Fine needle aspiration cytology of an unusual case of papillary thyroid carcinoma metastatic to the breast

Sharda Lallu, Sarla Naran and Catherine Koleda
Anatomic Pathology, Wellington SCL, Wellington

ABSTRACT
We report the fine needle aspiration cytology of a case of thyroid papillary carcinoma metastatic to the breast in a 63 year female who presented with a mobile lump in the right breast. She had past history of thyroid papillary carcinoma in 1991 with metastasis to the lung in 2005. Also, she had a right middle lobectomy for a bronchial carcinoid 30 years previously. Fine needle aspiration of the breast lump revealed a cellular sample composed of cell groups with a tubulopapillary architecture, with the cells showing mild atypia. A cell block preparation showed numerous papillary groups of cells exhibiting nuclear overlapping, occasional nuclear grooves, rare intranuclear inclusions and psammomatous calcifications. On immunohistochemical staining the tumour cells were positive for TTF-1, weakly positive for thyroglobulin and negative for ER, PR, GATA3, GCDFP-15, CD56, synaptophysin and chromogranin. The breast is an unusual site of metastasis for thyroid papillary carcinoma.

Key words: Fine needle aspiration, breast cancer, thyroid papillary carcinoma, metastasis.

INTRODUCTION
Papillary carcinoma of the thyroid is the most common form of thyroid malignancy, generally carries a good prognosis and tends to metastasize locally to regional lymph nodes. Distant metastases are uncommon and are usually to the lung and bone (1-3). Less common sites of metastases are the brain, liver, kidneys, skin and breast (1,3-5). Carcinoma of the thyroid metastasising to the breast is particularly uncommon.

In general, metastasis to the breast from an extra-mammary site is uncommon, constituting approximately 2 to 4% of all breast malignancies (5). Malignant melanoma is the most common tumour metastasize to the breast followed by lymphoma, lung cancer, ovarian carcinoma, soft tissue sarcoma, gastrointestinal and genitourinary tumours (4-6). In males, the most frequent site is from the prostate.

In this case report we describe the cytologic findings of thyroid papillary carcinoma metastasizing to the breast, after 24 years following total thyroidecomy along with histologic confirmation. We also discuss the differential diagnosis and usefulness of immunohistochemical staining to distinguish a metastasis from a breast tumour.

CASE REPORT
A 63 year old female with past history of a well differentiated papillary thyroid carcinoma of the left thyroid lobe, diagnosed in 1991, presented with a new breast lump. The thyroid tumour was treated with total thyroidecomy plus radioiodine ablation. She was diagnosed with lung metastases in 2005 with further radioiodine treatment. Also, she had a previous right middle lobectomy for a bronchial carcinoid some 30 years ago. On examination she had a small mobile mass in the inner upper aspect of her right breast, 24 years following total thyroidecomy. There was no obvious axillary lymphadenopathy. Serum thyroglobulin was increased at 1060 μg/L (normal: <58 μg/L). Fine needle aspiration (FNA) and simultaneous core biopsy of the right breast mass were performed.

MATERIALS AND METHODS
FNA material was collected in Thin Prep cytolyt (TP, Hologic cytyc, Malborough, Massachusetts, USA) fixative for liquid-based, thin-layer preparations. The aspirate sample was spun at 3700 rpm for 2 minutes and from the sediment, 1-2 drops were added to a Thin Prep Preserv-cyt vial. A Thin Prep slide was prepared using a TP 2000 processor, fixed in 95% ethanol and stained by the Papanicolaou method. The remainder of the sediment was used to make a cell block, fixed in 10% formalin, embedded in paraffin, routinely processed, and stained with hematoxylin-eosin (H & E).

Immunohistochemical studies were carried out on the cell block and core biopsy sections using antibodies TTF-1 (1:200; Leica), thyroglobulin (1:1000; Dako), ER (1:50; Dako), PR (premade; Leica), GATA3 (1:200; Cell Marque), GCDFP-15 (1:500; Leica), CD56 (Premade; Leica), synaptophysin (1:200; Dako), chromogranin (1:200; Cell Marque), PAX8 (1:100; Cell Marque), villin (1:100; Leica), CK 7 (1:400; Dako) and CK20 (1:200; Novocastra).

RESULTS
The Thin Prep sample was highly cellular showing blood, scattered macrophages, and numerous groups of cells with a tubulopapillary architecture and mild cytologic atypia (Figure 1a). Also seen were some cells with nuclear grooves (Figure 1b). The cell block showed numerous papillary structures (Figure 2) lined by cells which exhibited overlapping of nuclei, occasional nuclear grooves and rare intranuclear inclusions (Figure 6). Scattered psammomatous calcifications were seen.

Histologic findings
A H & E stained section of the breast core biopsy showed multiple fragments of low grade papillary tumour comprising fibrovascular cores lined by cells with overlapping nuclei, occasional nuclear grooves and rare intranuclear inclusions (Figure 3).
Figure 1a. Thin prep from FNA showing numerous groups of cells with a tubulopapillary architecture (Papanicolaou stain X 100).

Figure 1b. Thin prep from FNA showing numerous groups of cells with nuclear grooves (Papanicolaou stain X 400).

Figure 2. Cell block preparation from FNA showing papillary groups of cells with fibrovascular cores (Papanicolaou stain X 200).

Figure 3. Breast core biopsy section showing papillary fragments of cells with overlapping nuclei, occasional nuclear grooves and rare intranuclear inclusions (Haematoxylin-eosin X 400).

Figure 4. Immunohistochemical stain on cell block showing nuclear positive staining for TTF-1 (TTF-1 stain X 400).

