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OLGU SUNUMU/CASE REPORT

Hormon-Negatif Retroperitoneal Ekstra-Adrenal Paraganglioma

Hormone-Negative Retroperitoneal Extra-Adrenal Paraganglioma

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ÖZ

Paragangliomalar, parasempatik sinir sisteminden kaynaklanan nadir görülen nöroektodermal tümörlerdir. Bu olgu sunumunda retroperitoneal yerleşimli bir hormon negatif ekstra-adrenal paraganglioma olgusu sunulmaktadır. 50 yaşında kadın hasta sağ yan ağrısı ile kliniğimize başvurdu. Hastanın laboratuvar incelemelerinde idrar ve kan katekolamin yıkım ürünleri dahil patoloji saptanmadı. Bilgisayarlı tomografide vena kava inferiora bası yapan ve pankreasın alt kısmına yakın 80x50 mm boyutlarında izo-hipodens solid lezyon saptandı. Kitle rezeksiyonu için cerrahi planlandı. Diseksiyonu sırasında fentolamin ile kontrol altına alınan ciddi bir hipertansif atak meydana geldi. Kitlenin çıkarılmasından sonra intraoperatif ve postoperatif dönemde kan basıncı normal sınırlarda seyretti. Hasta postoperatif 5. günde komplikasyonsuz olarak taburcu edildi.

ABSTRACT

Paragangliomas are rare neuroectodermal tumors originating from the parasympathetic nervous system. In this case report, a case of hormone-negative extra-adrenal paraganglioma located retroperitoneally is presented. A 50-year-old female patient was admitted to our clinic with right flank pain. No pathology including urine and blood catecholamine degradation products was detected in the laboratory examinations of the patient. Computed tomography revealed an iso-hypodense solid lesion of 80x50 mm in size, compressing the inferior vena cava and close to the lower part of the pancreas. Surgery was planned for mass resection. During dissection, a severe hypertensive attack occurred, which was controlled with phentolamine. After removal of the mass, blood pressure remained within normal limits in the intraoperative and postoperative periods. The patient was discharged without complications on the 5th postoperative day.

Introduction

Paragangliomas are rare neuroectodermal tumors. They can develop anywhere paraganglia tissue is present (1). Paraganglioma is the general name given to tumors arising from neuroendocrine cells associated with the sympathetic or parasympathetic nervous system. If the tumor originates from the adrenal medulla, it is called pheochromocytoma (2). Paragangliomas arising from the parasympathetic system are usually nonfunctional, while those arising from the sympathetic ganglia are functional and secrete catecholamines (3).

The clinical picture of the patient varies depending on whether the paragangliomas are hormone active or not. Functional tumors cause the synthesis and release of many polypeptides, especially catecholamines. Symptoms and signs that occur in patients are due to excessive catecholamine release. The most common symptoms are mainly palpitations, hypertension, headache, sweating, flushing, abdominal pain and weight loss (2).

Curative treatment of extra adrenal paraganglioma is total resection of the mass (3). In the surgery of catecholamine-producing masses with positive serum/urine hormone levels, hypertensive episodes are expected during anesthesia induction or during surgery. On the other hand, although serum/urine hormone levels are negative, there are cases with hypertensive episodes during surgery, which are important because they are life-threatening. Therefore, it should be kept in mind that hypertensive episodes can be seen in the surgery of extra-adrenal paraganglioma cases, whether the serum/urine hormone levels are high or within normal limits.

In this case, the diagnosis and treatment process of an extra-adrenal paraganglioma case who had normal serum and urinary catecholamine degradation product levels in the laboratory examinations performed in the preoperative period, and who developed a hypertensive attack during the mass dissection is presented.

Case Report

A 50-year-old female patient was admitted to Erzurum Regional Education and Research Hospital, Erzurum, Turkey with right flank pain in June 2020. On her medical history, the patient had only diabetes mellitus. There was no history of surgery. At her preoperative physical examination, vital findings of the patient were as follows: blood pressure: 135/80 mm Hg, pulse rate: 74 beats per minute, oxygen saturation on room air: 97%, and body temperature: 36.8°Celsius. In addition, she had abdominal pain on deep palpation in the epigastrium. Digital rectal examination was also normal. Other system examinations were normal.

