

Pathology in Focus

Colonic carcinoma metastasis to the thyroid: a case of skip metastasis

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Abstract

Colonic carcinoma metastasis to the thyroid is rare. Here the authors present the case of an 81-year-old lady who presented with metastatic colonic adenocarcinoma in her thyroid gland. This case is unique as it is the first to demonstrate metastasis from the colon to the thyroid with no other site involvement. The use of cytokeratin immunohistochemical staining is reviewed along with the current perspectives on the concept of skip metastasis.

Key words: Neoplasm Metastasis; Colon Carcinoma; Thyroid Gland; Cytokeratin

Clinical summary

An 81-year-old woman presented to our head and neck service with a three-month history of a left thyroid swelling. Two years previously she had undergone a bowel resection for a Dukes C adenocarcinoma. Fibre-optic nasendoscopy confirmed extension of the thyroid swelling into the supraglottis and a paralysed left vocal fold. A trucut biopsy of her thyroid mass confirmed moderately differentiated adenocarcinoma in fibrous and inflammatory stroma (Figure 1). No normal thyroid tissue was present and the tumour was thyroglobulin-negative. Immunohistochemical staining was performed and showed the tumour to be positive for cytokeratin 20 (CK20) and negative for cytokeratin 7 (CK7) (Figure 2). This immunophenotype, although not pathognomonic, is typical of colorectal carcinomas. A CT scan of her neck, chest and abdomen failed to show metastasis at any other site. Arrangements were made for the patient to have a total thyroidectomy and laryngectomy.

Discussion

A wide range of primary sites may metastasize to the thyroid gland. These include kidney, malignant melanoma, breast, lung, followed by head and neck tumours, haematological malignancies, gastrointestinal tumours, genital tract tumours and sarcomas in decreasing order of frequency. Colonic carcinoma metastasis to the thyroid is rare, although microscopic metastasis in the thyroid gland has been found in 4–9 per cent of autopsy studies.^{1,2}

This is not the first case of metastatic colonic carcinoma to metastasize to the thyroid, but is unique as it demonstrates colon to thyroid metastasis with no other

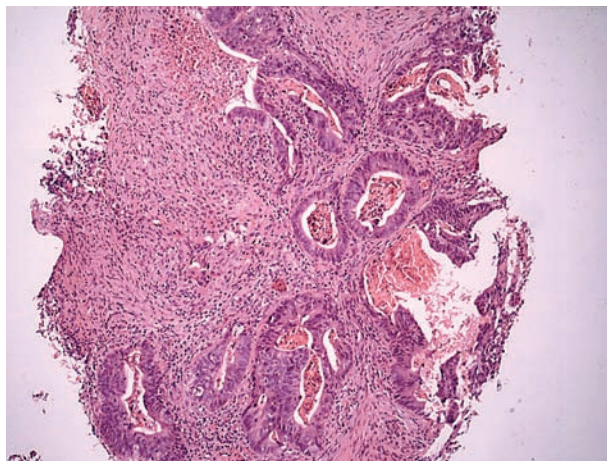


FIG. 1
Metastatic adenocarcinoma. No thyroid tissue is present (H&E; ×100).

site involvement (Table I).^{3–11} The absence of disease at sites between the primary and secondary disease can lead to the misassumption that the two disease processes are isolated. The majority of previous cases of colon to thyroid metastasis involve other major organs; in a third of cases the primary disease had metastasized to the liver. Eighty per cent of the published cases were female with an age distribution ranging from 37 to 81 years. Eighty per cent of these cases presented primarily with a neck mass. This is interesting, as without any other obvious indications of metastatic disease, and often no concurrent indications of

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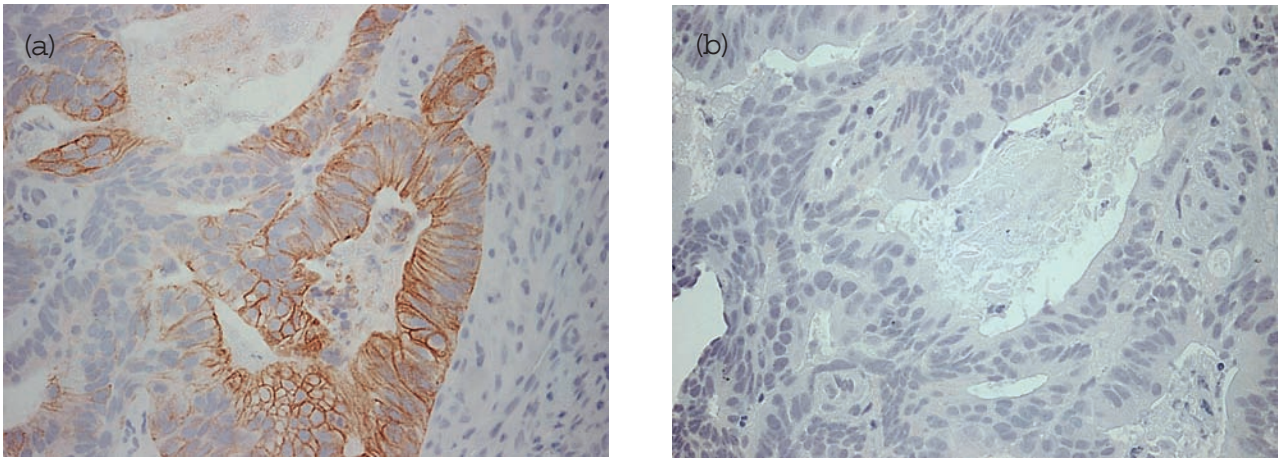


