

CASE REPORT

¹⁸F-Fluorine-18-L-dihydroxyphenylalanine (¹⁸F-DOPA) positive isolated peritoneal carcinomatosis from a MENII-related medullary thyroid carcinoma. About an atypical metastatic site and utility of ¹⁸F-FDOPA

Anne-Laure Aziz¹, Lawrence Dierickx¹, Frederic Courbon¹, David Taïeb² & Slimane Zerdoud¹

¹Nuclear Medicine, Institut Claudius Regaud, Toulouse, France

²Nuclear Medicine, Assistance Publique-Hôpitaux de Marseille, Marseille, France

Correspondence

Anne-Laure Aziz, Nuclear Medicine, Institut Claudius Regaud, Toulouse, France.
Tel: 05 31 15 56 22;
Fax: 05-61-32-27-54;
E-mail: anne-laure.aziz@hotmail.fr

Funding Information

No funding information provided.

Received: 2 May 2014; Revised: 20 July 2014; Accepted: 23 August 2014

Clinical Case Reports 2015; 3(2): 81–83

doi: 10.1002/ccr3.159

Key Clinical Message

A patient, operated for a medullary thyroid carcinoma (MTC) with a positive RET mutation, showed several peritoneal nodes on a computed tomography (CT), with increased Thyrocalcitonine. A ¹⁸F-Fluorine-18-L-dihydroxyphenylalanine (¹⁸F-FDOPA) positron emission tomography (PET/CT) showed isolated tracer uptake on the nodes. A biopsy confirmed that it was from the MTC, with the same RET mutation as in blood.

Keywords

¹⁸F-DOPA (¹⁸F-Fluorine-18-L-dihydroxyphenylalanine), medullary thyroid carcinoma, multiple endocrine neoplasia, peritoneal carcinomatosis.

Introduction

Medullary thyroid carcinoma (MTC) is a relatively rare type of thyroid cancer, originating from parafollicular cells. It occurs in a sporadic (75%) and in a familial form (25%): multiple endocrine neoplasia (MEN) II syndrome. Distant metastases from MTC usually occur in lungs, bones, liver, and infrequently in brain.

Peritoneal carcinomatosis is defined as an advanced stage of abdominal neoplastic disease (gynecological tumors, gastrointestinal carcinomas, and rarer peritoneal sarcoma or mesothelioma). An extraabdominal primary cancer causing peritoneal carcinomatosis is rare (it has been reported with lung cancer or breast cancer). The prevalence could be underestimated, as suggested by autopsy findings. Besic et al. reported that in 13% of 45 patients with anaplastic thyroid carcinoma, a mesentery or peritoneum site of distant metastasis was detected at autopsy [1]. In our patient, peritoneal carcinomatosis was isolated, which remains uncommon.

To our knowledge, this is the first case of an isolated peritoneal carcinomatosis associated with MTC.

Case Report

A 38-year-old male presenting with voluminous cervical lymph nodes, a thyroid solid tumor on computed tomography (CT) scan, and high calcitonine (8050 ng/L) was diagnosed with MTC. He underwent surgery (total thyroidectomy, central and lateral lymph node dissection). Pathological examination revealed a 9-cm MTC with extrathyroidal extension and 11 positive lymph nodes of the 87 examined, staged pT4apN1b. Radiotherapy (63 Gy) on cervical site was performed after surgery.

A familial genetic screening revealed the same RET (rearranged during transfection) proto-oncogene mutation (L790F, Leucine790 Phenylalanine) in the patient's blood, in his father considered as index case (72 years old) and in his daughter (10 years old).

