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CASE REPORT

THE MALIGNANT PARAGANGLIOMA: ABOUT A MOROCCAN CASE TREATED IN THE MEDICAL ONCOLOGY DEPARTMENT OF FEZ [CASE REPORT]

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ABSTRACT

Head and neck paragangliomas are tumors of a neuroendocrine nature originating from neural crest cells. These tumors are often difficult to diagnose and treat. We report a case of an 86 years old female presenting with a right tumefaction of the neck who had tumor localized at the carotid bifurcation. The serum catecholamine levels were normal. The tumor was unresecable. The radiological exploration concluded the diagnosis of a paraganglioma and confirmed the presence of visceral metastasis. The treatment was based on a local radiotherapy and systemic treatment with antiangiogenic agents.

INTRODUCTION

Paragangliomas are neoplasms that develop from the paraganglia tissues, which are themselves of neural crest origin. Non-functional paragangliomas pose a significant diagnostic challenge. In the absence of typical symptoms of catecholamine excess, the diagnosis of such tumors is often delayed. There is no consensus in the literature regarding a specific treatment modality for malignant paraganglioma of the head and neck region. We report the case of a patient who presented a paraganglioma of the head and neck with metastases. She was treated with sunitinib stopped by digestive toxcity. Patient remained stable for 3 years under surveillance.

Case Presentation: An 86 years old female was referred to our department with a right tumefaction that had progressed over several years. The patient has no symptoms of excess catecholamine or history of hypertension or other comorbidities. There was no family history of illness. The physical examination found a mass measuring 5 cm (fig 1). Computed tomography (CT) scan showed hyper vascularized tumor mass on the right carotid bifurcation measured 6*4.5*3.5 cm extending mandibular angle. It represses the external carotid forward; the internal carotid back and jugular vein laterally. This aspect evokes paraganglioma. No distance metastasis was found. (Fig 2) Magnetic resonance imaging (MRI) showed tumor mass measuring 47 * 34 * 43 mm repressing the carotid bifurcation and the internal jugular vein. (Fig 2) This was suggestive of a paraganglioma of the carotid bifurcation.24-hour urine catecholamine levels were negative. Surgery was denied the sight of the anatomical mass connections. The patient was referred to radiotherapy department where she received external radiation of 50 Gy to the tumor mass. Another Computed tomography (CT) scan revealed a stable paraganglioma in the carotid bifurcation, multiple diffuse lung nodules measuring 17.6 mm, lesion in the left adrenal gland measuring 32 * 21 mm and hypo dense lesion in the IV segment of liver. Abdominal MRI showed a heterogeneous lesion T1 hypo intense and T2 hyper intense measuring 20 * 32 mm diameter of the left adrenal gland and the presence of a liver lesion in segment V measuring 29 * 47mm in diameter. The patient was referred to the medical oncology department. After a normal transthoracic ultrasound with left ventricular ejection fraction at 62%, the patient was treated with sunitinib at a dose of 50 mg (4 weeks on 2 weeks off). After two weeks, the patient returns with uncontrollable vomiting with abdominal pain and impaired performance status. Doses were reduced to 37.5 and 25 mg with the same toxicity profile after each reduction. The decision was “wait and see”. Three years later, the patient has a clinical, a biological and a radiological stabile disease.

DISCUSSION

Paragangliomas are rare vascularized extra-adrenal tumors of neuroectodermal origin.

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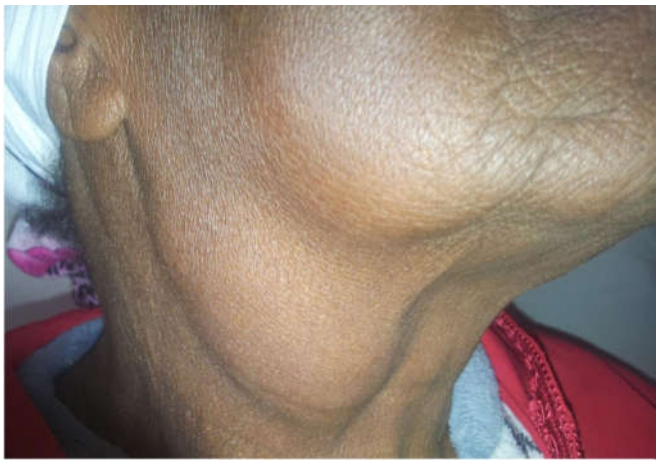

