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Malignant retroperitoneal paraganglioma treated with radiotherapy: A case report

Radyoterapi ile tedavi edilen malign retroperitoneal paraganglioma: Olgu sunumu

Ghammad Sanae [1], Chebihi Hassani Ghita [1], Allouche Fadwa [1], Alami Zineb [1], Bouhafa Touria [1], Hassouni Khalid [1]

[1] **Department of Radiotherapy, Chu Hassan II Hospital, Fez, Morocco**

ORCID ID of the authors
GS: 0000-0002-7940-8396
CHG: 0000-0003-2714-1957
AF: 0000-0002-6793-4911
AZ: 0000-0003-3349-1793
BT: 0000-0002-9857-1594
HK: 0000-0002-1442-255X

Abstract

Paragangliomas are rare tumors arising from undifferentiated cells of the primitive neural crest. We report a case of a 33-year-old female patient who presented a large firm retroperitoneal tumor situated on the left flank above the left kidney. Levels of the serum epinephrine and norepinephrine were high. We performed a scanned biopsy; the histopathological examination and the immunohistochemical analyses concluded the diagnosis of a retroperitoneal paraganglioma. The tumor was judged secreting and inoperable; therefore it was decided to be treated with radiotherapy.

Keywords: Retroperitoneal paraganglioma, Radiotherapy, Secretory tumor, Pheochromocytoma

Öz

Paragangliomalar, ilkel nöral krest'in farklılaşmamış hücrelerinden kaynaklanan nadir tümörlerdir. Sol böbreğin sol böbrek üzerinde yer alan geniş retroperitonal tümör hastası olan 33 yaşında bir kadın hastayı sunduk. Serum epinefrin ve norepinefrin düzeyleri yüksek bulundu. Taranmış bir biyopsi yaptık; Histopatolojik inceleme ve immunohistokimyasal analizler retroperitoneal paraganglioma tanısını koydu. Tümör salgılanıp inoperabl olarak değerlendirildi; Bu nedenle radyoterapi ile tedavi edilmeye karar verildi.

Anahtar kelimeler: Retroperitoneal paraganglioma, Radyoterapi, Secretory tumor, Pheochromocytoma

Corresponding author / Sorumlu yazar:
Ghammad Sanae
Address / Adres: Department of Radiotherapy, Chu Hassan II Hospital, Fez, Morocco
e-Mail: sanoua1010@gmail.com

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Introduction

Retroperitoneal paragangliomas are uncommon neoplasms. They are usually non-functional tumors, as only a minority of cases secretes catecholamines [1]. It seems that 50% of these tumors are malignant, as metastases to distant organs may appear even years after the initial diagnosis [2,3]. Clinical presentation, diagnosis and treatment are similar to adrenal tumors. Patients should be closely monitored with serum and urine catecholamine determination. Traditionally the most common treatment has been surgical removal, but now there are repeated cases treated by radiotherapy [4]. We report in this article the case of a secretive retroperitoneal paraganglioma treated by radiotherapy with a favorable clinical response.

Case presentation

We describe an inoperable case of a large retroperitoneal paraganglioma diagnosed in a 33-year-old woman. The patient complained of an abdominal distention and a pain in the left lumbar inguinal and ombilic area with palpitation without other clinical signs. Blood tests, including liver and renal biochemistry were normal. On the physical exam, the patient is clinically stable with a mild arterial hypertension along with a firm and sensitive abdominal mass taking place in the lumbar fossa, the left flank and part of the umbilical region measuring approximately 15 cm in longest diameter. A computed tomography of the abdomen revealed a large retroperitoneal and abdominal mass (17x11cm in diameter) with mixed component fleshy and liquid, covering the aorta and the left renal pedicle with an unknown starting point (renal, adrenal gland, pancreas) and without distant metastases in the cerebral, thoracic and pelvic stages (Figure 1 and 2).

