Muscular metastasis heralding medullary carcinoma of the thyroid

Rawdha Tekaya,[1] Manel Haouel,[1] Kehena Bouzid,[2] Rafik Zouari[1]

Departments of [1]Rheumatology and [2]Biochemestry, Charles Nicolle Hospital, University Tunis El Manar, Tunis, Tunisia

Abstract

Medullary thyroid carcinoma (MTC) commonly metastasizes locally to the cervical lymph nodes and distantly to the liver, lungs and bones. Metastatic involvement of the muscles is extremely rare. We reported an unusual case of undiagnosed MTC presenting with symptoms related to metastatic lesions of the brachoradialis and the gluteus medius muscles. A 53-year-old man consulted for a painful mass of the right forearm and atrophy of the quadriceps. Ultrasonography revealed a heterogeneous collection in the forearm. Computed tomographic scan showed a mass in the right lung, an enlargement of mediastinal lymph nodes and solid masses in the right gluteus medius and the left iliopoas muscle extending to the left iliac bone. Pulmonary biopsies displayed findings consistent with metastatic MTC. Fine needle aspiration cytology from the right arm swelling revealed a lesion with the same calcitonin immunostaining patterns as the lung metastasis. The diagnosis of multiple metastases (lung, muscle and bone) of MTC is established. The patient has received local radiation therapy and was planned for chemotherapy. Muscular metastases from MTC are rare and although their prognosis is poor, local treatment may be worthwhile.

Introduction

Medullary thyroid carcinoma (MTC) is a neuroendocrine tumor arising from parafollicular C cells that produce calcitonin. It represents only approximately 4% of all thyroid tumors.[1] MTC commonly metastasizes locally to the cervical lymph nodes and distantly to the liver, lungs and bone. Metastatic involvement of the muscles is extremely rare. We report the clinical and radiological features of a case of metastatic MTC in the muscles along with a brief review of literature.

Case Report

A 53 year-old man was admitted to our department complaining of severe right thigh pain with functional impairment. He also reported a weight loss of 10 kg within the past three months. On physical examination, he had a 3×2 cm mass fixed to the right forearm in the brachoradialis muscle without ulceration of the skin, atrophy of the right quadriceps muscle and supraclavicular lymph node enlargement on the left side of the neck. Ultrasound of the brachioradialis muscle confirmed a 32×21 mm solid inhomogeneous mass. No other abnormal findings were evident on clinical examination. Laboratory investigations revealed an erythrocyte sedimentation rate of 80 mm/hour (normal value <20 mm/hour), a C-reactive protein of 20 mg/L (normal value <6 mg/L), a lactate dehydrogenase of 600 IU/L (normal range: 190-390 UI/L) and a slightly elevated calcemia of 3 mmol/L (normal range: 2.2-2.6 mmol/L).

On metastatic work up, chest X-ray ant computed tomographic scan (CT) showed a mass in the apical segment of the right upper lobe of the lung and enlargement of mediastinal lymph nodes. CT of abdomen and pelvis demonstrated an inhomogenously solid mass measuring 13×16 mm in the right gluteus medius involving the homolateral iliac bone and another solid mass measuring 33×21 mm in the left iliopoas muscle extending to the left iliac bone (Figure 1). Multiple biopsies were obtained from the right lung mass. These displayed sheets of spindle-shaped, polygonal cells separated by fibrous stroma, with abundant eosinophilic cytoplasm. All the slides stained positively for calcitonin in immunohistochemical analysis. These findings were consistent with metastatic medullary carcinoma of thyroid. Fine needle aspiration cytology from the right arm swelling revealed a lesion with the same calcitonin immunostaining patterns as the lung metastasis. The diagnosis of multiple metastasis (lung, muscle and bone) of medullary carcinoma of thyroid is established.

Thyroid ultrasound examination detected a single hypoechoic nodule. Thyroid function tests were normal: free thyroxine (FT4) was 1.02 ng/dL (normal range: 0.70-1.48 ng/dL) and thyroid-stimulating hormone (TSH) was 1.5 mcUI/mL (normal range: 0.35-4.94 mcUI/mL); thyroglobulin level was 13,7 ng/mL (normal range: <35 ng/mL) but calcitonin level was slightly increased at 60 pg/mL (normal range <56 pg/mL).

As a palliative measure for pain relief the patient was trigged for a short course of external radiotherapy to the right forearm and the right thigh with only modest improvement. The patient is being planned for systemic chemotherapy.

Correspondence: Rawdha Tekaya, Department of Rheumatology, Charles Nicolle Hospital, University Tunis El Manar, Tunis, Tunisia.
E-mail: tekayarawdha@yahoo.fr

Key words: muscular metastasis, medullary thyroid carcinoma, calcitonin.

Conflict of interests: the authors declare no potential conflict of interests.

Received for publication: 23 August 2012.
Revision received: 10 August 2012.
Accepted for publication: 24 September 2012.