Patient's hematological and biochemical laboratory parameters were normal, including tumor markers. Abdominal ultrasonography (USG) was performed at first imaging tool. On USG, there were a few millimetric calculus in the gallbladder. In addition, computed tomography (CT) was performed on the patient due to observing a 73x42 mm hypoechoic solid lesion adjacent to the pancreatic head on USG. On CT scan, an iso-hypodense solid lesion, 80x50 mm in size, compressing the inferior vena cava, close to the pancreas inferior and close to the right kidney, was observed. Hormone status was investigated, considering that the retroperitoneal mass might be a paraganglioma (Table 1). Non-functioning extra-adrenal paraganglioma was considered in the patient whose serum and 24-hour urine hormone levels were normal. Surgery was decided when the mass was over 50 mm in size. The abdominal cavity was entered with right Kocher's incision. On exploration, a hyper vascular approximately 80 mm in size mass, which extends between the head of the pancreas and the upper pole of the kidney was seen. The mass was pressing on the vena cava. However, there was no organ invasion, and it has a clear border with the surrounding tissues (Figure 1 and 2). With the traction of the mass, the patient's blood pressure increased rapidly to 250/160 mm/Hg and her pulse rate increased to 150 beats per minute. Phentolamine (5 mg/2 ml) intravenously

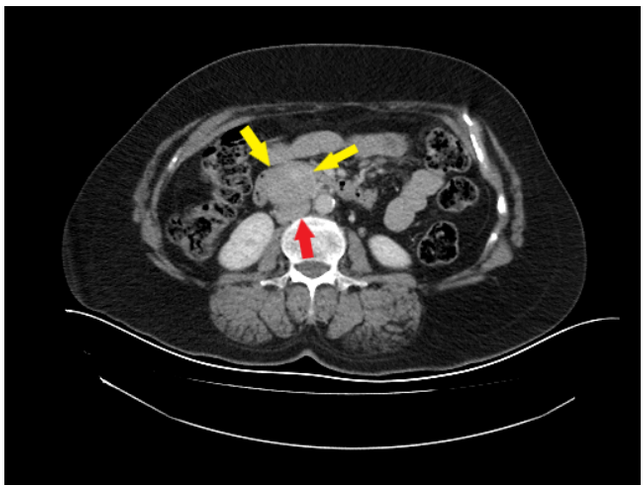

Figure 1. CT scan of a 50-year-old women with extra adrenal paraganglioma located anterior to the inferior vena cava (Yellow arrows show the mass, and red arrow shows inferior vena cava).

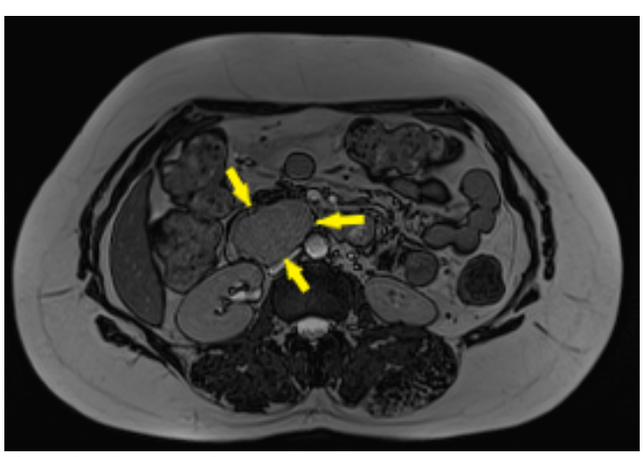

Figure 2. MRI image of the patient (yellow arrows show the mass).

Table 1. The patient's laboratory results of the catecholamine breakdown products.

Laboratory Test	First Value	Normal Range
Serum		
• VMA		
• Adrenaline	31.57 pg/mL	0-85 pg/mL
• Noradrenaline	360 pg/mL	70-480 pg/mL
• Metanephrine	32.17 pg/mL	0-90 pg/mL
• Normetanephrine	150.34 pg/mL	0-180 pg/mL
24-hour Urine		
• VMA	5.11mg	1.8-6.7 mg
• Metanephrine	269.83 mcg	0-350 mcg
• Dopamine	172.62 mcg	0-600 mcg
• Noradrenaline	17.27 mcg	0-80 mcg
• Normetanephrine	300.11 mcg	0-600 mcg
• Adrenaline	11.6 µg	0-20 µg
• 5-HIAA	4.19 mg	0.5-8.2

infusion was started to control hypertensive attack. Phentolamine infused at the rate of 1–6 μg/kg/min according to the blood pressure (her weight was 95 kilograms). Also, cholecystectomy was performed in the same session due to cholecystolithiasis. The mass was completely resected. After resection of the mass, her blood pressure remained within normal limits at operation room. The operation was completed by placing a drain in the pararenal area.