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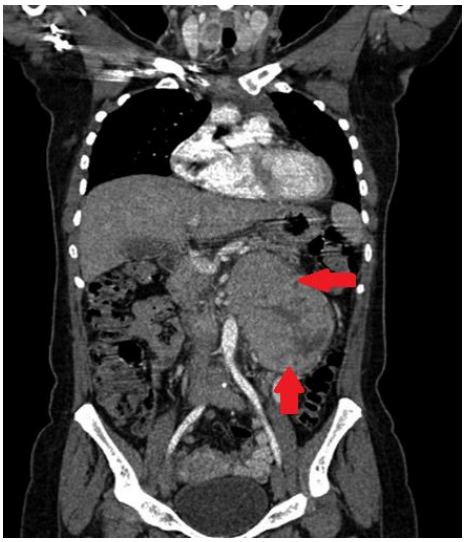

Figure 1: The coronal cuts of the computed tomography of the abdomen

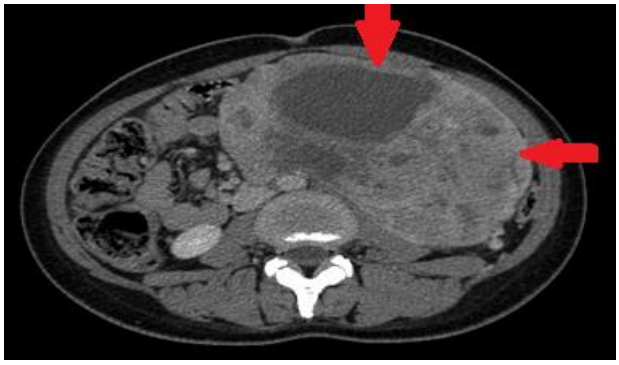

Figure 2: Axial contrast enhanced computed tomography of abdomen at portal time shows a hypervascular retroperitoneal mass with enlarged surrounding vessels

In the magnetic resonance imaging (MRI) the mass of the left flank measures 17 x 13 x 12 cm and it sits in front and below of the left kidney which is pushed up. Inside it exceeds the median line and pushes the small intestines to the right. The left colon is laminated to the left. The lesion remains relatively good limited with lobulated contours, with a vascular structure of a 13 mm axis at the level of the lower part, compatible with a dilation of the left ovarian vein

We performed a biopsy guided with scan and the histological examination revealed a tumor with an organoid 'zellballen' pattern of cellular growth (Figure 3). Immuno-histochemical examination for neuron-specific enolase and vimentin were also positive (Figure 4), whereas epithelial and endothelial markers S-100, actin, myosin and CD117 (c-kit) were negative. The tumor was characterized as a 'retroperitoneal paraganglioma'.

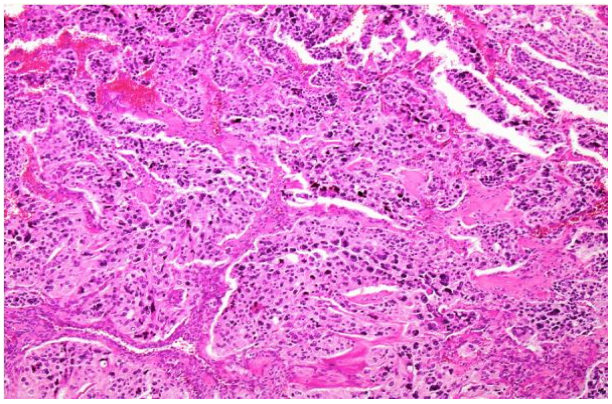

Figure 3: Hematoxylin and eosin stain, paraganglioma

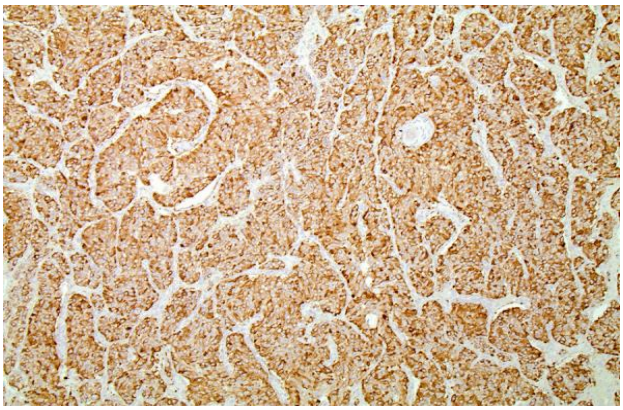

Figure 4: Immunohistochemistry, cells expressing chromogranin

Dosage of catecholamine is higher than normal

* Normetanephrine (catabolite of norepinephrine): 23444.1 µg / 24h (normal value is 0,04µg /L)