Six months after treatment, calcitonine decreased to 48 ng/L. However, an important increase of calcitonine was observed 6 (613 ng/L) and 9 months later (1314 ng/L). Carcino-embryonic antigen (CEA) and urinary catecholamines were both negative. No evidence of pheochromocytoma was found. CT and magnetic

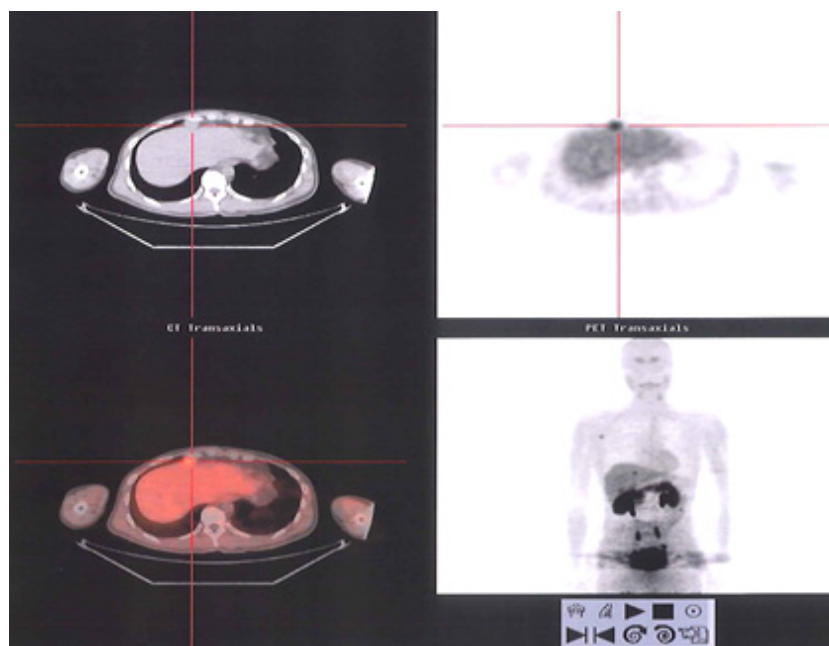


Figure 1. ¹⁸F-DOPA PET/CT showing high uptake in several peritoneal and retroperitoneal nodes.

resonance imaging (MRI) showed several peritoneal and retroperitoneal nodes: in cardio-phrenic angle (size of 14 mm), at the back of the right kidney (size of 18 mm), at the back of the left kidney (size of 13 mm), showing increased T2 and increased diffusion signal on MRI.

¹⁸F-FDG-PET/CT (¹⁸Fluorodeoxyglucose positron emission tomography/CT) and ¹⁸F-F DOPA-PET/CT (¹⁸F-Fluorine-18-L-dihydroxyphenylalanine) (Fig. 1) showed significant uptake in the peritoneal nodes (higher in ¹⁸F-DOPA than in ¹⁸F-FDG), without increased uptake on the head and neck region. MiBg-I123 scintigraphy and Somatostatin Receptor Scintigraphy (SRS) were both negative.

A retroperitoneal node's biopsy was performed and showed a morphological and immunohistochemical profile confirming the medullary carcinoma's origin (tumoral cells with positive calcitonine, synaptophysine, and TTF1 (thyroid transcription factor 1). CEA was negative. RET mutation was positive in the node (with the same mutation as found in blood: L790F, exon 13).

A treatment with tyrosine kinase inhibitors (VANDE-TANIB) was started.

Discussion

We report the case of a patient presenting with a hereditary form of MTC, without pheochromocytoma or hyperparathyroidism and with a L790F mutation in the RET proto-oncogene, in blood test and in a retroperitoneal node.

Hereditary MTC is caused by autosomal dominant gain-of-function mutations in the RET proto-oncogene. Germ-line mutation in the RET proto-oncogene in exons 10, 11 and less frequently in 13, 14, 15, and 16 are found in most of the familial cases (nearly 95%) [2]. L790F is a point mutation of DNA (deoxyribonucleic acid) change from TTG to TTT, resulted amino acid change from Leucine to Phenylalanine, first reported in 1998 by Berndt *et al.* [3]. Several studies report an association between the L790F mutation and the development of pheochromocytoma [4]. L790F mutation is usually associated with indolent disease; however, our patient presented bad prognosis criteria such as short CEA doubling time (from 613 to 1314 ng/L in 3 months).