She was followed up in the intensive care unit postoperatively. The first vital findings of the patients in the intensive care unit were as follows: blood pressure: 138/77 mm Hg, pulse rate: 110 beats per minute, oxygen saturation on room air: 95%, and body temperature: 37.2° Celsius. Oral intake was started at the 6th hour postoperatively. On the first postoperative day, 100 cc serohaemorrhagic fluid came from the drain. She was followed in the intensive care unit for 2 days. On the second postoperative day, 50 cc serous fluid came from the drain. During her follow-up in the intensive care unit, no hypertensive attacks were observed. She was followed up in the service from the 3rd postoperative day. Her drain was removed on the 4th postoperative day. She was discharged on the 5th postoperative day without complications. At the pathological evaluation of the operation specimen, it was suitable with chronic cholecystitis and paraganglioma, weighing 98 g and measuring 80*55*40 mm. In the immunohistochemical examination of the mass, chromogranin, synaptophysin, neuron-specific enolase, CD56 and s100 were stained positively, while inhibin, HMB45, GATA3, p53 and CD99 were stained negative. In addition, In PASS (Pheochromocytoma of the Adrenal gland Scaled Score) score, periadrenal invasion (-), cell monotony (-), mitosis >3 (-), atypical mitosis (-), necrosis (-), tumor cellular spindle morphology (+), pleomorphism (+), large nests or diffuse growth (+), high cellularity (+), capsular invasion (-), vascular invasion (-) and hyperchromasia (-). PASS score of the patients was 7.

The patient agreed us to use her medical records and signed the consent form.

Discussion

Retroperitoneal masses constitute a heterogeneous group of lesions originating from the retroperitoneal region (4). While the majority of the masses are malignant tumors such as lymphoma, leiomyosarcoma, neurogenic tumors, a few of them are benign tumors such as retroperitoneal fibrosis. These masses can be solid or cystic. Neurogenic tumors are solid lesions arising from cells of the nervous system. On the other hand, lymphangioma and hydatid cysts are cystic lesions (5,6).

Retroperitoneal paragangliomas are rare tumors of the autonomic nervous system originating from sympathetic and parasympathetic neural crest cells. Paragangliomas are most commonly encountered in the bifurcation of the common carotid artery, aortic arch, and retroperitoneal region (7). Retroperitoneal paragangliomas are more common in women and slow growing tumors (8).

It has been reported that retroperitoneally located paragangliomas are more functional than other regions and 30-50% of them are malignant. It is most often seen in the area between the aorta and the inferior vena cava (9). In our case, the mass was in similar localization.

Functional paragangliomas secrete epinephrine and norepinephrine. The most prominent diagnostic symptom in functional paragangliomas is attacks of paroxysmal hypertension. Our patient had no episodes of hypertension in his anamnesis, if retroperitoneal paraganglioma is non-secretory, abdominal pain and intra-abdominal mass may be the main symptom. The diagnosis is usually made by the mass image detected incidentally in imaging methods. The diagnosis is confirmed by the detection of catecholamine breakdown products, metanephrine and vanil-mandelic acid in the urine (10). Although recent advances in diagnostic imaging, pharmacologic treatment, surgical techniques, and molecular profiling have contributed to a better understanding of the disease, it still represents a dilemma for physicians (11). Pheochromocytoma attacks can be seen during anesthesia induction and operation, especially in cases where blood and urine catecholamine breakdown products are normal in the preoperative period like our case.

Surgery, chemotherapy, radiotherapy and Iodine-131–metaiodobenzylguanidine (MIBG) are used in the treatment of paragangliomas. Aggressive surgical treatment is the only option for disease-free survival (12). Care should be taken in surgical resection to avoid rupture of the tumor. Chemotherapy and radiotherapy are applied in cases where curative surgery cannot be performed due to organ involvement and resections may cause high mortality.

Benign and malignant paragangliomas have the same histopathological appearance. Except for metastasis and recurrence, there are no definitive morphological criteria for malignancy. The criteria predicting malignancy can be summarized as extra-adrenal location, coarse nodularity, extensive necrosis, absence of hyaline globules, young

age, tumor size and Ki-67 index (13). Extra-adrenal location, tumor diameter, high Ki-67 index, mitotic activity, and focal nuclear atypia were the poor prognostic features of our case.

In addition, Pheochromocytoma of the Adrenal gland Scaled Score (PASS) score is used to distinguish between benign and malignant neoplasm. The criteria used to calculate the PASS score are shown in Table 2. In our case, PASS score of the patients was 7. Surprisingly, despite her PASS score of 7, no recurrent mass was observed in the contrast-enhanced abdominal magnetic resonance imaging of the patient with contrast at the 3rd and 6th months.

