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Endobronchial metastasis in breast cancer

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ABSTRACT Ten patients with endobronchial metastasis from primary breast cancer were found among 1200 fibreoptic bronchoscopies. Six of these patients had radiological signs suggesting bronchial obstruction. The diagnosis was verified in nine cases by means of bronchoscopic biopsy or cytology and in one by thoracotomy. Endobronchial metastasis should be considered when symptoms or chest films suggest endobronchial disease in a patient with a history of breast cancer.

Endobronchial metastasis from nonpulmonary carcinoma is uncommon, occurring in only 2–5% of patients with cancer at necropsy.[1 2] Antemortem diagnosis is unlikely unless airways obstruction, severe cough, or haemoptysis occurs. Our personal experience seemed to indicate a more common occurrence and prompted a review of our fibreoptic bronchoscopy records. This review yielded 10 well-documented cases of breast cancer that had metastasised to bronchial mucosa.

Methods

Cases were selected by careful review of the fibreoptic bronchoscopy records of the Thoracic Medicine Department at Geisinger Medical Center from January 1974 to June 1978. Twelve hundred records were reviewed for either suspected or proven endobronchial metastasis from breast cancer. Metastases from other possible primary organs were excluded by clinical means. Extensive searches for other primary tumours were not carried out as these are not generally felt to be worthwhile in the absence of clinical evidence.[3]

All the bronchoscopies were performed by us using the standard transnasal approach[4] with either the Olympus BF5B2 or BFB2 fibreoptic bronchoscope. Topical anaesthesia with 1% lignocaine was used. Atropine 0·8 mg intramuscularly was given before the procedure.

Bronchial washings were collected with a standard suction trap and fixed in 50% ethyl alcohol before transport to the cytology laboratory. The method of Papanicolaou[5] for fixing and staining of specimens was followed. Criteria for classification of slides were those described by Koss.[6]

Geisinger Medical Center has an active oncology programme including chemotherapy protocols for breast cancer. The incidence of breast cancer seen at Geisinger is approximately that seen nationally. The Geisinger tumour registry shows that 17–20% of female cancers originated in the breast, with a range of 116 to 139 new cases each year during the period of this study.

Results

The 10 case histories are summarised in the table. Eight of the 10 patients had infiltrating ductal carcinoma. Six (patients 1, 2, 5, 6, 7, 9) of the 10 patients had radiographic findings of loss of volume, atelectasis, or persistent segmental or lobar infiltrates suggesting bronchial obstruction. Mucosal biopsy was carried out in all 10 cases and was diagnostic of metastatic breast carcinoma in seven.

There was nothing to suggest primary lung cancer and none of the 10 patients had ever smoked tobacco. In nine, the bronchoscopic appearance was definitely abnormal with firm oedematous mucosa. Varying degrees of bronchial obstruction occurred in eight. Exophytic tumour was found once. In patient 3 the mucosa appeared grossly normal; the chest film showed multiple small nodules and bronchial mucosa was obtained during attempts at transbronchoscopic lung biopsy. Histologically tumour was demonstrated in the submucosa of the bronchi. Bronchial biopsies in three patients with visible bronchial abnormalities were not diagnostic because of inadequate depth of biopsy. In two of these the bronchial cytology was

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Table *Endobronchial metastases in breast cancer: case summaries*

