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Highly aggressive behaviour of occult papillary thyroid carcinoma

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Abstract
Occult papillary thyroid carcinoma is generally associated with an excellent prognosis. Distant metastasis of this tumour is extremely rare. A case of occult papillary thyroid carcinoma with metastases to the lungs, cervical lymph nodes, skeleton, and the brain is reported. The tumour expressed itself in extremely aggressive clinical behaviour and responded only partially to aggressive therapy. The controversial methods of treatment for occult papillary thyroid carcinoma are also discussed.

Key words: Thyroid neoplasms; Carcinoma, papillary, occult; Neoplasm metastasis

Introduction

Papillary carcinoma is the most common malignant tumour of the thyroid gland. It is predominantly a curable disease with a mortality rate of 11–17 per cent (Lipton *et al.*, 1987; McCaffery and Lipton, 1990). The term occult thyroid carcinoma is used for an occasional incidental finding of thyroid carcinoma during surgery for other indications (Vassilopoulou-Sellin and Weber, 1992), or when the tumour has already metastasized in a patient without a history of thyroid disease, with no clinical symptoms, with normal physical examination of the thyroid gland, and when thyroid scan, ultrasound, CT scan and thyroid functions demonstrated no abnormality in the thyroid gland (Matsuda *et al.*, 1991; Sasaki *et al.*, 1991; Vassilopoulou-Sellin and Weber, 1992).

Recently, the term occult thyroid carcinoma has been used for a tumour of less than 1.5 cm in diameter (Salvadori *et al.*, 1993). Because of its small size, the tumour is hardly detected by some of the methods of examination, and therefore is not easily found. This occult papillary thyroid carcinoma (PTC) does not differ from the usual PTC with respect to morphological, clinical, and prognostic factors. It differs only in the size of the tumour (Salvadori *et al.*, 1993).

Distant metastasis of PTC is rare (Noguchi *et al.*, 1970), and is extremely rare in occult PTC. We report a case of occult PTC with extensive metastatic process which presented itself in aggressive clinical behaviour, and discuss the controversial methods of treatment for occult PTC.

Case history

A 56-year-old woman was admitted to Rambam Medical Centre because of a dry cough, and shortness of breath which had progressively increased for three months prior to admission. It was accompanied by weakness and severe back pain. Physical examination revealed a decrease in breathing sounds and crepitation in both lungs, predominantly on the right side. The rest of the physical examination was within normal limits. X-ray of the chest showed a diffused reticulo-nodular shadowing of both lungs as well as an infiltrate in the right upper lobe (Figure 1). Thin-section of high-resolution CT of the lungs demonstrated a 5 × 5 cm mass in the upper right lung, and a diffused reticulo-nodular process in both lungs, more pronounced on the right. These findings are compatible with a diffuse interstitial metastatic process in both lungs

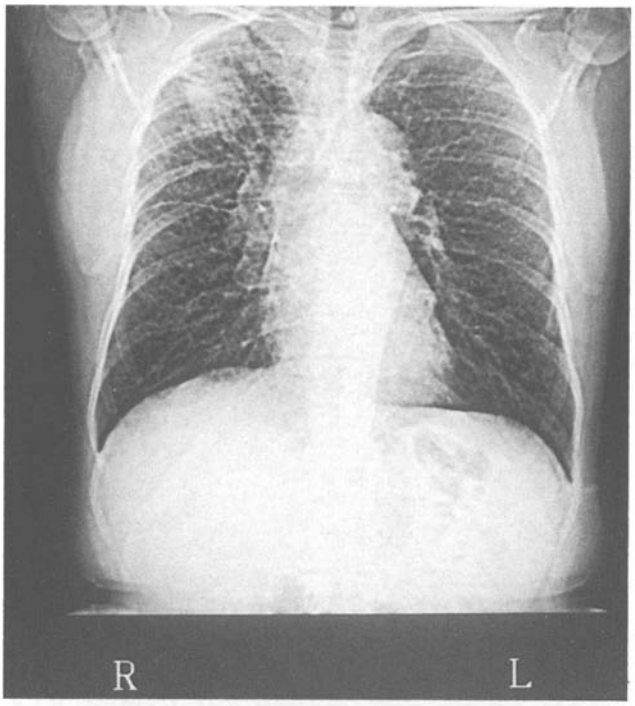

Fig. 1
X-ray of the chest showing a diffused interstitial process in both lungs as well as an infiltrate in the right upper lobe.

