

SHORT REPORT

Role of the Genetic Study in the Management of Carotid Body Tumor in Paraganglioma Syndrome

M. Antonello ^{a,*}, M. Piazza ^a, M. Menegolo ^a, G. Opocher ^b,
G.P. Deriu ^a, F. Grego ^a

^a Department of Cardiac, Thoracic and Vascular Sciences, Section of Vascular and Endovascular Surgery, University of Padua, Italy

^b Endocrinology Unit, University of Padua, Italy

Submitted 31 March 2008; accepted 17 June 2008
Available online 8 August 2008

KEYWORDS

Succinate dehydrogenase;
Carotid body tumor;
Paraganglioma

Abstract Diagnosis of carotid body tumor (CBT) was made in a 36 years old woman. The pre-operative examination included genetic analysis of the succinate dehydrogenase that showed a mutation in his subunit D responsible of multiple paraganglioma at slow growth. Subsequently a thoraco-abdominal CT and indium¹¹¹ octreotide body scan were performed and another paraganglioma was detected in the anterior mediastinum. CBT was surgically removed; differently the thoracic lesion due to his benign genetic profile was not treated. During a 3-years follow-up the thoracic paraganglioma as expected, didn't increase. Genetic analysis of succinate dehydrogenase, should be performed in the management of CBT.

© 2008 European Society for Vascular Surgery. Published by Elsevier Ltd. All rights reserved.

Introduction

Carotid body tumours (CBT) can cause significant disability and death. The succinate dehydrogenase (SDH) genes encode three subunits (B,C,D) of mitochondrial complex II, a heterotetrameric complex involved in the Krebs cycle and the aerobic electron-transport chain. Mutations of SDH are implicated in familial and sporadic form of CBT.¹ Transmission is autosomal dominant with incomplete penetrance.

When related to one of these mutations, CBT is frequently associated with other silent paraganglioma (PGL).¹

Report

A 36 year old female was referred with a right CBT. At age 16 a jugulotympanic PGL had been resected. Five years later a local recurrence was treated in another institution which required ligation of the left internal carotid artery. The operation was complicated by cranial nerve palsies. For the present admission, the patient presented with a right-sided neck mass, left tongue deviation, motor impairment of the scalene muscle block and paralysis of the IX, X, XI

* Corresponding author. Tel.: +39 498212638; fax: +39 498212637.
E-mail address: michele.antonello.1@unipd.it (M. Antonello).

and XII left cranial nerves. A magnetic resonance angiography of the neck showed a mass of 3.5 by 3 cms splaying the carotid artery bifurcation (Fig. 1). Normal levels of plasma and urinary metanephrine and chromogranin-A were found.

Single nucleotide polymorphism of SDH was assessed using a Big-Dye Terminators v.3.1 Cycle Sequencing Kit and ABI Prism 3100 DNA Analyzer (Applied Biosystems). These studies demonstrated a mutation (c.341G>C p.Y114C) of the sub-unit D gene. This polymorphism has been associated with a high risk of multiple PGL.² A thoraco-abdominal CT angiogram was performed and demonstrated a mass of 3.5 by 2 cm in the anterior mediastinum, suggestive of PGL (Fig. 2A). An indium¹¹¹ octreotide body scan confirmed the diagnosis.

After a multidisciplinary discussion involving an endocrinologist, thoracic and vascular surgeons it was decided, because of the age of the patient and the benign nature of PGLs, to defer the treatment of the thoracic lesion and to follow it with annual MR scans. Because of the natural history of Shamblin Type II CBT (surrounding carotid vessels or partly enclosing them) and the likelihood of future symptoms related to local compression, the CBT was resected. The patient's postoperative course was unremarkable and she was discharged on postoperative day 4. The patient was followed-up with annual carotid duplex scan and thoracic MR that showed no signs of local recurrence or enlargement of the thoracic PGL at 3-years (Fig. 2B).

Discussion

Mutation of the sub-unit D of the SDH gene is found in 79% of head and neck paraganglioma (HNP), in 53% of adrenal pheochromocytoma, in 39% of extra-adrenal pheochromocytoma and in 78% of multifocal benign tumors.² Therefore,

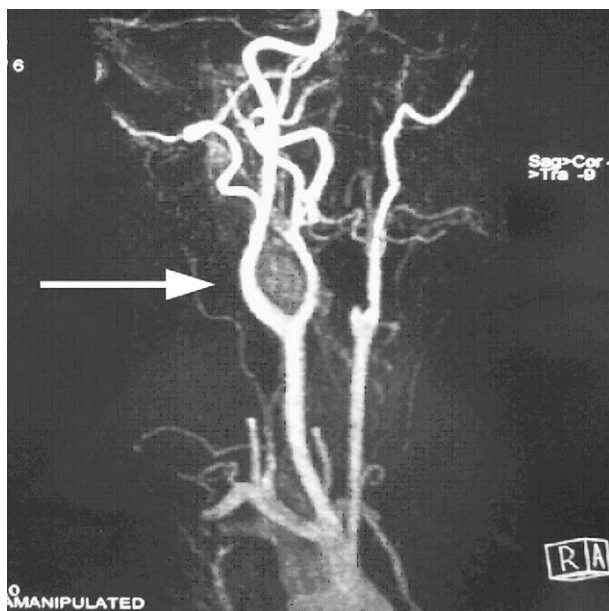


Figure 1 Preoperative MR showing the carotid body tumor on the right carotid bifurcation.