Fig. 1. Tumefaction of the right carotid region

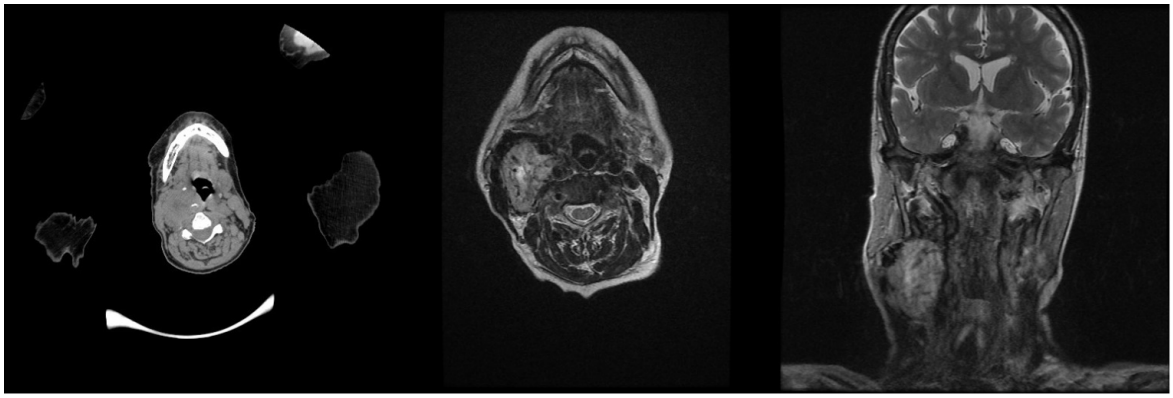

Fig. 2. Computed tomography (CT) scan and Magnetic resonance imaging (MRI) showed hyper vascularized tumor mass on the right carotid bifurcation

Table 1. Shamblin criteria for carotid body paragangliomas

Group	**Relation to Carotid Artery and Resectability**
I	Includes small tumors that are only loosely adherent to the adventitia of the artery and are easily removed
II	Tumors are somewhat larger and are more densely adherent to the artery and even infiltrate the vessel wall; sharp adventitial dissection is required for their removal
III	Includes very large tumors that encircle or encompass the artery to such an extent that aportion of the vessel must be resected for complete removal of the tumor with subsequent grafting

They have an important role in organismic hemostasis by acting directly as chemoreceptors or by the secretion of catecholamine in response to stress (Sevilla, 2007 and Zak, 1954). The incidence of paragangliomas of the head and neck varied between 1/300 000 to 1/1000000 and only less than 5% of these tumors are malignant. The mean age at diagnosis is 34.5 years and represents 0.6% of head and neck tumors (Sevilla, 2007; Zak, 1954 and Jin, 2008). The majority of paragangliomas of the head and neck are present along the glossopharyngeal and vagus nerve, and the most common clinical sites are the bifurcation of the carotid artery, the middle ear, and the jugular fossa (Semaan, 2008). Over the past 10 years, we are more interested in the genetic status of paraganglioma patients. The paragangliomas of the head and neck are most often in the form of sporadic tumors. About 30% to 40% is now included in the entity of autosomal dominant hereditary tumors, although only 10% of patients have a family history of paraganglioma (Neumann, 2002 and Klein, 2008). Clinical diagnosis of these syndromes is difficult and some researchers advocate genetic evaluation for all paraganglioma patients to allow for a more accurate estimate of the risk of multiple primary tumors, malignant potential and advice on family risk. The most common hereditary syndromes known to predispose to paraganglioma and / or pheochromocytoma are multiple endocrine neoplasia type 2, von Hippel-Lindau disease and neurofibromatosis type 1. Familial paraganglioma syndromes are associated with mutations. The succinate dehydrogenase (SDH) gene is recognized as the main cause of hereditary paraganglioma in the head and neck region (Neumann, 2004; Ricketts, 2010; Brandi, 2001; Kirmani, 1993). It was not possible to determine whether the case of our patient was sporadic or familial because of the lack of screening technique in our institute to confirm or reject a genetic mutation. Patients with functional paragangliomas producing catecholamine may present hypertension, hot flashes, tachycardia, palpitations, anxiety, headache and / or profuse diaphoresis. People with non-functional paragangliomas can be diagnosed accidentally or with symptoms of compression. Serum levels of chromogranin A, NSE or vimentin are elevated with most neuroendocrine tumors and can be differentiated from non-neuroendocrine tumors using a blood or urine hormone analysis.