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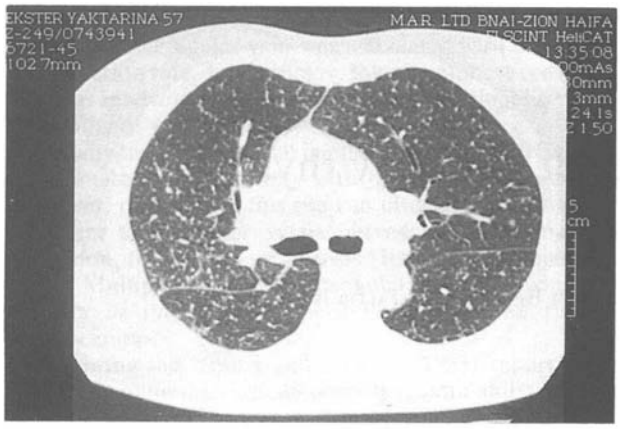

FIG. 2

Thin-section of high-resolution CT of the lungs showing a diffused reticulo-nodular process in both lungs, more pronounced on the right.

(Figure 2). Histopathological examination of a specimen from the mass in the right bronchus which was obtained by bronchoscopy showed tiny fragments of respiratory mucosa with many foci of metastatic papillary carcinoma. A few metastases were located in lymphatic spaces (Figure 3). Immunoperoxidase stain for thyroglobulin disclosed focal cytoplasmatic staining in a few malignant cells – all of these findings support the diagnosis of PTC metastasis.

Physical examination of the thyroid gland as well as

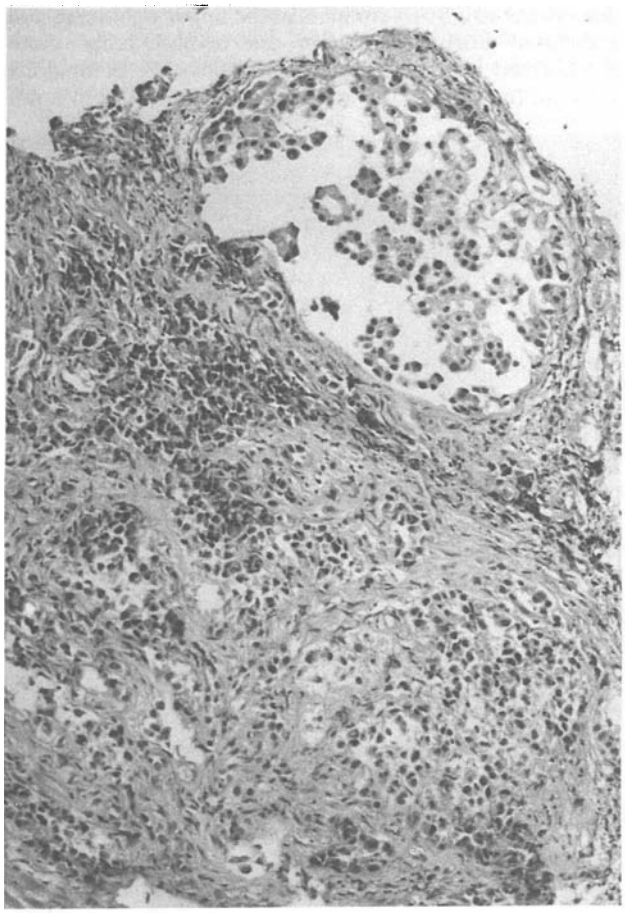

FIG. 3

A fragment of bronchial tissue showing islands of carcinoma (bottom) and a tumour implant in an open lymphatic vessel (top). (H&E; × 125).

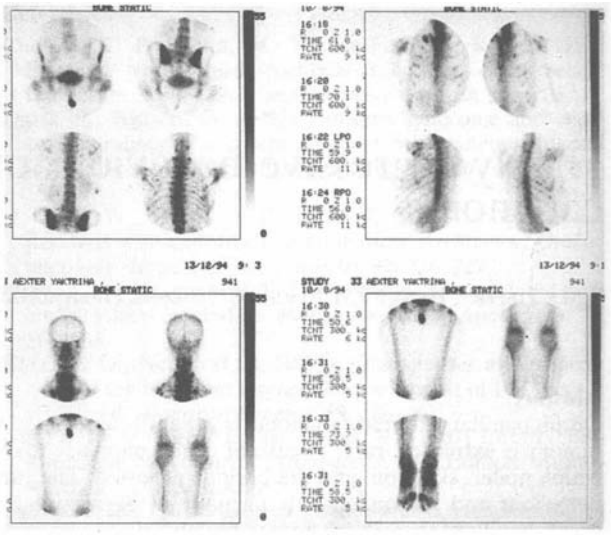

FIG. 4

A bone scan showing multiple small areas of an increased uptake in most of the skeleton.

thyroid functions, thyroid scan, ultrasound, and CT scan of the neck demonstrated no abnormality in the thyroid gland or in the neck.