Rheumatology Reports 2013; 5:e2
doi:10.4081/rr.2013.e2

Discussion

MTC is mainly sporadic in nature, but a hereditary pattern is present in 20-30% of cases, transmitted as an autosomal dominant trait.[1] The familial form of MTC usually occurs as a component of MEN type IIa (Sipple syndrome), characterized by the combination of MTC, adrenal pheochromocytomas (often bilateral), and hyperplasia of the parathyroid glands.[2] Our case was a sporadic one without adrenal or parathyroid involvement. Sporadic MTC can arise clinically at any age but its incidence peaks during the fourth and sixth decades of life.

MTC is a subset of thyroid tumors characterized by aggressiveness. Metastases are more frequent in lymph nodes and less in the lung and bone. Clinical neck lymph node metastases are detected in half of patients and may reveal the disease.[2,3] Metastases outside the neck, in the liver, lungs, bones and less frequently brain and skin, are present initially in 20% of cases. Distant metastases are usually multiple in involved organs. Although MTC is an aggressive tumor with early metastases, the clinical course is often long, with continued morbidity and mortality extending up to 20 years after the initial diagnosis.[4] Isolated MTC typically demonstrates a relatively indolent biologic progression, as seen in our case.

Serum calcitonin is the most specific and sensitive marker of MTC for both the primary diagnosis and the postsurgical follow-up; it is produced in abnormally high concentrations by almost 100% of primary and metastatic MTCs. However in rare cases, as described here, serum calcitonin can be negative or at moder-

ate high level.[5] Although our patient had a MTC with multiple metastases, serum calcitonin was slightly elevated. It is possible that rare forms of MTC go along with mutations in the calcitonin/*CGRP* gene which might be responsible for the normal or even relatively reduced calcitonin levels.[5] It would be interesting to examine the calcitonin/*CGRP* gene structure in these patients. In this patient, the tumour showed positivity for calcitonin in the immunhistochemistry which is in line with the latter hypothesis that calcitonin production is active but secretion mechanisms might be altered.

Prognostic factors relevant to outcome in MTC include age at diagnosis, male gender, the initial extent of the disease including lymph node and distant metastases, tumour size, extra-thyroid invasion, vascular invasion, calcitonin immunoreactivity and amyloid staining in tumor tissue.[6,7] Metastases at unusual sites are typical of dedifferentiation and often arise several years from onset. We reported an unusual case of MTC associated with diffuse initial metastases to the skeletal muscles, lungs and bones. The muscle is uncommonly involved by metastatic disease. The rare cases of muscle metastasis described in the literature are all connected with follicular thyroid carcinoma,[8,9] and exceptionally with papillary thyroid carcinoma.[10] In this patient, we have considered that the lesions were due to invasion of muscle metastasis towards the bones rather than direct progression of bone metastasis towards the muscular tissues as there was no bone involvement in the arm and there was no pattern of bone metastasis in the iliac bone such as cortical bone reacts or marrow changes on CT scan. To the best of our knowledge, this is the first report of a MTC metastasizing to the forearm and thigh muscles. The exact pattern of dissemination to the muscle is not clear from the available literature. It is believed that muscle pH and muscle's contractile ability contribute to the resistance of skeletal muscles to metastatic disease. Psoas, iliopsoas, paraspinal muscles and proximal musculature of the upper and lower limbs represent the most frequently involved skeletal muscle sites. Although various imaging studies have been used to identify metastasis to muscle, none are specific for differentiating among carcinomas, sarcomas or other muscle disorders. On unenhanced CT scans, muscle metastasis is revealed as an enlargement of the muscle. Occasionally, the findings may be subtle because the tumor is isodense to the surrounding muscle, and contralateral asymmetry is necessary to make the diagnosis. Management of metastatic disease is first orientated towards the relief of symptoms. External radiation therapy is indicated for bone and muscular metastases not amenable to surgery, especially when they are painful or located in the spine, the base of the skull, and in pelvic or long bones. It procures rapid relief of bone and muscular pain, and slower recalcification of bone lesions. This patient underwent a short course of external radiotherapy to the forearm and the thigh with modest relief of pain. Treatment with radioactive iodine is pointless, because C cells do not take up radioiodine and radioactive iodine covalently linked to ^{123}I-meta-iodobenzylguanidine (MIBG) offers no significant benefit.[11]

