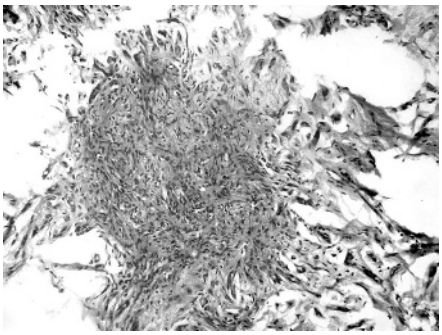

Figure 1 A focus of myoepitheliosis showing proliferation of cuboidal to spindle-shaped myoepithelial cells leading to the formation of a nodule.

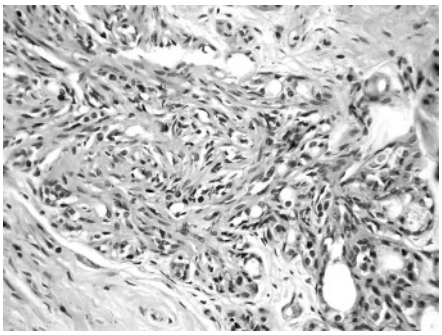

Figure 3 High-power photomicrograph showing the proliferating oval to spindle myoepithelial cells.

The larger nodule showed an IDC, grade II, on microscopy (Elston and Ellis modification of Bloom Richardson classification).[3] The tumour extended close to the deep resection plane; however, it was free. The smaller nodule showed multiple foci of proliferating oval to spindle cells, involving almost all the TDLUs as well as the surrounding areas (figs 1 and 2). Similar foci were also identified in the sections taken from peritumoural (fig 3) and tumour-free areas. The intervening stroma showed fibrosis. No atypia or mitosis was noted. The myoepithelial nature of these cells was confirmed by smooth muscle actin (SMA) and S-100 immunostaining. There was no evidence of any malignant change in the epithelial component in this nodule. Considering the above features, a diagnosis of IDC with multifocal myoepitheliosis was made. The lymph nodes from the axillary tail were free of tumour.

Discussion

Myoepithelial lesions of the breast range from the myoepithelial proliferations accompanying benign lesions—for example, sclerosing adenosis, ductal hyperplasia and nipple adenoma—to malignancies such as adenoid cystic carcinoma, adenomyoepithelioma and myoepithelial carcinoma. Myoepitheliosis is a benign condition characterised by multifocal proliferation of spindle to cuboidal myoepithelial cells generally located in the TDLUs. It can occur in two forms: the intraductal form, in which there is variable distention and occlusion of the TDLUs, and periductal form, which is often associated with sclerosis. The periductal variety, now considered a variant of sclerosing adenosis, may sometimes be misdiagnosed as an invasive carcinoma, particularly in the background of atrophy.[2] The present case highlights a mixed pattern with both intraductal and periductal components. Myoepitheliosis generally does not present as a mass lesion. However, if myoepithelial cells form aggregates, it may sometimes be felt as a nodule, as was seen in our case.[2] Immunohistochemically, the cells exhibit positivity for protein markers such as SMA and S-100 protein.[4] The recently described nuclear protein p63 is also considered to be sensitive and specific for identification of myoepithelial cells.[5] Our case showed positivity for SMA as well as S-100 protein, but the intensity of staining was stronger for SMA. Tavassoli[2] described three patients with myoepitheliosis in a series of myoepithelial lesions of the breast. None of her patients, however, had a coexisting IDC.

The exact contribution of myoepithelial cell proliferation to ductal carcinomas is unclear. Several reports suggest that 2–18% of the IDC show focal or diffuse myoepithelial differentiation by immunohistochemical protein markers (eg, basal cytokeratins, actin, calponin, caldesmon and S-100 protein). Experimental studies have shown a considerable overlap between the genetics of lesions arising from myoepithelial and epithelial cells, and it has been suggested that the two cell types are derived from the same precursor.[6] Also, the myoepithelial cells have been shown to secrete a variety of tumour-suppressor molecules, such as maspin, laminin-1 and Wilms' tumour-1, which are thought to have anti-invasive and anti-angiogenic effects on carcinoma and precancer cells. The loss of these molecules due to myoepithelial cell injury may lead to cell proliferation, angiogenesis and invasion.[7 8] Excision is the treatment of choice in myoepitheliosis. However, in the present case, the future course of treatment and outcome depend on the coexistent malignancy.[2]

To conclude, we document the presence of a rare multifocal myoepitheliosis in a case of IDC. However, the link between the two lesions in the same breast cannot be explained from this single case report. Future studies are needed to establish the exact role of such proliferations of myoepithelial cells in breast malignancies.