¹⁸F-FDOPA PET/CT showed isolated high uptake in the peritoneal nodes. We know that ¹⁸F F-DOPA PET/CT is a useful supplement to morphological diagnostic imaging [5]. A recent study of Imperiale *et al.* suggests that ¹⁸F-DOPA is a sensitive functional imaging for the detection of primary neuroendocrine tumors occult on SRS, particularly if the tumor shows a low proliferation index and high level of serotonin or calcitonine [6]. Our case report suggests that ¹⁸F-FDOPA PET/CT could be used with a good accuracy in patients presenting MTC, especially with a L790F-RET mutation, to diagnose metastatic spread (such as peritoneal carcinomatosis); other studies with more patients are necessary to determine the place of ¹⁸F-FDOPA in the diagnosis of peritoneal metastases from MTC.

Therapeutic options in metastatic MTC are limited. In 10–20% of cases, a short and moderate response is reported using doxorubicin. Tyrosine kinase inhibitors (TKI) are proposed for the treatment of progressive MTC without possibility of surgical treatment, in locally advanced or metastatic disease [7].

After discussion in national multidisciplinary meeting, we proposed a treatment by TKI (Vandetanib). After 3 months of treatment, we observed an excellent response with a major decrease of Calcitonine (from 1250 to 33 ng/mL) and significant decrease of the metastatic nodes on MRI. Only minor adverse effects were observed (passing skin rash, minor diarrhea).

A surgical treatment of peritoneal carcinomatosis by cytoreductive surgery and hyperthermia intraperitoneal chemotherapy (HIPEC) was discussed, as it is classically used in disseminated peritoneal surface malignant disease and offers good results in tumoral control. However, there are currently no reports on literature for this aggressive treatment in this particular context. Other studies are necessary to determine its potential efficiency.

Conclusion

We report the first case of MTC with proved metastatic isolated localization of peritoneal carcinomatosis, confirmed by pathological examination. This case suggests that ¹⁸F-FDOPA may be interesting in the diagnosis of peritoneal nodes of unknown primitive in patients presenting with MTC, especially if bad prognosis criteria are observed. We observed an excellent response at 3 months of treatment by Vandetanib. The place of other specific treatments as HIPEC has to be evaluated in this particular context.

Conflict of Interest

I certify that neither I nor my co-authors have a conflict of interest that is relevant to the subject matter or materials

included in this work, in particular no employment or consultancy within the past 2 years for any entity involved with this research.

References

1. Basic, N., and B. Gazic. 2013. Sites of metastases of anaplastic thyroid carcinoma : autopsy findings in 45 cases from a single institution. *Thyroid* 23:709–713.
2. Komminoth, P. 1997. The RET proto-oncogene in medullary and papillary thyroid carcinoma. Molecular features, pathophysiology and clinical implications. *Virchows Arch.* 431:1–9.
3. Berndt, I., M. Reuter, B. Saller, K. Frank-Raue, P. Groth, M. Grussendorf, et al. 1998. A new hot spot for mutations in the RET protooncogene causing familial medullary thyroid carcinoma and multiple endocrine neoplasia type IIA. *J. Clin. Endocrinol. Metab.* 83:770–774.
4. Gimm, O., B. E. Niederle, T. Weber, M. Bockhorn, J. Ukkat, M. Brauckhoff, et al. 2002. RET protooncogene mutations affecting codon 790/791: a mild form of multiple endocrine neoplasia type IIA syndrome? *Surgery* 132:952–959.
5. Hoegerle, S., C. Althoefer, N. Ghanem, I. Brink, E. Moser, and E. Nitzsche. 2001. ¹⁸F-DOPA positron emission tomography for tumour detection in patients with medullary thyroid carcinoma and elevated calcitonin levels. *Eur. J. Nucl. Med.* 28:64–71.
6. Imperiale, A., E. Rust, S. Gabriel, J. Detour, B. Goichot, B. Duclos, et al. 2014. ¹⁸F-Fluorodihydroxyphenylalanine PET/CT in patients with neuroendocrine tumours of unknown origin: relation to tumour origin and differentiation. *J. Nucl. Med.* 55:367–372.
7. Wells, S. A. 2011. Vandetanib in patients with locally advanced or metastatic medullary thyroid cancer: a randomized, double-blind phase III trial. *J. Clin. Oncol.* 5:5–9.