Patient	*Age (yr)*	*Primary diagnosis*	*Positive lymph nodes*	*Metastases*	*Symptoms*	*Chest film*	*Bronchial appearance*	*Bronchial biopsy*	*Cytology*	*Metastases elsewhere*
1	50	Infiltrating ductal carcinoma. Right radical mastectomy April 1973	0	Bronchial biopsy May 1975	Cough (5 months) haemoptysis, wheezing	Atelectasis RML; elevation right hemidiaphragm	Obstruction RML; 50% narrowing RLL below superior segment by mucosal oedema	Infiltrating adeno-carcinoma replacing mucosa and invading smooth muscle	Class 1	Bone and liver scans negative
2	47	Infiltrating ductal carcinoma. Left radical mastectomy April 1974	1	Bronchial biopsy September 1975	Cough and dyspnoea on exertion (3 weeks)	Elevation right hemidiaphragm; densities RML and RLL; widening of right superior mediastinum	Obstruction of medial segment RML by mucosal oedema	Adenocarcinoma; nests of large tumour cells in the submucosa	Class 1	Bone and liver scans negative
3	58	Infiltrating ductal carcinoma. Left radical mastectomy July 1974	0	Bronchial biopsy January 1976	None	Multiple small nodules bilaterally	Normal	Adenocarcinoma; small groups of tumour cells in the submucosal lymphatics	Class 3	Bone brain and liver scans normal
4	57	Stromal cell sarcoma Left radical mastectomy October 1972	0	Bronchial biopsy April 1976	Cough for 6 months	Large density in the lateral portion of the left mid lung	Marked mucosal oedema with obstruction of the LLL bronchus below the superior segment	Stromal cell sarcoma in the submucosa	Class 1	Bone scan positive (asymptomatic); liver scan normal
5	58	Anaplastic carcinoma. Left radical mastectomy September 1972	7	Bronchial biopsy August 1976	Cough for 7 weeks	RML atelectasis	Oedema and fixation of the bronchi with obstruction RML	Poorly differentiated carcinoma invading the mucosa	Class 3	None
6	58	Infiltrating ductal carcinoma. Right radical mastectomy February 1975	0	Bronchial biopsy October 1975	Cough and dyspnoea on exertion (1 month)	RML atelectasis Right pleural effusion	Thick oedematous mucosa entire right side; obstruction RML; 50% obstruction RLL; 25% obstruction RUL	Anaplastic carcinoma	Class 3	Bone scan positive (asymptomatic); brain scan negative
7	58	Infiltrating ductal carcinoma. Modified left radical mastectomy December 1976	8	Bronchial cytology November 1977	None	Mass with associated atelectasis RLL	Mucosal oedema RML and RLL RML 70% obstruction; RLL 25% obstruction	Tissue inadequate	Class 4 Adenocarcinoma	None
8	54	Infiltrating ductal carcinoma. Right radical mastectomy March 1974	0	Transthoracic needle biopsy November 1977	Headache, blurred vision, left leg weakness	5·5 cm mass RLL Right hilar enlargement	Induration and narrowing RUL	Tissue inadequate	Class 5	Brain scan positive Bone scan negative Liver scan equivocal
9	68	Mucinous infiltrating ductal carcinoma. Left total mastectomy April 1973	0	Thoracotomy May 1978	Cough, fever, haemoptysis	LLL pneumonia	Mass LLL	Fragments—not diagnostic	Class 3	None
10	54	Infiltrating ductal carcinoma. January 1976 right radical mastectomy; April 1976 left modified radical mastectomy	2	Bronchial biopsy July 1978	Cough, dyspnoea haemoptysis, weight loss	Patchy infiltrate adjacent to the right hilum	Severe mucosal infiltration obstructing (70%) the bronchus intermedius and extending into the RUL and RLL	Adenocarcinoma	Class 1	None

RML=right middle lobe RUL=right upper lobe RLL=right lower lobe LLL=left lower lobe

considered positive (classes 4 and 5), while the other diagnosis was verified at thoracotomy (patient 9). The bronchial cytology was negative in four and suspicious (class 3) in four.

The patients ranged in age from 47 to 68 years (mean 56 yr). The time from diagnosis of the primary tumour to documentation of endobronchial metastasis ranged from nine to 61 months (mean 32·4). Four patients had spread to local lymph nodes (one to eight nodes) at the time of their original mastectomy. The mean interval from the time of diagnosis of the primary tumour to discovery of bronchial metastasis was shorter (26 months) for those with deposits in nodes than those without (36 months).