Figure 5. Immunohistochemical stain on cell block showing focal cytoplasmic positive staining for thyroglobulin (thyroglobulin stain X 400).
Immunohistochemical findings

Immunohistochemical stains on the cell block showed the tumour cells were positive for TTF-1 (Figure 4) and they showed focal weak positivity for thyroglobulin (Figure 5). The tumour cells were negative for ER, PR, GATA3, GCDFP-15, CD56, synaptophysin and chromogranin.

Immunohistochemical stains on the core biopsy showed the tumour cells were positive for TTF-1, PAX8, CK7 and occasional cells were positive for thyroglobulin. The tumour cells were negative for ER, PR, CK20, villin, and GCDFP-15.

Figure 6. Cell block preparation from FNA showing cell with intranuclear inclusion (Papanicolaou stain X 400).

DISCUSSION

Papillary and follicular carcinomas of the thyroid gland are often referred to together as differentiated thyroid cancer (DTC). They are typically low-grade and slowly progressive. The prognosis is usually favourable and the 10 year survival rate is as high as 80-95%. Papillary carcinoma of the thyroid is the most common form of thyroid malignancy and generally carries a good prognosis since it usually remains confined to the thyroid gland and tends to metastasize locally to regional lymph nodes alone. However, distant metastasis mainly to lung and bone occurs uncommonly (1-3, 5, 7-9). Metastasis to other sites is distinctly rare and includes brain, breast, liver, kidney, muscle and skin (1,3,5,8,9). The presence of distant metastasis is a poor prognostic factor for survival, with only 50% of patients surviving after 10 years. Recognizing distant metastasis from DTC has a significant impact on clinical decision making. Metastasis to the breast from DTC is extremely rare. To date, only 11 cases have been described in the literature. All of the patients were female.

Metastasis to the breast from extra-mammary primary cancer in general is rare. The first reported case of metastasis to the breast was in 1903 by Trevithick who reported a reticulum cell sarcoma metastasis to the breast (4). The incidence of breast metastases from extra-mammary tumours in an autopsy series was reported between 1.4 and 6.6% (5). Malignant melanoma, lymphoma, lung cancers, neuroendocrine-like tumours, ovarian carcinoma, soft tissue sarcoma, gastrointestinal and genitourinary tumours are the most common cancers metastasize to the breast. Differentiating primary mammary disease from extra-mammary sources may be difficult on the clinical examination alone. The suspicion of metastasis to breast is generally straightforward when a known primary tumour is present. It is important to differentiate metastatic malignancies from primary breast tumours to avoid surgery such as mastectomy. Immunohistochemical staining is helpful for accurate diagnosis. Anti-thyroglobulin antibody, as in this case, is a good marker in confirmation of the pathological diagnosis of differentiated thyroid cancer metastasis.

The majority of breast metastases present as palpable, rapidly growing, well-circumscribed and painless breast masses with predilection to the upper outer quadrant. Unlike primary tumours, the vast majority of metastases do not demonstrate retraction of the skin or nipple, despite their superficial location (6). Distinguishing a breast metastasis from a primary mammary adenocarcinoma, based on mammographic findings, may be extremely difficult due to the wide range of imaging manifestations of the metastatic lesions. Thus, metastasis may mimic a primary malignancy or even a benign breast tumour. Occasionally, metastases to the breast demonstrate features that lead the pathologist to a correct diagnosis, such as cells with nuclear grooves, intranuclear inclusions, powdery chromatin and psammoma bodies as seen in our case. However, carcinomas with micropapillary components have been described in many organs including the breast, urinary bladder, ovary, salivary gland, thyroid and lung. Multiple psammoma bodies may be seen in metastatic ovarian carcinoma, papillary carcinoma of the thyroid, primary breast and lung carcinoma (6).

Thyroglobulin positivity excludes a breast primary, metastatic ovarian carcinoma and metastatic lung adenocarcinoma. The positive staining for TTF-1, thyroglobulin, and negative staining for ER, PR, GCDFP-15, GATA3 ruled out primary breast papillary carcinoma, papilloma and tubular carcinoma. CD56, chromogranin and synaptophysin were negative which ruled out a neuroendocrine tumour as our patient had a remote history of carcinoid of the lung. A panel of markers must be used as no single antibody is 100% sensitive and false negative results do occur. In our case TTF-1 and thyroglobulin positivity directed towards metastatic papillary carcinoma from thyroid. Metastatic disease to the breast, although rare, should be considered in differential diagnosis of malignant breast lesions as the treatment and prognosis differ significantly.

Life-long follow up is recommended for all patients with papillary carcinoma of the thyroid since the tumour may metastasize even decades after thyroid surgery. Metastatic thyroid papillary carcinoma to the breast, although rare, should be considered in the differential diagnosis of mammary tumours particularly those with a papillary pattern. The contribution of immunohistochemistry to the correct diagnosis is important. Thyroidectomy, postoperative iodine ablation, thyroxine replacement and careful follow up with serum thyroglobulin levels are associated with fewer cancer recurrences and tumour related deaths (9).

ACKNOWLEDGEMENTS

The authors acknowledge Louise Goossens for her photographic assistance and Ian Tompson for formatting images.

AUTHOR INFORMATION

Sharda Lalulu, BSc CFIAC, Cytotechnologist
Sarla Naran, BSc CFIAC, Cytotechnologist
Catherine Koleda, FRCPA MBBS BMedSc(Hons), Histol and Cytopathologist

Department of Cytology, Anatomic Pathology, Wellington SCL, Wellington Hospital
Address for correspondence and reprint requests:
Dr Catherine Koleda, Cytology Unit, Anatomic Pathology, Wellington SCL, Wellington Hospital, Wellington, New Zealand. E-Mail: Catherine.Koleda@wellingtonscl.co.nz.

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