To rule out the possibility of papillary carcinoma of origin other than the thyroid, breast examination and mammography (to rule out breast cancer), CT scan of the abdomen (to rule out pancreatic carcinoma), pelvic examination, pelvic CT and ultrasound (to rule out ovarian carcinoma) were carried out and no evidence of any pathology was found.

A bone scan which was performed because of persistent complaints of back pain revealed multiple small areas of increased uptake in the sacroiliac region on both sides, along the whole lumbar spine and in the anterior and posterior sides of the ribs, on both sides (Figure 4). These pathological uptakes in the bone scan are compatible with an extensive metastatic process.

During the evaluation mentioned above, she started to complain about increased weakness, dizziness, and disequilibrium. Physical examination revealed a pack of enlarged non-tender lymph nodes 3 × 2 cm in size in the right supraclavicular region which were not present on admission, ataxia, and a pathological Romberg test, all signs which did not exist before. Contrast enhanced CT of the brain revealed small enhanced lesions, one in the vermis behind the fourth ventricle, and one in the right temporo-parietal region which were compatible with metastasis (Figures 5, 6).

The supraclavicular lymph nodes were removed and were submitted for pathological examination. All the nodes showed metastases of the same papillary carcinoma that was found in the bronchial biopsy. There were also tumour emboli in lymphatic vessels in the perinodal fatty tissue (Figure 7). A focal thyroglobulin positive-staining was demonstrated in some tumour cells.

A total thyroidectomy was performed. Multiple serial sections performed on the whole thyroid gland showed normal follicular structures with no evidence of malignancy. Four days after the operation a sudden convulsive attack occurred. Since no metabolic reason was found, it was assumed that the convulsion occurred due to the brain metastasis and external radiation therapy to the brain was started. The patient was also treated by chemotherapy [etoposide (VP 16) and cisplatin] but unfortunately, only with partial response. A total body radioiodine scan showed that the tumour had not absorbed iodine, and

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FIG. 5

Contrast-enhanced CT of the brain showing an enhanced lesion (arrowed) in the vermis behind the fourth ventricle.

consequently there was no place for radioiodine therapy. Five months after the initial diagnosis, the patient was still hospitalized and her condition critical.

FIG. 6

Contrast-enhanced CT of the brain showing a small enhanced lesion (arrowed) in the right temporo-parietal region.

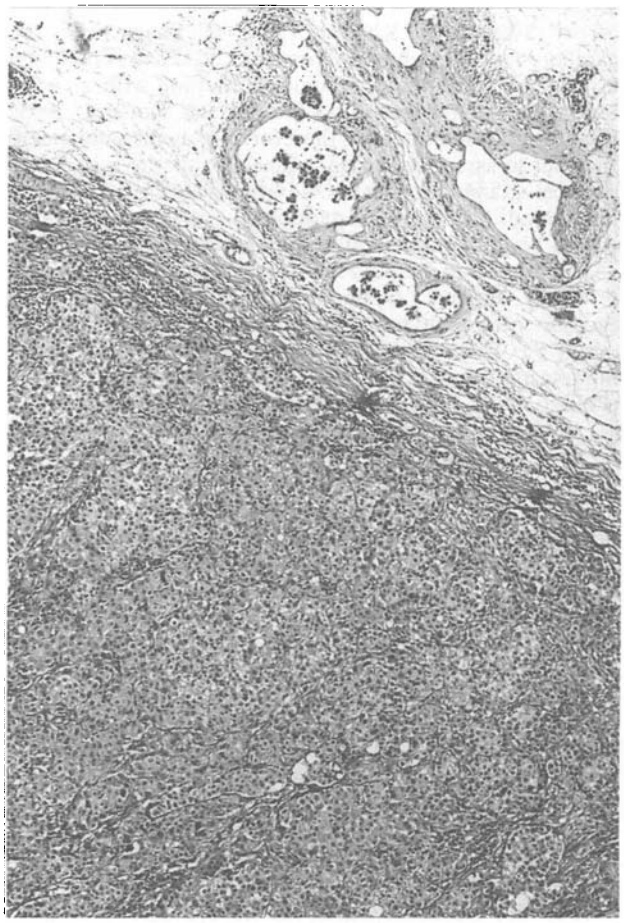

FIG. 7

The whole lymph node is replaced by papillary carcinoma. There are also tumour emboli in the lumen of lymphatic vessels (at the top in the perinodal fat). (H&E; × 50).

Discussion

PTC is the most common malignant tumour of the thyroid gland. This tumour was found in 4.6–11.3 per cent of postmortem examinations of people without a history of thyroid disease (Pelizzo *et al.*, 1990; Yamamoto *et al.*, 1990; Furmanchuk *et al.*, 1993; Martinez-Tello *et al.*, 1993). Occasionally, the occult thyroid cancer is found in surgery of the neck for other indications (Vassilopoulou-Sellin and Weber, 1992). Since PTC most frequently and preferentially spreads via the lymphatics, cervical lymph node metastases are common and are the most usual presenting sign of the disease when the thyroid cancer is occult (Matsuda *et al.*, 1991; Takami and Kodaira, 1993).