* Metanephrine (catabolite of adrenaline): 7812.8 µg / 24h (normal value is 0,02 µg / L)

* 3-Methoxytyramine (catabolite of dopamine): 95845.5 µg / 24h (normal value is 0,02 µg / L)

The tumor is judged secreting and inoperable. The patient was referred to the Radiotherapy-Oncology Department. After conformal radiotherapy planning (Figure 5 and 6), the patient started a course of fractionated radiotherapy using 2 Gy daily fractions to a total dose of 50 Gy (in 5 weeks) with a good tolerance to radiotherapy.

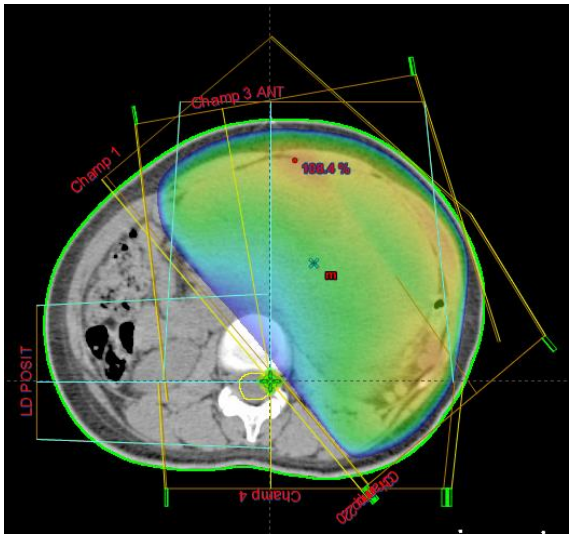

Figure 5: Radiotherapy planning of retroperitoneal paraganglioma using 4 treatment fields

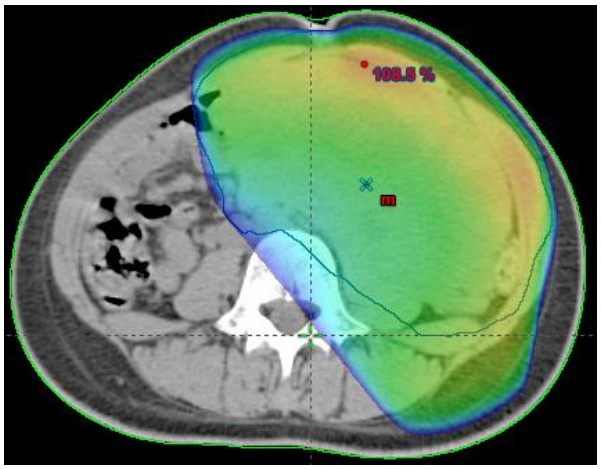

Figure 6: Dose distribution on retroperitoneal paraganglioma (blue structure is PTV)

Full symptomatic relief was rapidly achieved. The tumor was slowly regressing (computed tomography scans carried out every three months) and a 30% regression of dimensions with extensive central necrosis of the tumor heterogeneously enhanced after injection of contrast product was documented 8 months after ending treatment, clinically disappearing from the abdominal mass 12 months later.

Discussion

Paraganglioma is a rare tumor commonly seen in the 3rd to 4th decade, with no sex predilection. 40% of paragangliomas produce high catecholamine levels, which result in symptoms such as headache, palpitations, excessive sweating, and elevated urinary metanephrine or vanillylmandelic acid levels. In the retroperitoneum the most common site for a paraganglioma is the organs of Zuckerkandl, which are located anterior to the aorta at the origin of the inferior mesenteric artery. [5]