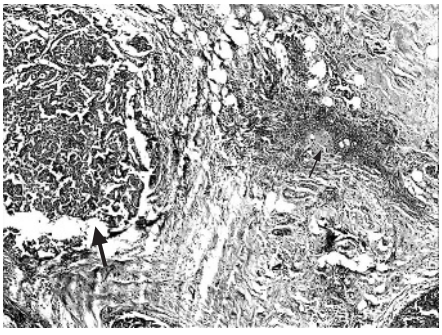

Figure 2 Infiltrating ductal carcinoma (broad arrow) with a focus of myoepitheliosis in the adjoining breast (arrow).

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Primary hyperparathyroidism and metastatic carcinoma within parathyroid gland

Involvement of the parathyroid glands by metastatic tumour is rare. In autopsy studies of known cancer patients, it was noted in 0.2–11.9% of individuals.[1] Hypoparathyroidism and hypocalcaemia as a result of parathyroid destruction by tumour is unusual.[2 3] We report a case of hyperparathyroidism due to parathyroid hyperplasia with simultaneous occurrence of metastatic bronchogenic adenocarcinoma to a parathyroid gland.

Case report

A 75-year-old woman was referred with hypercalcaemia. Six months earlier she had presented to an osteoporosis clinic with generalised pain in the upper limbs. She reported anorexia and mild weight loss but was otherwise asymptomatic. Specifically there were no respiratory symptoms. A bone density scan revealed osteoporosis. Routine biochemical investigations revealed hypercalcaemia, raised parathyroid hormone level and normal renal function (table 1). A parathyroid pertechnetate/MIBI subtraction scan suggested the presence of an enlarged left superior parathyroid gland. The patient was a non-smoker and had no significant past medical history. Plain radiographs of the chest and renal tracts taken 6 months prior to surgery were normal. A diagnosis of primary hyperparathyroidism seemed secure and surgical exploration advised. Prior to operation a hard palpable lymph node in the right submandibular region

Table 1 Blood biochemistry results

	At presentation 6 months before surgery	Preoperative 5 months before surgery	Postoperative Day 2 post-surgery	Normal range
Calcium (mmol/l)	2.73	2.77	2.16	2.22–2.66
Albumin (g/l)	35	34	30	35–50
Corrected calcium (mmol/l)	2.83	2.89	ND	
Phosphate (mmol/l)	0.70	0.88	1.03	0.80–1.55
Alkaline phosphatase (U/l)	109	123	ND	35–120
Parathyroid hormone (pg/ml)	181	191	ND	10–85
Urea (mmol/l)		6.7	5.2	3.3–8.8
Creatinine (μmol/l)		51	55	40–110

ND, not done.

was noted and it was planned to excise this at the same time as neck exploration.

A unilateral left sided neck exploration was carried out using the surgical strategy which we have previously described.[4] At operation, an enlarged left superior parathyroid gland was identified and removed. A normal sized left inferior parathyroid gland was excised for comparative biopsy and the right submandibular node resected. Intraoperative pathological examination was not done. The right side of the neck was not explored. The postoperative period was uneventful and the serum calcium returned to normal. On receipt of the histopathological report the patient was readmitted for further investigations. Ear, nose and throat examination showed no abnormality. Computed tomography of the neck and chest now showed marked mediastinal lymphadenopathy and left lower lung consolidation associated with a pleural effusion. A subsequent FDG-PET (fluorodeoxyglucose positron emission tomography) scan revealed abnormal FDG uptake in the right occipital lobe of the brain, in mediastinal, pulmonary hilar, paraaortic and supraclavicular lymph nodes, in the right adrenal gland and both iliac bones, and in lumbar (L2) and thoracic (T5) vertebral bodies. The findings were consistent with widespread metastatic disease from a presumed primary bronchial carcinoma. The patient was unfit for any further diagnostic procedure. She underwent a course of palliative radiotherapy but died a few months later. Autopsy was not performed.