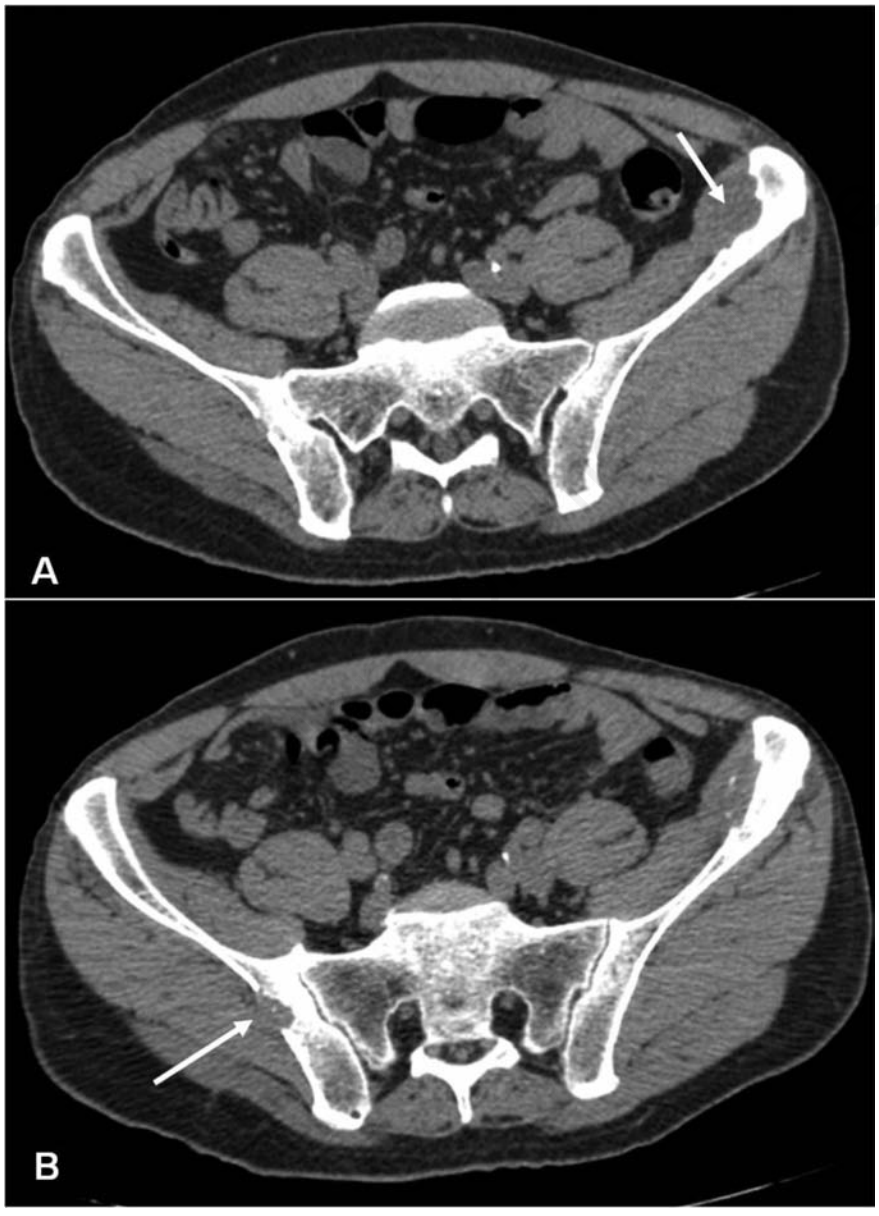

Figure 1. Transversal computed tomography view of the pelvis showing an enlargement of the right gluteus medius involving the homolateral iliac bone (A) and another muscular metastasis in the left iliopoas muscle extending to the iliac bone (B).

Conclusions

In a patient with MTC, although skeletal muscle metastases are rare, it should be considered along with other benign lesions in the differential diagnosis. An accurate diagnosis of this muscular metastasis is important to avoid unnecessary surgical procedures and to implement an appropriate systemic therapy although the presence of skeletal muscle metastases in the setting of disseminated disease offers less hope for curative treatment.

References

1. Hundahl SA, Fleming ID, Fremgen AM, et al. A National Cancer Data Base report on 53,856 cases of thyroid carcinoma treated in the US, 1985-1995. Cancer 1998;83:2638-48.
2. Moley JF, DeBenedetti MK. Patterns of nodal metastases in palpable medullary thyroid carcinoma: recommendations for extent of node dissection. Ann Surg 1999;229:880-7.
3. Scollo C, Baudin E, Travagli JP, et al. Rationale for central and bilateral lymph node dissection in sporadic and hereditary medullary thyroid cancer. J Clin Endocrinol Metab 2003;88:2070-5.
4. Kebebew E, Clark OH. Medullary thyroid cancer. Curr Treat Options Oncol 2000;1:359-67.
5. Sand M, Gelos M, Sand D, et al. Serum calcitonin negative medullary thyroid carcinoma. World J Surg Oncol 2006;4:97.
6. Pacini F, Castagna MG, Cipri C, Schlumberger M. Medullary thyroid carcinoma. Clin Oncol 2010;22:475-85.
7. Kebebew E, Ituarte PH, Siperstein AE, et al. Medullary thyroid carcinoma: clinical characteristics, treatment,prognostic factors, and a comparison of staging systems. Cancer 2000;88:1139-48.
8. Iwai H, Ohno Y, Ito H, et al. Renal rupture associated with a poorly differentiated follicular thyroid carcinoma metastasizing to the thigh muscle, lung and kidney. Intern Med 2005;44:848-52.
9. Chaffanjon PCJ, Sturm N, Caravel JP, et al. Pelvic muscular metastasis of well differentiated thyroid carcinoma. Ann Chir 2004;129:100-2.
10. Bruglia M, Palmonella G, Silvetti F, et al. Skin and thigh muscle metastasis from papillary thyroid cancer. Singapore Med J 2009;50:61-4.
11. Leboulleux S, Baudin E, Travagli JP, Schlumberger M. Medullary thyroid carcinoma. Clin Endocrinol 2004;61:299-310.