Seven of the patients had postoperative radiotherapy or chemotherapy. There was no difference between them and the three patients with no radiotherapy or chemotherapy.

In eight of the 10 patients it was possible to compare the histology of the metastasis with the primary tumour. In all eight, the histology was similar. In one case the primary tumour was not available for comparison and in the other only cytological proof of metastatic disease was obtained. In the former (case 6), however, the clinical course and response to hormonal management strengthened the diagnosis of metastatic breast carcinoma.

Follow-up on this group of patients as of July 1979, indicated that six patients (1, 3, 4, 7, 8, 10) had died as a result of tumour. No necropsies had been performed. Four patients (2,5,6,9) are well on hormonal or drug therapy. Patient 2 is alive almost four years after the diagnosis of endobronchial metastasis having responded to testosterone and melphalan.

Case reports

The following case histories (patients 1 and 9) illustrate the presentation and evaluation of two of our patients in further detail.

CASE 1

The first patient was a 50-year-old woman who was admitted to Geisinger Medical Center in May 1975 for evaluation of a cough of five months' duration with recent haemoptysis and occasional wheezing. In April 1973, she had a right radical mastectomy for infiltrating ductal carcinoma. Six lymph nodes contained no tumour. During the May 1975 admission, a chest film showed right middle lobe atelectasis and elevation of the right hemidiaphragm (fig 1). Bone and liver scans were

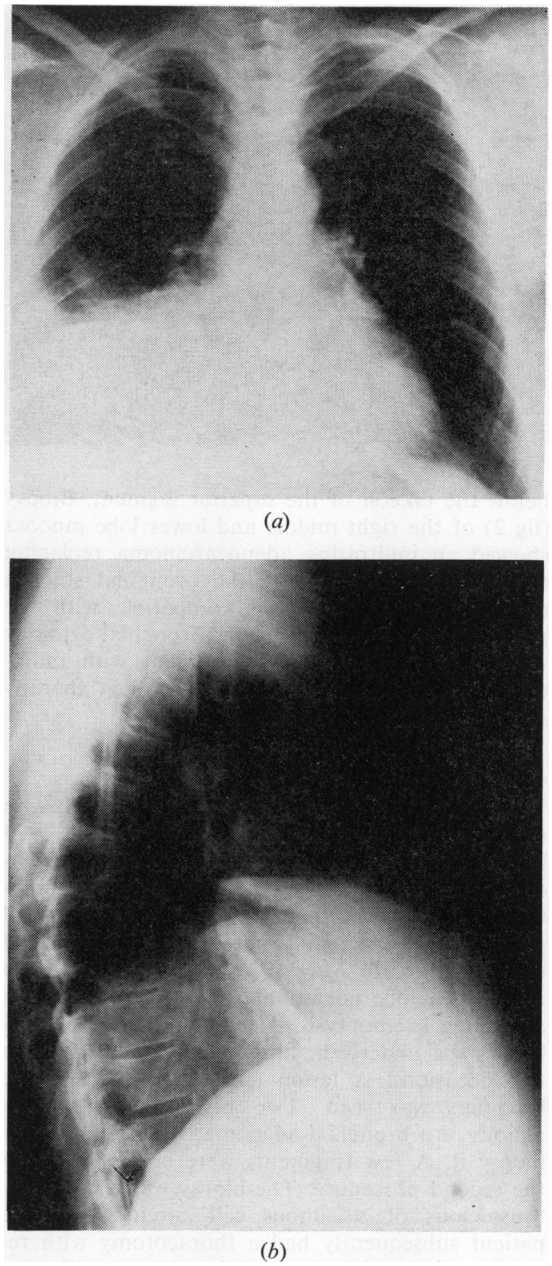

Fig 1 *Posterior-anterior (a) and lateral (b) chest films (case 1) showing atelectasis of the right middle lobe and elevation of the right hemidiaphragm.*

negative. Fibreoptic bronchoscopy demonstrated a thick, oedematous, firm mucosa with total obstruction of the right middle lobe bronchus and 50% narrowing of the right lower lobe bronchus