The most common criteria for carotid body paragangliomas are classified according to Shamblin criteria (Table 1). This classification helps to describe the anatomical location as well as the extension of the tumor, thus helping to guide the surgical management (Shamblin, 1971). A new trend in the genetic classification of paragangliomas also appears due to the prevalence of 30% germline mutations in paragangliomas of the head and neck (Boedeker, 2009). Treatment of metastatic paraganglioma should be selected based on the patient's age, performance status, tumor site, and number of occurrences. The multidisciplinary approach must be advocated, following the lack of therapeutic standards to our knowledge. The therapeutic strategy aims to control excessive secretion of catecholamine and tumor burden, but no cure is possible. Treatment options include a "wait-and-see" surveillance, locoregional therapies, systemic chemotherapy and radionucleotides. Because of the malignant potential of paragangliomas, surgical excision is the preferred treatment in the absence of metastasis. Resection is often difficult because these highly vascular tumors are frequently located near principal blood vessels.

If a tumor is judged unresectable, a reduction of its size by chemotherapy, radiotherapy or embolization may be indicated, since resection offers the only chance of curing (Bryant, 1982). Radiation therapy can also be used for inoperable tumors or for palliative treatment. In our case the tumor was unresectable and an external radiotherapy of 50 Gy on the tumor mass was delivered for a local control. Inoperable paragangliomas can be treated with radionucleotides. Van Hulsteijn, reported seventeen studies including 243 patients with paraganglioma / pheochromocytoma malignant treated with 131I-MIBG therapy. He suggested that stable tumor volume and partial hormonal response could be achieved in 50% of cases, if treated with 131I-MIBG (Mikhail, 1986 and van Hulsteijn, 2014).

In our case, the radionucleotide treatment is not available. Cyclophosphamide and dacarbazine-based chemotherapy associated with vincristine (CVD) or doxorubicin (CVDD or CDD) are the best-studied regimens. In the largest study published to date (n = 52 patients), 40% of patients treated with CVD, MC, or CVD had clinical benefits, including a reduction in tumor size in 25% of patients. case (Berruti, 2012). Antiangiogenic agents represent a new therapeutic approach. Chougn et al reported that seventeen patients with progressive metastatic pheochromocytoma and / or paraganglioma were treated with sunitinib at a dose of 50 mg (four weeks of treatment / two weeks of rest) with a reduction in height. tumor, stabilization of the disease and improvement of hypertension in some patients (Chougnet, 2012). In our case, the multidisciplinary consultation meeting proposed sunitinib instead of chemotherapy protocols taking into account the tolerance profile of the targeted therapy. Despite this approach, targeted therapy was poorly supported and active surveillance was proposed because of the slow nature of the disease and the absence of symptoms.

Conclusion

Paragangliomas are neuroendocrine tumors developed at the expense of the parasympathetic nervous system Paragangliomas of the nonfunctional head and neck are rare tumors. They are often asymptomatic. Management of paragangliomas should be multidisciplinary but only surgical treatment is curative. Complementary therapies such as chemotherapy and external radiotherapy may find their place in metastatic forms, but without significantly affecting the prognosis.

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