Primary retroperitoneal neoplasms are rare benign and malignant mesenchymal tumors that arise in the retroperitoneum, outside of the major organs [6]. Paragangliomas are extra-adrenal pheochromocytomas that arise from chromaffin cells in the sympathetic (localized in retroperitoneum and thorax) or parasympathetic (next to aortic arch, neck, and skull base) neural paraganglioma [7]. They account for 10% of adult pheochromocytomas. About 70% of sympathetic paragangliomas are intraabdominal, usually found in the perinephric and paraaortic spaces. The remaining 30% are located in the chest. Malignant retroperitoneal paragangliomas range from 30% to 50% [8]. Paragangliomas metastasize approximately in 20% to 42% of the cases. Dissemination can be hematogenous or through the lymphatic system, with the most common site of metastasis being the regional lymph nodes, bone, lung, and liver. Because benign and malignant paragangliomas have the same histological appearance, the best predictor for outcome is metastasis or recurrence [7].

The diagnosis is usually established with high urine catecholamine metabolites, VMA, and metanephrine levels [9].

Thirty percent of the patients presented with these diseases in a hereditary context. The biological diagnosis relies on the identification of excessive secretion of the metanephrines which are more sensitive and specific than those of catecholamines. The published recommendations give the opportunity to choose between the metanephrines in serum or urines. The concentrations of the free plasmatic metanephrines reflect the ongoing production of the tumor. They are little sensitive to the renal failure. [10].

If a secretory tumor is diagnosed, the patients undergo paroxysmal episodic hypertension, as well as the typical triad of symptoms associated with pheochromocytomas: palpitations, headache, and profuse sweating. The nonsecretory type most commonly presents an abdominal pain or mass; a large proportion of these tumors are incidentally discovered in normotensive patients during imaging evaluation for other reasons [10].

Once the diagnosis of chromaffin tumor is established, the next step is to determine the extension of the disease. The imaging modality of choice for primary tumor evaluation and staging is a CT scan of the thorax, abdomen, and pelvis. If no lesion is detected, further imaging of the organ of Zuckerkandl and the bladder is performed. CT imaging demonstrates 93–100% sensitivity for localizing adrenal tumors, and 90% for extra-adrenal tumors [11]. In the CT scan the paraganglioma is usually seen as a large well-defined lobular tumor with areas of hemorrhage and necrosis. Punctate calcification is seen in 15% of cases, and a fluid-fluid level can be seen that is due to hemorrhage. Because of the hypervascular nature of paraganglioma, intense contrast enhancement is seen.

MRI is more sensitive than CT in detecting extra-adrenal tumors. At MR imaging, signal voids can be seen with T1-weighted spin-echo sequences. Variable signal intensity is seen on T2- weighted images. Although paraganglioma may be “bright”, the tumor is usually complex and heterogeneous (because of hemorrhage) and almost never demonstrates “lightbulb” high signal intensity with current imaging techniques [5]

Scintigraphy with 123-I labeled MIBG offers superior specificity than CT and MR imaging [12].

The possibility for malignant transformation of paragangliomas makes surgical excision the treatment of choice. Radiation therapy has been advocated for patients who cannot undergo surgery or for unresectable tumors [8]. Aggressive surgery is mandatory to obtain disease free survival. Therapy with radionucleotides may be used for tumors exhibiting uptake on diagnostic scan [11]. Octreotide can be used for treatment of inoperable paragangliomas [13]. Tumor recurrences can also be successfully excised surgically with low morbidity [14].

Traditionally, the main treatment for paragangliomas has been surgical removal but repeated cases were treated by radiation therapy alone for local control of these tumors [15,16]. The authors recommended doses in the 4000 to 4500 cGyrange delivered over 4-5 weeks. Essentially, chemotherapy has no defined role for their treatment, but only used for metastatic stage [16]. Metastatic lesions have a poor prognosis, with a 5-year survival rate of 36% according to one study [17].

Conclusion

Paragangliomas of the retroperitoneum are a rare group of tumors with malignant potential that cause considerable difficulty both in diagnosis and treatment [18]. The management of paragangliomas is controversial. Observation, surgery, EBRT and SRS may, alone or in combination, be appropriate depending on the size and the extent of the tumor, previous treatment, patient age, general health, and neurologic condition. Few data exists regarding long-term tumor control and late effects after EBRT or SRS, But most of these studies affirm that external-beam RT and SRS are safe and effective for large and/or symptomatic paragangliomas [19].

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