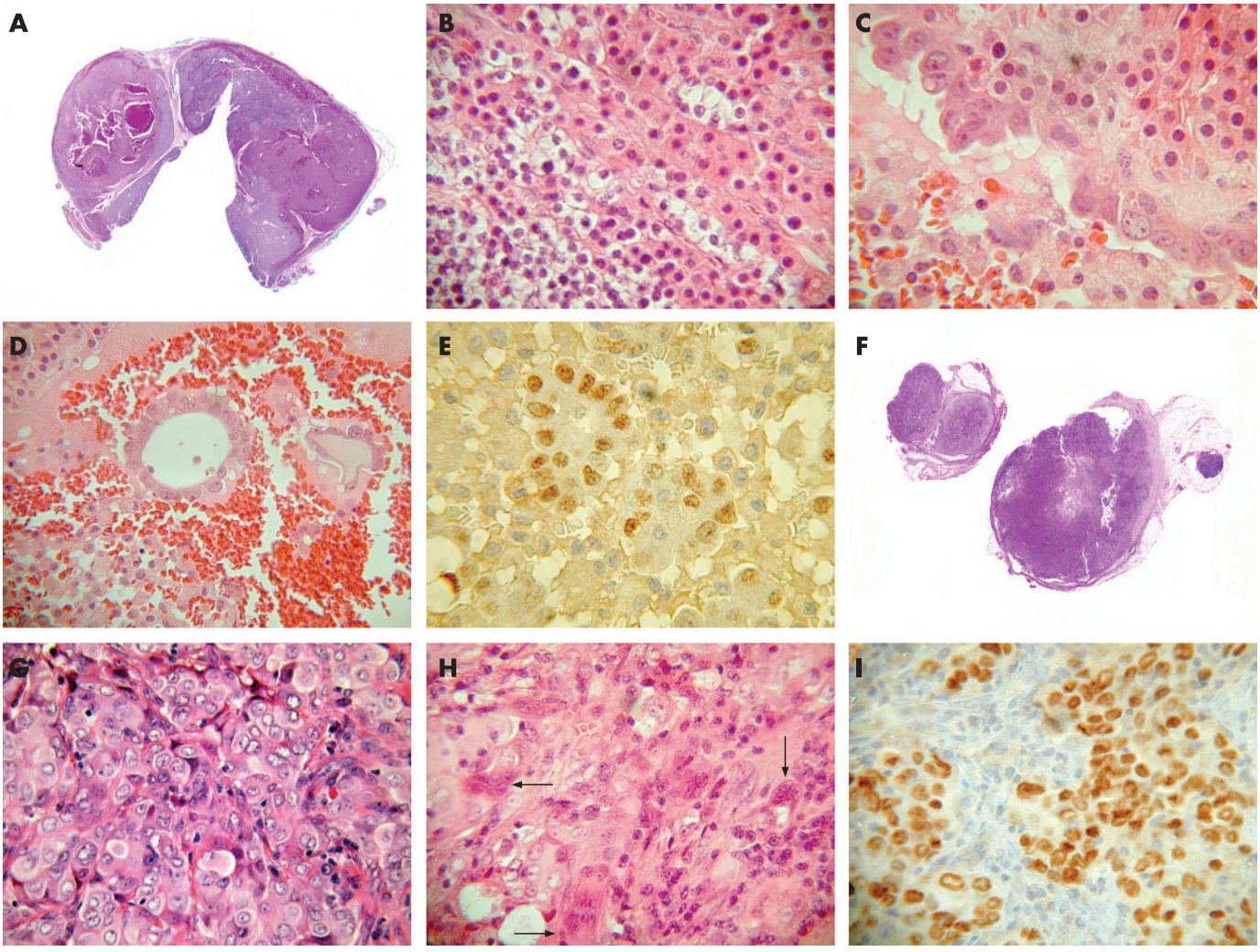

Figure 1 (A) Nodular hyperplasia of the left superior parathyroid gland with areas of haemorrhage and cystic degeneration. (B) Chief cells and oxyphil cells in the hyperplastic left inferior parathyroid gland. (C) Left superior parathyroid gland cyst lined by malignant cells contrasting with bland chief/oxyphil cells in the wall of the cyst. (D) Malignant glands within the left superior parathyroid gland cyst. (E) Malignant glands within left superior parathyroid cyst showing TTF-1 nuclear staining. (F) Section of lymph node replaced by metastatic carcinoma. (G) Sheet of carcinoma cells within the lymph node with occasional gland-like spaces. (H) Metastatic carcinoma with osteoclastic giant cells (arrows) within lymph node. (I) Metastatic carcinoma within lymph node showing TTF-1 nuclear staining.

Pathological findings

The left superior parathyroid gland measured 33 mm in maximum dimension and weighed 4173 mg. The cut surface was nodular and brown in colour. The left inferior parathyroid measured 5 mm in maximum dimension and weighed 120 mg. Microscopy showed nodular hyperplasia of chief cells and oxyphil cells in both glands. Areas of haemorrhage and cystic degeneration were present in the larger left superior gland. Hobnail cells with vesicular nuclei and prominent nucleoli lined one of these cysts. The cyst lumen contained a few malignant glands. A diagnosis was made of parathyroid hyperplasia of both glands with metastatic adenocarcinoma within the left superior parathyroid. The right submandibular lymph node measured 12 mm in diameter and was totally replaced by metastatic poorly differentiated carcinoma with a stroma rich in osteoclastic giant cells. The tumour cells had vesicular nuclei and prominent nucleoli similar to that of the metastatic carcinoma in the left parathyroid gland but neither glandular nor squamous differentiation was evident. Immunohistochemical staining showed the tumour cells staining positively with CK7, PE10 and TTF-1, within both the lymph node and the left superior parathyroid gland. There was no reactivity to WT-1, CA-125, CK20, and HMB-45. The immunoprofile suggested a diagnosis of primary bronchogenic carcinoma with metastasis to the right submandibular lymph node and the left superior parathyroid gland (fig 1).