FIG. 2

Immunohistochemical staining shows the tumour to be positive for CK20 (×400) (a) and negative for CK7 (×400) (b). This immunophenotype is usually seen in adenocarcinomas of the colon

past primary disease, attention may not be immediately drawn to the possibility of metastatic thyroid disease. The surgical management of thyroid gland metastasis is often considered to be palliative resection of the affected tissue. Radiation would be indicated as adjuvant treatment to control head and neck disease; the use of chemotherapy would be dependent on the location of the primary disease. Overall survival often depends on the behaviour of the underlying primary disease.

cell carcinoma. CK7 is a neutral-basic type II cytokeratin found in adenocarcinomas of the breast, lung, and other glandular tumour types. A combination of CK20 staining with CK7 staining is complementary and was essential in achieving a histological diagnosis that was compatible with the patient's previous colonic adenocarcinoma. Other authors have advocated the use of other agents, such as villin, CEA, thyroglobulin, calcitonin, chromogranin and synaptophysin, for further support of the diagnosis of metastatic colonic adenocarcinoma over a newly developed primary carcinoma of the thyroid.^{5,8,10-12}

The lymphatic spread of colorectal carcinoma is generally believed to take place in a sequential manner from submucosal lymphoid follicles through the bowel wall to epicolic, paracolic, intermediate and para-aortic lymph nodes.¹³ This is based on the original work of Dukes and Gabriel,^{14,15} who described a non-sequential spread or 'skip metastasis' in 1% of their cases. Later studies have reported the rate of histologically detected skip metastasis in colorectal cancer to occur in 1–3 per cent of cases^{16,17} and in 18 per cent of colorectal tumours when examined by lymph node mapping and K20 RT-PCR.¹⁸ Documented cases of skip metastasis have been reported in anatomical sites other than the lower gastrointestinal tract. Skip metastasis has been particularly described as related to the fallopian tubes,¹⁹ testes²⁰ and even the head and neck.²¹ The precise mechanism of skip metastasis is unclear, but non-sequential spread within the lymphatic bed (true skip metastasis), non-anatomic early lymphatic spread to a sentinel or primary draining lymph node, or even

- **Metastasis of colonic carcinoma to the thyroid gland is rare**
- **In this case thyroid metastasis was the only metastatic manifestation of the primary colonic disease**
- **The mechanism of 'skip metastasis' and the role of cytokeratin immunohistochemical staining are reviewed**

The role of anti-cytokeratin antibodies and their subtypes has been identified as important in determining the epithelial origin of poorly differentiated tumours. CK20 is a polypeptide subtype of the acidic small type I cytokeratin group, which has been demonstrated specifically for adenocarcinoma of the colon, mucinous ovarian tumours, transitional cell carcinomas and Merkel

TABLE I

PREVIOUS CASE SERIES OF COLON TO THYROID METASTASIS: OUR CASE IS UNIQUE IN THAT NO OTHER SITES WERE INVOLVED

Author	Age/sex	Stage of colon cancer	Other metastatic sites
Make B ³	68/M	NA	Liver
Rosen IB ⁴	46/F	NA	NA
Mesko TW ⁵	59/F	Dukes B	Vertebrae, kidney
Lester JW ⁶	55/F	NA	Liver, lung
Cristallini EG ⁷	64/F	NA	Liver
Nachtigal D ⁸	69/F	Dukes A	Lung
Kim S ⁹	37/F	NA	Lymph node, skin
Kim CH ¹⁰	68/F	Dukes B	Lung
Akimaru ¹¹	67/M	NA	Lung, brain, lymph node
Present case	81/F	Dukes C	None

differences in tumour biology have all been implicated.¹⁸

It is also important to consider what factors particularly influence metastasis to the thyroid gland. Kameyama *et al.* reviewed two proposed mechanisms, namely the 'mechanical' theory and the 'seed and soil theory'.¹² The 'mechanical' theory takes into consideration the fact that the thyroid gland is well vascularized and would therefore receive a large number of blood-borne tumour cells. The second 'seed and soil theory' suggests that tumour development is a consequence of the provision of a fertile environment (the soil) in which compatible tumour cells (the seed) can proliferate. Focal nutrition and immunological mechanisms may play a part in providing a fertile 'soil'. The thyroid gland is known to have a high level of local immunity and metastasis has been shown to be more likely to develop in a previously diseased gland.²²

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