	2/98 Br	4/4/97 Exc Biop		
22/06/99	44	Yes	U5	M2	C5	0	1a	0	Node -ve	+ve	8/99		13/6/97 Mast		
06/02/98	52	No		M2	C4	0	1a	0	Node -ve	+ve	2/98	3/98 Br	3/12/97 Loc Bio + Ax Diss		
<b>*06/08/98</b>	<b>64</b>	<b>No</b>	<b>U2</b>	<b>M2</b>	<b>C5</b>	<b>0</b>	<b>1a</b>	<b>0</b>	<b>Node +ve</b>	<b>-ve</b>	<b>9/98-12/98</b>	<b>2/99 Br, Supr</b>	15/7/99 Loc biop		
<b>*20/04/99</b>	<b>62</b>	<b>No</b>	<b>U2</b>	<b>M2</b>	<b>C5</b>	<b>0</b>	<b>1b</b>	<b>0</b>	<b>Node +ve</b>	<b>-ve</b>	<b>6/99-9/99</b>	<b>7/99 Br, Supra</b>	16/8/99 Mast		
06/02/96	69	No	U5	M2	C5	0	1b	0	Node +ve	-ve	2/96-6/96	7/96 Br, Supra	13/2/98 Loc biop	9/98 Gastric Ca	27/05/99
<b>*08/12/98</b>	<b>44</b>	<b>No</b>		<b>M2</b>	<b>C5</b>	<b>0</b>	<b>1b</b>	<b>0</b>	<b>Node +ve</b>	<b>+ve</b>	<b>12/98</b>	<b>12/98 Br, Supra</b>	4/1/99 Ax diss		

\*True 'occult' cases.

Diag., date of diagnosis; FH<sub>x</sub>, family history; USS, ultrasound scan; Orig. mam., original mammography M1-5; FNA Ax, fine needle aspiration from axillary node metastases; T, N, M, classification; ER, oestrogen receptor status for tumour; Date of chemo., chemotherapy; Date of DXT, deep X-ray treatment (radiotherapy); Surgery, date and type of surgery performed; Rec, recurrence date; Died, date patient died.

truly being 'occult'. Criteria analysed were: age at initial presentation, mammography and ultrasound findings, past histology from previous biopsies unrelated to the breast, histology from any surgery or investigations into the breast and axilla, family history and whether there was any recurrence.

## Results

Table 1 shows the data on these patients. Not all the patients labelled as having 'occult' primaries had complete data, hence the need to go systematically through the notes for each case.

From Table 1, it can be seen that out of all 25 cases initially labelled as 'occult', only 6 cases fulfilled the necessary criteria. These true 'occult' patients have been marked with an asterisk.

There was no family history of breast cancer in any of these patients. Only one had another tumour (a melanoma), but no pathological evidence in this case pointed to the axillary lymph node presentation being a secondary from the previous melanoma.

The earliest date of presentation was 1985 and the last date 1998. The age range of presentation was 38–78 years (mean, 56 years).

Of the original 6 patients identified, mammograms were either normal or inconclusive with the follow-up mammogram a year later being reported normal. Neither mammograms or ultrasound scans had subsequently shown any evidence of a suspicious lesion in either breast. None of the patients had MRI scans.

All 6 patients underwent axillary node dissection and 5 showed confirmation of adenocarcinoma compatible with a breast primary. One patient had a trucut biopsy from the palpable axillary node which showed adenocarcinoma and proceeded to have neo-adjuvant chemotherapy. The post-chemotherapy axillary dissection revealed nodes with lymphoid cells trapped in fibrocollagenous tissue with no malignant tissue being found.

Five of the six patients had grade three poorly differentiated carcinoma. None showed evidence of ectopic breast tissue or apocrine neoplasia. Three out of the six patients had axillary nodes with a positive oestrogen receptor (ER) status and were started on adjuvant tamoxifen therapy. The other three patients were ER negative. Two patients received neo-adjuvant chemotherapy and two patients received post-surgical adjuvant chemotherapy.

Two patients did not have chemotherapy. Five out of the six patients had radiotherapy treatment to the ipsilateral breast and axilla, whilst one patient had chemotherapy alone.