Discussion

We have reported a patient with primary hyperparathyroidism due to parathyroid hyperplasia and coincidental metastatic adenocarcinoma involving one of the enlarged parathyroid glands. While there are independent reports of metastatic tumour involving the parathyroids and primary hyperparathyroidism associated with disseminated malignancy, a literature search revealed no reported case similar to ours wherein the metastatic adenocarcinoma was identified as a result of parathyroid gland excision for hyperparathyroidism.

Metastasis of tumour to the parathyroid glands has been described previously in autopsy studies of known cancer patients with widespread tumour.[1 2] The commonest sites of primary tumour in these circumstances were breast, lung, and soft tissue, also leukaemia and cutaneous melanoma.[3] Secondary involvement of the parathyroid gland by local invasion of thyroid and laryngeal carcinomas is also reportedly infrequent.[5] Tang *et al* have described involvement of the parathyroid gland by papillary thyroid carcinoma in 20 of 911 cases; 2% of these had metastases as opposed to direct invasion.[6] Our case therefore appears to be unique in that the patient presented with symptoms related to hypercalcaemia and the primary lung tumour was undetected prior to removal of the parathyroid glands.

The association of hypercalcaemia with non-parathyroid cancer is well recognised. The mechanisms of the hypercalcaemia include osteolytic metastasis and hypercalcaemia developing as a non-metastatic phenomenon consequent to production of a parathyroid hormone-like humoral agent by the tumour.[5 7 8] There are several case reports of hypercalcaemia due to primary hyperparathyroidism associated with cancer of the lung, and non-medullary carcinoma of the thyroid, breast and larynx, but the frequency of this association is not precisely known. Many of these cancer patients had hypercalcaemia in the absence of metastatic disease; the presence of raised parathyroid hormone levels led to evaluation of the parathyroid glands.[9–13] Godsall *et al* noted primary hyperparathyroidism with concomitant non-parathyroid cancer in 8 of 133 patients with disseminated cancer. The types of cancer included squamous lesions of the head and neck, lung, and colon, breast adenocarcinoma and myeloma.[14] Honda *et al* reported primary hyperparathyroidism occurring in association with aldosterone-producing adrenocortical adenoma and breast cancer, and suggested relation to MEN1 gene mutations.[15] However, there are others who suggest that the occurrence of the two diseases is coincidental rather than due to a shared aetiology.[13] Primary hyperparathyroidism due to parathyroid adenoma has also been reported with a slightly increased frequency in non-aggressive breast cancer patients.[9 10] In our patient, despite the gross impression of a parathyroid adenoma, microscopy of the left superior and inferior parathyroid glands showed hyperplasia with asymmetric enlargement of the left superior parathyroid gland. The serum calcium reverted to normal after parathyroid exploration. It seems probable that removal of the larger parathyroid gland was responsible for normalisation of the serum calcium and that the microscopic hyperplasia of the second parathyroid gland was functionally insignificant.

In conclusion, this report describes the rare incidental discovery of metastatic adenocarcinoma within a hyperplastic parathyroid gland resected for surgical management of primary hyperparathyroidism. It is important for clinicians and pathologists to be aware of this possibility in patients evaluated for osteoporosis and hypercalcaemia.

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Granulomatous reaction to injectable hyaluronic acid (Restylane) diagnosed by fine needle biopsy

The hyaluronic acid (HA) derivative Restylane is now the most common injectable soft tissue filler used for facial wrinkle augmentation. Although it is generally well tolerated and absorbed within months, nodule formation at the injection site has been documented.

A 62-year-old woman with a history of carcinoma of the breast six years previously was referred to a fine needle aspiration (FNA) clinic for biopsy of a subcutaneous facial nodule. On palpating the nodule six weeks prior to presentation she was referred for ultrasound examination; findings were reported as being consistent with a lymph node, raising concern of possible metastatic carcinoma of the breast. Serendipitously the same ultrasound examination led to discovery of a thyroid nodule that was aspirated and found to be papillary carcinoma, broadening the differential diagnosis of the facial nodule to metastatic thyroid carcinoma.

On physical examination the lesion was a 1 cm subcutaneous nodule overlying the lower third of the mandible, a location felt to be consistent with a slightly ''high'' submental node. However, the nodule had irregular contours on palpation, and although it could be moved over the underlying bone, seemed to be fixed to the overlying skin. No cellular material was obtained by initial sampling with