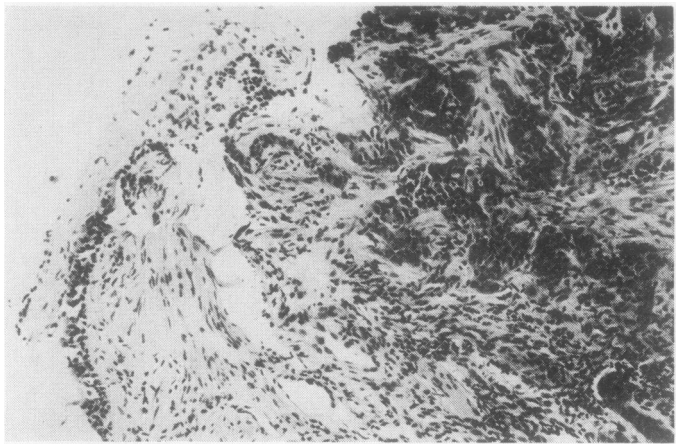

Fig 2 *Bronchial biopsy (case 1) showing infiltrating adenocarcinoma invading the submucosa. Haematoxylin and eosin, original magnification ×125.*

below the takeoff of the superior segment. Biopsy (fig 2) of the right middle and lower lobe mucosa showed an infiltrating adenocarcinoma replacing the mucosa and invading the bronchial smooth muscle. The histology was compatible with the previous primary in the breast. Bronchial cytology was negative. In spite of treatment with radiotherapy to the lung and oral androgen therapy she died at home five months later.

CASE 9

The second patient was a 68-year-old woman who underwent a left total mastectomy in April 1973 because of a mucinous infiltrating ductal carcinoma. She received a postoperative course of radiotherapy. In November 1977, she developed pneumonia in the right lower lobe which responded to antibiotics. In May 1978 she again developed right lower lobe pneumonia (fig 3), this time with associated haemoptysis. After treatment with antibiotics she underwent fibreoptic bronchoscopy on two occasions. A lesion in the right lower lobe bronchus was seen. Two bronchoscopists, suspicious of a bronchial adenoma, were reluctant to biopsy it. A few fragments were obtained during the second procedure. The biopsy was reported as "suspicious of squamous cell carcinoma". The patient subsequently had a thoracotomy with resection of the right lower lobe. Adenocarcinoma (fig 4) compatible with the breast primary was seen obstructing the left lower lobe bronchus. She was last seen in March 1979 with no evidence of recurrence of disease.

Symptoms of metastatic disease were lacking in two patients in whom metastasis was first detected by routine chest radiography. Symptoms in the other eight consisted of cough in seven, dyspnoea

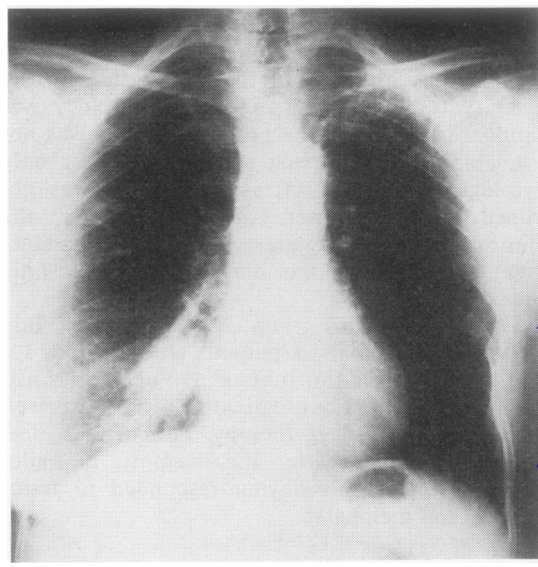

Fig 3 *Chest film (posterior–anterior) of case 9 showing a left lower lobe pneumonia.*

in four, haemoptysis in three, recurrent pneumonia, weight loss and neurological symptoms caused by cerebral metastases in one each. Four patients had symptoms or laboratory evidence suggesting metastatic disease elsewhere. Two of these consisted of asymptomatic abnormalities on bone scans.