Distant metastases of PTC are uncommon (Noguchi *et al.*, 1970). Distant metastases as a presenting sign or symptom of occult PTC are extremely rare. We found only two such reports in the literature (Sasaki *et al.*, 1991; Takami and Kodaira, 1993). In one report the occult thyroid cancer was associated with pulmonary metastasis which had been considered for 15 years as a long-standing coin lesion on chest X-ray (Sasaki *et al.*, 1991), and the other osseous metastatic lesions were found in two patients with occult PTC. No reports of brain metastases in occult PTC were found. In the case reported here, the patient was suffering from pulmonary, osseous, cervical lymph nodes, and brain PTC metastases, with no evidence of the primary tumour in the thyroid gland or elsewhere in the body, and therefore it is a unique case of extremely disseminated canceromatosis.

The diagnosis of metastatic cancer is made either by fine needle aspiration (FNA) (Matsuda *et al.*, 1991), or by

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biopsy (Takami and Kodaira, 1993). The diagnosis of the papillary lesion originating from thyroid tissue is made by using the rapid immunoperoxidase method with an antibody against thyroglobulin (Takami and Kodaira, 1993) which is a fast method, and therefore highly recommended. In order to assess the primary cancer in the thyroid gland, physical examination of the thyroid gland, thyroid scan, ultrasound, CT scan, and blood test for thyroid function should be performed in all the patients with occult PTC.

The preferred method of treatment of occult PTC is primarily surgery. Opinions differ on how extended excision of the thyroid gland should be in the case of occult PTC incidentally discovered without any evidence of metastatic lesions. Some surgeons perform a lobectomy (Pelizzo *et al.*, 1990), or subtotal thyroidectomy (Chou *et al.*, 1993), but most advocate total thyroidectomy (Chou *et al.*, 1993: Ley *et al.*, 1993; Witterick *et al.*, 1993).

Most physicians agree that when the occult PTC presents with metastatic lesions, even if the primary tumour is not detected in the thyroid gland (by palpation, scan, ultrasound and CT), total thyroidectomy followed by radioiodine therapy or external beam radiotherapy is recommended as the chosen treatment. In spite of this, it is important to point out that Vassilopoulou-Sellin and Weber (1992) suggested that differentiated thyroid cancer metastases in cervical lymph nodes, discovered incidentally during surgery for another potentially more aggressive malignancy, should be approached conservatively when the thyroid gland does not demonstrate clinical or radiological lesions. Some of their patients who suffered from squamous cell carcinoma of tongue had occult PTC metastases, which incidentally were found in the cervical lymph nodes, were treated conservatively and remained without any evidence of the thyroid disease for periods from 15 months to four years.

All physicians agree that when the occult PTC presents with a symptomatic metastatic lesion, aggressive therapy which includes surgery, accompanied by adjuvant therapy is recommended as the chosen treatment for this condition.

The prognosis for occult PTC which is discovered incidentally without evidence of metastases is excellent (Vassilopoulou-Sellin and Weber, 1992), similar to the prognosis of another PTC in the same clinical condition (Salvadori *et al.*, 1993). When the occult tumour has already metastasized, a good prognosis for the patient is decreased. Since most of the studies were carried out as postmortem examinations, or published as case reports, the exact survival rate cannot be estimated exactly.

We report a case of occult PTC with an extensive metastatic process in the lungs, cervical lymph nodes, skeleton and brain (a site which has never been reported previously). The extensive spread of the metastatic lesions and their locations, as well as the severe clinical symptoms they produced, are unique. Because of the highly aggressive behaviour of the tumour, aggressive therapy, which included total thyroidectomy, radiotherapy, and chemotherapy were given to the patient. Unfortunately, in spite of this aggressive treatment, and in spite of the fact that PTC is generally a curable disease with a good prognosis (Flint *et al.*, 1991), in our patient control of the disease was not achieved.

Conclusions

Occult PTC is not a common condition, and is usually found during surgery for other reasons, or when the tumour has already metastasized. Overall, it is associated with an excellent prognosis (Martinez-Tello *et al.*, 1993), but unfortunately not in the case reported here. We recommend aggressive treatment in any case of occult PTC. Treatment should include total thyroidectomy when the tumour is located only in the thyroid gland but when the occult PTC has already metastasized, total thyroidectomy accompanied by extensive adjuvant therapy are recommended as the treatments of choice for this condition.

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