All these patients have been followed-up in the breast clinic and a primary site has still not been found. No recurrence had occurred over a time-period ranging from 8 to 168 months. The mean disease-free survival time was 57 months from date of diagnosis (approximately 5 years). Two out of the six patients have survived 5 years or more.

Of the remaining 19 patients who did not have 'true' occult breast cancer, 6 have died with metastatic disease arising from the ipsilateral breast, and 13 are still alive to date and disease-free. All 19 of these patients had radiotherapy treatment to the ipsilateral breast and axilla – 14 had chemotherapy and all 19 underwent surgery.

## Discussion

In 1954, Owen *et al.*<sup>1</sup> attempted to estimate the incidence of occult breast cancers. This was one of the first pieces of research into this enigma. They found 25 cases in 5451 patients with the disease. It is from this research that we owe this 0.3% incidence rate found commonly in literature written about this phenomenon. The true incidence is probably much lower since, with crude diagnostic imaging, Owen (in 1954) over-estimated the number of patients he labelled as 'occult' and with modern imaging techniques many of these primary carcinomas would have been located. We should, therefore, think of all those historic reports as 'apparent occult cancers' and not 'true occult cancers'. With further improvements in imaging techniques in the future, there will probably be no more true occult breast cancer cases.

No study has reported the length of time between diagnosis of so called 'occult' breast cancer and the discovery of a primary in the breast. Such data are scanty since, in most instances, the breast has either been removed or irradiated. Halstead<sup>2</sup> reported on just three patients and said vaguely that the time between diagnosis and a primary source being found in the breast was 'a few months' to 'two and a half years'.

In the past, postmortem section of the breasts from patients with axillary lymphadenopathy showed a primary site in the breast in a variable number of patients from 55% to 100% depending on which study is read.<sup>2,4,8,9</sup> In these apparently occult cases, one must also look at previously excised specimens to ensure that what one thought of as an axillary lymph node presentation of breast cancer was not in fact a secondary from a histopathological misdiagnosis.

Studies of angiogenesis in the growth, progression and metastasis of occult breast cancer may point to the primary carcinoma metastasis occurring at a sub-clinical

level whilst the angiogenesis was switched on within the axilla and not in the breast.<sup>10</sup> This is the more recent thinking regarding the genesis of occult breast cancers.

This is quite different to the thinking of Rosen<sup>3</sup> 20 years ago who gave a number of possible explanations for the finding of metastatic carcinoma in axillary nodes with only non-invasive carcinoma in the breast such as: (i) despite careful sectioning of tissue, a focus of invasive cancer may be missed; (ii) invasion may be present even though not detectable by light microscopy; (iii) metastases may cross from the contralateral breast; (iv) carcinoma from ectopic breast tissue may be present in a lymph node; (v) invasive cancer may be present in the axillary fat which is not examined; or (vi) heterotopic glands in a lymph node may be misinterpreted as carcinoma.

Rosen suggested that due to the very nature of 'occult' breast cancers, it may be impossible to detect them on a mammogram. This is because it is the dense stroma and intraductal proliferation of cells with consequent degenerative calcium deposition which create the image seen on a positive mammogram. This is not present in patients with 'occult' disease for some reason. Although pathologists have not identified any particular type of breast cancer as more likely to present in this occult manner, one would expect that more poorly differentiated tumours would be 'occult' and the prognosis of such cases would be poor, but this does not seem to be so. These views in the light of the research into angiogenesis seem somewhat dated and should not be overly relied upon.

Quadrantectomy of the upper lateral quadrant of the breast was recommended by Feigenberg<sup>4</sup> in 1976, but failed to show any better outcome for those patients.

In 1995, an accumulation of most recent data was presented by Rosen at the 12th Annual International Breast Cancer Conference. It was still stated that fewer than 1% of patients with breast cancer present with occult axillary lymph node metastasis as the first clinical manifestation of the disease. The age range found in Rosen's study was 30–83 years (mean, ~57 years), although the number of cases examined is not stated. A positive family history was reported in nearly 50% of such patients with about 25% having a first degree relative affected. Mammography has failed to show a consistent correlation between location of the radiological abnormality and the site at which the carcinoma is ultimately located.

