extent macrophages, are the main inflammatory cells, with only a small number of B cells.⁶ Class II major histocompatibility antigens are usually not expressed in the normal resting mammary epithelium,⁷ although occasionally weak staining may be seen. Strong class II MHC expression in the normal breast is only seen during pregnancy and lactation. The intensity of HLA-DR staining in women with sclerosing lymphocytic lobulitis varies from weak to strong, sometimes within a single biopsy specimen. Thus the patchy epithelial expression of HLA-DR in both cases reported here is consistent with sclerosing lymphocytic lobulitis, but is not strong supportive evidence. The significance of the absence of epithelial staining by LN3 in the series of Tomaszewski *et al* is difficult to judge as they give limited detail of the immunohistochemical method. The association with diabetes mellitus in both of the cases reported previously and one of our cases is another similarity with the disorder in women.

The pattern and immunophenotype of the inflammation, the presence of stromal fibrosis with epithelioid fibroblasts, as well as the

association with diabetes mellitus support the view that this disorder in the male breast is the equivalent of sclerosing lymphocytic lobulitis seen in women.

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Association between thyroid cancer of cribriform variant and familial adenomatous polyposis

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Abstract

A case of a 20 year old Japanese woman who developed thyroid cancer exhibiting unusual cribriform structures while being followed up for familial adenomatous polyposis/Gardner's syndrome is reported. The patient presented with osteomas, pigmented retinal lesions, and adenomas of the duodenum and the papilla of Vater, in addition to numerous adenomatous polyps in the colorectum. On ultrasonography, the thyroid cancer was localised to the right lobe and was identified as an irregular, internal echo tumour with a peripheral hypoechoic zone, measuring 1.8 cm in diameter. Histological examination of the resected tumour showed a concomitance of papillary proliferation and cribriform structures with follicles of varying sizes. These features can be distinguished from sporadic thyroid cancer.

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Keywords: familial adenomatous polyposis, thyroid cancer.

Familial adenomatous polyposis (FAP)/Gardner's syndrome is an inherited disorder caused by a germline mutation of the APC gene. It is characterised by intestinal adenomatous polyps predisposing to cancer. Recent long term, follow up studies have clarified that patients with this condition are also susceptible to malignancies involving multiple sites.^{1,2} The thyroid gland, particularly in women, is reported to be the most frequently involved organ.² Here, we present a young Japanese woman with thyroid cancer exhibiting unusual histological features of cribriform proliferation. These features are similar to those described recently by Harach *et al*.³ We also review previous cases described in the literature.^{4–9}

Case report

A 20 year old Japanese woman was admitted to hospital in July 1993 for treatment of colonic polyposis. The patient had been diagnosed as having familial adenomatous polyposis at the age of 11 years, when her mother had undergone a total colectomy for colon cancer involving adenomatosis of the colorectum. The patient's condition had been good and she had

Figure 1 Ultrasonographic image showing an irregular internal echo tumour with a peripheral hypoechoic zone localised in the right lobe of the thyroid gland.

no history of exposure to radiation. Physical examination was normal, except for a nodular goitre palpable in the right thyroid gland, a small osteoma posterior to the right ear, and pigmented lesions on the right ocular fundus. There were no significant findings on laboratory tests, which included assessments of serum free thyroxin (0.12 ng/l), thyrotropin (1.2 μ U/ml), thyroglobulin (6.0 ng/ml), and thyroxin binding globulin (21.5 μ g/ml) concentrations. Thyroid ultrasonography using a 7.5 MHz concave linear array probe revealed a solitary mass with an irregular internal echo pattern, with a peripheral hypoechoic zone in the middle of the right thyroid gland (fig 1). The mass measured 1.8 cm in diameter. Ultrasonography of the left lobe was normal and there was no lymphadenopathy. Fine needle aspiration, guided by ultrasonography, provided material with cytology consistent with

Figure 2 Histological examination of the resected specimen revealed an encapsulated thyroid cancer exhibiting cribriform structures with follicles of varying sizes (haematoxylin and eosin, $\times 190$).

thyroid cancer. Follow up radiography of the colon revealed an increasing number of colonic adenomatous polyps, although no evidence of malignancy was found on histological examination of biopsy specimens. Gastroduodenoscopy and histology also revealed adenomatosis of the duodenum and the papilla of Vater.