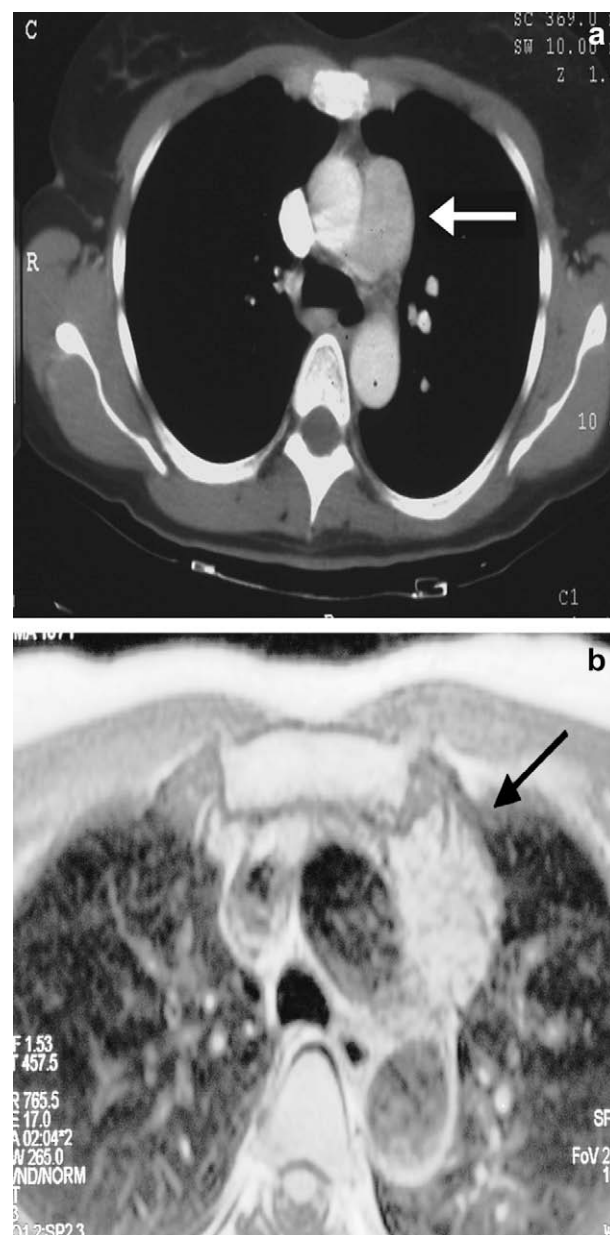


Figure 2 (a) Preoperative CT showing a paraganglioma in the anterior mediastinum; (b) MR performed after 3 years of follow-up showing the unchanged size of the paraganglioma in the anterior mediastinum.

all patients with this mutation should undergo other studies such as contrast enhanced thoracoabdominal CT scan and Indium¹¹¹ octreotide body scan to evaluate other possible PGL sites.

Management of these lesions should be based on their malignant potential and on their likelihood of causing symptoms by local growth and compression of adjacent structures. For most CBTs early surgical excision represents the treatment of choice to minimize risks of cranial nerve and carotid artery involvement or injury. When CBT is classified as Shamblin type I or II surgical excision is strongly recommended.

To treat the thoracic PGL a traditional surgical approach is the only method to obtain a radical resection of the mass

allowing a long-term survival of about 84% as opposed to 50% when resection is performed with other minimally invasive techniques. The surgical procedure itself has an operative mortality of about 6%.³ In the case reported the multidisciplinary team decided, considering the young age of the patient, the operative risk and the benign character of PGL suggested by the genetic analysis, to treat the thoracic PGL conservatively. As predicted by its genetic profile the mediastinal PGL did not enlarge during the three year follow-up.

Molecular screening for mutations in genes coding for the subunit B, C and D of SDH, is recommended in cases of familial and sporadic HNP to guide a multidisciplinary team in the diagnosis and management of the lesions. In sporadic

HNP with a SDH mutation screening should also be performed on the family.

References

- 1 Baysal BE. Hereditary paraganglioma targets diverse paraganglia. *J Med Genet* 2002 Sep;39(9):617–22.
- 2 European-American Paraganglioma Study Group. Distinct clinical features of paraganglioma syndromes associated with SDHB and SDHD gene mutations. *JAMA* 2004 Aug 25;292(8):943–51.
- 3 Andrade CF, Camargo SM, Zanchet M, Felicetti JC, Cardoso PF. Non functioning paraganglioma of the aortopulmonary window. *Ann Thorac Surg* 2003 Jun;75(6):1950–1.