Table 2. Pheochromocytoma of the adrenal gland scoring scale (PASS).

Histomorphological parameter	Score
• Large nests or diffuse growth	+2
• Central necrosis or confluent necrosis	+2
• High cellularity	+2
• Cell monotony	+2
• Tumor cell spindling	+2
• Mitotic figures 3/10 hpf	+2
• Atypical mitotic figures	+2
• Extension into adipose tissue	+2
• Capsular invasion	+1
• Vascular invasion	+1
• Pleomorphism	+1
• Hyperchromasia	+1
≥ 4 potential aggressive behavior	
< 4 behave in a benign fashion	

Recurrence has been reported in 8-20% of patients treated with surgery. Metastasis to regional lymph nodes, lung, liver and bone develops in 28-50% of patients by hematogenous and lymphatic routes (14).

Conclusion

Paragangliomas should be considered in the differential diagnosis of retroperitoneal masses. Especially, hormone-active paragangliomas can be detected at an earlier period with their prominent symptoms, while non-functional paragangliomas are mostly found incidentally when being investigated for nonspecific symptoms. Surgical complete resection is the most effective treatment method for paragangliomas. It is necessary to be prepared for hypertensive attacks and cardiac arrhythmias that may develop during the operation in the preoperative and intraoperative period.

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References

1. Cunningham SC, Suh HS, Winter JM, Montgomery E, Schulick RD, Cameron JL et al. Retroperitoneal paraganglioma: single-institution experience and review of the literature. Journal of Gastrointestinal Surgery 2006;10:1156-1163.
2. Elder EE, Elder G, Larsson C. Pheochromocytoma and functional paraganglioma syndrome: no longer the 10% tumor. Journal of Surgical Oncology 2005;89:193-201.
3. Rha SE, Byun JY, Jung SE, Chun HJ, Lee HG, Lee JM. Neurogenic tumors in the abdomen: tumor types and imaging characteristics. Radiographics 2003;23:29-43.
4. Nishino M, Hayakawa K, Minami M, Yamamoto A, Ueda H, Takasu K. Primary retroperitoneal neoplasms: CT and MR imaging findings with anatomic and pathologic diagnostic clues. Radiographics 2003;23:45-57.
5. Chaudhari A, Desai PD, Vadel MK, Kaptan K. Evaluation of primary retroperitoneal masses by computed tomography scan. Int J Med Sci Public Health 2016;5:1423-1429.
6. Arda I, Fırat D, Korkmaz S, Demiryılmaz İ, Yılmaz İ. Atipik Prezente Kist Hidatik: Pankreas Başında Kitle. Sakarya Tıp Dergisi 2018;8:149-152.

7. Lightfoot N, Santos P, Nikfarjam M. Paraganglioma mimicking a pancreatic neoplasm. JOP Journal of the Pancreas 2011;12: 259-261.

8. Türkyılmaz A, Yener Aydın, Kurt A, Dostbil A, Eroğlu A. Paragangliomada Geç Pulmoner Metastaz. The Eurosian Journal of Medi-cine 2007;39:78-80.

9. Parithivel VS, Niazi M, Malhotra AK, Swaminathan K. Paraganglioma of the pancreas: literature review and case report. Digestive Diseases and Sciences 2000;45:438-441.

10. Sangster G, Do D, Previgliano C, Li B, LaFrance D, Heldmann M. Primary retroperitoneal paraganglioma simulating a pancreatic mass: A case report and review of the literature. HPB Surgery 2010; 645728.

11. Adas M, Koc B, Adas G, Yalcin O, Celik S, Kemik Ö. Pitfalls in the diagnosis of pheochromocytoma: A case series and review of the literature. Journal of Epidemiological Research 2015;2:49-55.

12. Yang JH, Bae SJ, Park S, Park H-K, Jung HS, Chung JH et al. Bilateral pheochromocytoma associated with paraganglioma and papillary thyroid carcinoma: Report of an unusual case. Endocr J 2007;54:227-231.

13. Çelik S, Demir Ö, Tuna B, Yörükoğlu K, Esen A. Retroperitoneal Paraganglioma: Olgu Sunumu. Bulletin of Urooncology 2014; 13:184-186.

14. Nap R, Meinardi J, Van Den Berg G, Dullaart R, de Vries J, Wolffenbuttel B. Long-term follow-up is indicated after surgery for a phaeochromocytoma. Nederlands Tijdschrift Voor Geneeskunde. 2006;150:1045-1049.