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Short Report

Retrospective Evaluation of The Cases with Malignant Pheochromocytoma: A Single Center Experience

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Pheochromocytomas are neuroendocrine tumors that arise from chromaffin cells of the adrenal medulla.[1] It is a rare disease with an estimated annual incidence of 0.8 per 100.000 person years.[2] Pheochromocytomas are most common in the fourth to fifth decade with equal distribution in men and women.[3] The disease is mostly sporadic but forty percent of the cases are part of the familial disorders such as von Hippel-Lindau (VHL) syndrome, multiple endocrine neoplasia type 2 (MEN2), and less commonly, neurofibromatosis type 1 (NF1).[4] Approximately 10 percent of pheochromocytomas are malignant (8.3% to 13%).[5] Local invasion into surrounding tissues and organs or distant metastases that may occur anytime can allow to make a distinction of benign from malignant type.[6,7] All pheochromocytomas have some metastatic potential according to World Health Organization (WHO) because metastasis can appear as many as 53 years after resection.[8] Metastasis may occur frequently in lymph nodes, bone, liver and lungs.[9]

The clinical picture is almost same as benign pheochromocytoma. The classic triad of symptoms in cases consists of episodic headache, sweating, and tachycardia.[10] Pheochromocytoma sometimes is diagnosed with imaging methods in patients with unrelated symptoms.[11] After the biochemical diagnosis, localization of the tumor is made by computed tomography (CT), magnetic resonance imaging (MRI) first. If the tumor is not find by abdominal and pelvic CT or MRI, metaiodobenzylguanidine (MIBG) scintigraphy, fludeoxyglucose-positron emission tomography (FDG-PET) and gallium 68 1, 4, 7, 10-tetraazacyclododecane-1,4,7,10-tetraacetic acid-octreotate-positron emission tomography (68-Ga DOTATATE PET) can be done.[12-14]

There is no curative treatment for malignant pheochromocytoma. If possible both primary and metastatic lesions should be resected which may improve symptoms and possibly survival.[15,16]

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Table 1. Clinical characteristics of the patients and some features of the tumors

Characteristics		Number (n)
Gender (female)		3
Age at presentation (years)		45
Type of presentation		
Hypertension		3
Asymptomatic		2
Macroscopic features		
Tumor localization	Right adrenal	2
	Left adrenal	2
	Bilateral	1
Tumor size (mm)		58
Microscopic features	Capsular invasion	1
	Vascular invasion	1
	Extension into periadrenal adipose tissue	2

External radiation therapy for bone metastasis, cryoablation, radiofrequency ablation or transcatheter arterial embolization for hepatic metastasis are other treatment modalities for malignant pheochromacytoma.[17] I123 MIBG treatment is another therapeutic option for palliation.[18] Chemotherapy may prolong the survival of the cases and play a role in the palliation.[17] Furthermore, medical control of symptoms with adrenergic blockage is important. The prognosis of malignant pheochromocytoma is variable; the overall 5-year survival that range widely from 12 to 84 percent.[19]

In this study, we evaluated the patients with malignant pheochromocytoma who were followed up by our clinic. We retrospectively evaluated the data of cases admitted to our department between 2013 and 2020 and diagnosed with malignant pheochromocytoma in this study. Three patients with a diagnosis of malignant pheochromocytoma were female and mean age at presentation was 45 years. The baseline characteristics of the patients, imaging and pathological features of the tumors were demonstrated in Table 1.

Among five cases, three were diagnosed with pheochromocytoma after hypertensive attack. Two cases were diagnosed after detection of adrenal mass in one with abdominal pain and one with elevated liver enzymes. Noradrenergic functionality was detected in all cases. Primary site of the tumor was the left side in two patients, the right side in two patients and bilateral in one patient. The average diameter of the adrenal mass of the cases was 58 mm. There was no familial pheochromocytoma syndrome in our cases. Transperitoneal surrenalectomy was performed in all cases. Extension to periadrenal adipose tissue was detected in two patients, vascular invasion in one patient and capsule invasion in 1 patient in the surgery-resected specimen. Intraabdominal lymph node metastasis was found in 1 patient and metastatic focus was seen in the liver in 1 patient at the time of the diagnosis. During follow-up, metastasis was detected in the perirenal region in 1 patient. Bone metastasis was seen in 3 patients, lymph node metastasis in 2 patients and lung metastasis in 1 patient. Surgery followed by Lutetium-177 treatment as an adjuvant therapy in two patients. Transperitoneal surgery was performed for a patient with metastasis in the perirenal area and resection of the mass was performed. Also, a patient with a liver metastasis at the time of the diagnosis was underwent surgery and the metastatic focus was resected. Two patients received radiotherapy for bone metastases. The mean follow-up period of the cases was 44 months. Three patients died from progression of the disease or acute complications and the other 2 patients are still under follow-up.

There is no curative therapy for malignant pheochromocytoma. After resection of primary tumor, metastatic foci should be resected entirely as possible. Multidisciplinary and individualized approach to treatment of patients with metastatic pheochromocytoma is warranted. Our study has retrospective design and the relatively low number

of patients. Better therapeutic approach can be established by future studies.

Conflict of Interests

Authors declare that there are none.

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