A number of approaches were recommended by Rosen regarding the treatment of occult breast cancer. It was suggested that if mastectomy was delayed, repeat mammograms of patients who initially had negative studies often reveal new findings suggestive of carcinoma. Exact figures have not been given for this 'wait and see'

approach, *i.e.* the time interval between diagnosis and the detection of the primary.

Although not clinically palpable, the majority of carcinomas were thought to be found upon gross examination of a mastectomy or excisional biopsy specimen. The majority of lesions are still thought to occur in the upper outer quadrant of the breast.

Mohr and Queiser<sup>6</sup> followed up 5 patients who were thought to have 'occult' breast cancer. The conclusions drawn from this paper suggested that 'ectopic' breast cancer might be a rare variant and should be differentiated from 'occult' breast cancer with lymph node metastases or other primary tumours of the axillary tissue, for example the rare apocrine gland carcinoma. If we assume the patient has an ectopic breast tumour, axillary dissection should be combined with local irradiation and/or hormonal chemotherapeutic treatment and primary resection of the breast seems to be unnecessary.

New techniques including ultrasonography and magnetic resonance imaging (MRI) have now made impalpable cancers a common event and of these in the past some have been called occult cases. Very little has been written on the use of MRI in patients with axillary metastases of occult breast cancer. A study by the University Hospital of Rotterdam<sup>7</sup> in 1997 investigated 4 women with 'occult' axillary lymph node presentation to assess whether MRI of the breast could detect a clinically and mammographically occult breast tumour. MRI detected a single lesion in each of the three women and two lesions in the ipsilateral breast of the fourth woman. MRI fine needle aspiration cytology confirmed the 5 lesions detected as breast carcinomas. Even though the sample number was few, it has been suggested that MRI of the breast should be added to clinical examination mammography before defining it as an occult primary and planning therapy. Currently, no MRI compatible biopsy system for lesions not detectable by mammography exists in this country. The first of this kind is about to be introduced into the Middlesex Hospital.

## Conclusions

True occult cancers in which imaging totally fails to show the primary will become increasingly rare. The prognosis of these, however, may not be particularly worse than average from the nature of their presentation.

## References

1. Owen HW, Dockerty MB, Gray HK. Occult carcinoma of the breast. *Surg Gynecol Obstet* 1954; **98**: 302–8.

2. Halstead W. The results of radical operations for the cure of carcinoma of the breast. *Ann Surg* 1970; **46**: 1–19.
3. Rosen PP. Axillary lymph node metastases in patients with occult non-invasive breast carcinoma: *Cancer* 1980; **36**: 1298–306.
4. Feigenberg Z, Zer M, Dintsman M. Axillary metastases from an unknown primary source. *Isr J Med Sci* 1976; **12**: 1153–8.
5. Rosen PP. Occult carcinoma presenting with axillary lymph node metastases. *Non-Serial, 12th Annual International Breast Cancer Conference, Miami, FA, March 16–18, 1995*.
6. Mohr T, Queiser W. Cancer presenting as anterior axillary mass – ectopic breast cancer? Report of five cases: *Onkologie* 1996; **19**: 260–4.
7. Tilanus-Linthorst MMA, Obdeijn AIM, Bontenbal M. Oudkerk M. MRI in patients with axillary metastases of occult breast carcinoma. *Breast Cancer Res Treat* 1997; **42**: 179–82.
8. Haupt HM, Rosen PP, Kinne DW. Breast carcinoma presenting with axillary lymph node metastases: an analysis of specific histopathologic features. *Am J Surg Pathol* 1985; **9**: 165–75.
9. Patel J, Nemoto T, Rosner D *et al*. Axillary lymph node metastasis from an occult breast cancer. *Cancer* 1981; **47**: 2923–7.
10. Locopo N, Fanelli M, Gasparini G. Clinical significance of angiogenic factors in breast cancer. *Breast Cancer Res Treat* 1993; **52**: 159–73.