In August 1993 the patient underwent right hemithyroidectomy with lymph node dissection following total colectomy and mucosal proctectomy. The resected right thyroid gland contained a well circumscribed, firm tumour measuring 1.8 $\times$ 1.2 cm. Histological examination revealed an encapsulated tumour, composed of carcinoma cells with grooved nuclei proliferating in a concomitant papillary and cribriform fashion with follicles of varying sizes (fig 2). There was neither lymph node metastases nor vascular invasion. The entire mucosal surface of the resected bowel was studded with numerous polyps (>1000) up to 1 cm in diameter. All of the polyps were adenomas with mild to moderate epithelial atypia, containing no cancerous foci.

Six months later, ileo-anal anastomosis with a J-pouch procedure was completed. The patient's postoperative course has been stable, and follow up ultrasonography of the left thyroid gland in May 1995 was unremarkable.

Discussion

The early recognition of extracolonic malignancies is of increasing importance in patients with FAP as advances in prophylactic colectomy have resulted in a reduction in the number of deaths from colorectal cancer.^{1 2} Iwama *et al*¹ reviewed the case records of 1050 Japanese patients with FAP, and estimated that the relative risk of those patients developing thyroid cancer is 21 times greater than that of the general population. In addition, Plail *et al*⁶ have indicated that the risk in women with FAP under 35 years of age is 160 times normal. Therefore, patients with FAP should be monitored closely for signs of thyroid cancer, particularly women.

The use of ultrasonography has improved assessment of thyroid disease, even when lesions cannot be detected on clinical examination.¹⁰ It is the most suitable screening method because of it is simple, cost-effective and highly sensitive. High resolution ultrasonography can detect lesions as small as 1 mm. In addition, fine needle aspirates provide direct and specific information once a thyroid nodule has been identified on ultrasound images.¹⁰ Our patient was accurately diagnosed with thyroid cancer on the basis of ultrasonographic and aspiration biopsy findings.

To our knowledge, 40 cases of thyroid cancer in patients with FAP have been fully documented in the English literature³⁻⁹; this estimate excludes rare cases complicated by multiple endocrine neoplasia. According to the literature and our own findings, thyroid cancer associated with this condition is characterised by a female preponderance (90.0%), a papillary structure (88.6%), and occurs in patients under 35 years of age (83.8%). More than half

of the tumours (56.7%) showed multicentricity. In addition, the recognition of thyroid cancer preceded the diagnosis of intestinal polyposis in about 25% of these patients. For patients with thyroid cancer manifesting these features, examination of the colon is therefore essential.

Recently, Harach *et al*⁸ reported four cases of thyroid cancer associated with FAP, which manifested the papillary form and also had a cribriform pattern. These authors suggest that this tumour is characteristic of patients with FAP, although it has been described as a papillary cancer in previous reports because of its structure. Our patient also manifested the cribriform features, which are distinct from thyroid cancer in the general population. This histological property may suggest a relation between thyroid cancer and a genetic abnormality associated with the APC gene. Recent genetic investigations¹¹ suggest that mutation of the APC gene is unlikely to play a part in the development of a common sporadic form of papillary thyroid cancer. This finding may support the morphological distinction of thyroid cancer in patients with FAP.

Prognosis of patients with FAP and thyroid cancer is difficult to assess. Two patients with FAP and thyroid cancer have died.⁷ In addition, thyroid cancer has recurred following surgery in two^{4,5} of 29 patients with average observation periods of 7.1 years. Both of these patients underwent lobectomy at the initial surgery. Considering the incidence of multifocal development, total or near-total thyroidectomy may be a more appropriate treatment for patients with thyroid cancer and FAP.

Nevertheless, we performed a hemithyroidectomy in the present patient to maintain postoperative thyroid function as the tumour was a solitary, encapsulated cancer which did not involve the lymph nodes. Further observation using thyroid ultrasonography is mandatory to prevent recurrence. Periodic fine needle aspiration biopsy may also be necessary.

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