Discussion

DeBeer *et al*[7] reported what they felt was the first case of carcinoma of the breast metastasising to the mucosa of a major bronchus. Subsequently

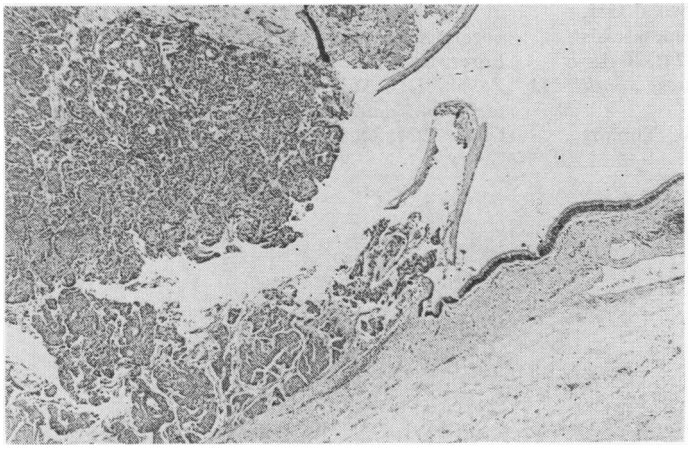

Fig 4 *Section of left lower lobe obtained at thoracotomy (case 9) showing mucosal and submucosal invasion by adenocarcinoma. Haematoxylin and eosin, original magnification ×375.*

Tenholder *et al*[8] reported seven patients with metastatic breast cancer proven by bronchial biopsy. Fitzgerald[9] reported six cases of breast cancer among 17 patients with endobronchial metastases. Our experience has reflected that of the latter two groups. We have found endobronchial involvement to be fairly common in metastatic breast cancer and have rarely seen endobronchial metastasis from other tumours.

Because it is believed to be rare, endobronchial metastatic breast cancer is not usually a prime consideration when segmental or lobar abnormalities appear on chest radiographs in association with symptoms suggesting endobronchial disease. The diagnosis of metastatic disease may also be delayed by the lack of symptoms or evidence of metastatic disease elsewhere, as in six of our patients.

The endobronchial appearance is generally one of mucosal oedema and thickening. The tumour usually involves the submucosal lymphatics rather than the surface of the mucosa. This probably explains the low incidence of positive bronchial cytology and emphasises the need for a deep mucosal biopsy.

The fact that 80% of this group of patients had infiltrating ductal carcinoma is not surprising, as McDivitt[10] reported that 78% of all breast cancer showed this cell type. Smoking or carcinogen exposure did not appear to have an effect. None of our patients smoked, all lived in rural communities, and none had worked with industrial carcinogens.

There are few studies of diagnostic techniques in breast carcinoma metastatic to the lung. Zavala[11] had a yield of 50% using transbronchial lung biopsy in metastatic carcinoma of all types. Cytological yield with brushing was only 30%. In our series with endobronchial metastasis it appears that deep mucosal biopsies have the highest yield (70%), but bronchial cytology should not be dismissed since it may provide the diagnosis when the biopsy is inadequate, as in two of our cases. Fibreoptic bronchoscopy with deep mucosal biopsy is safe and well tolerated in most patients. Its high yield in the presence of endobronchial disease makes it the procedure of first choice in the evaluation of the patient with suspected endobronchial metastases.

Endobronchial metastasis from breast cancer is not uncommon and should be strongly considered when someone with a history of breast cancer presents with symptoms or radiological findings suggesting endobronchial disease.

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