The European Research Journal 2023;9(1):173-177 Case Report

DOI: 10.18621/eurj.1022302 Child Health and Diseases

Paraganglioma admitting with stage 4 hypertensive retinopathy

İsa Yılmaz[1], Fatma Özcan Sıkı[2], Mehmet Öztürk[3], Fuat Buğrul[4], Zeliha Esin Çelik[5], Şükrü Arslan[1]

[1]Department of Child Health and Diseases, Division of Pediatric Nephrology, Selçuk University School of Medicine, Konya, Turkey; [2]Department of Pediatric Surgery, Selçuk University School of Medicine, Konya, Turkey; [3]Department of Radiology, Selçuk University School of Medicine, Konya, Turkey; [4]Department of Child Health and Diseases, Division of Pediatric Endocrinology, Selçuk University School of Medicine, Konya, Turkey; [5]Department of Medical Pathology, Selçuk University School of Medicine, Konya, Turkey

ABSTRACT

Objectives: Paragangliomas and pheochromocytomas are rare tumors originating in chromaffin cells which are predominantly located in adrenal glands. This tumor is generally bilateral and much more rarely seen in pediatric patients. Sustained or paroxysmal hypertension is the most frequent sign of paragangliomas /pheochromocytoma. Here, we present a 15-year-old patient diagnosed with the complaint of blurred vision.

Keywords: Extraadrenal gland neoplasms, paraganglioma, pheochromocytoma, hypertension, childhood

Paragangliomas and pheochromocytomas (PGL/PHEO) are rare neuroendocrine tumors producing catecholamines and other neuropeptides [1]. Pheochromocytomas originate mainly from the adrenal medulla; however, they usually secrete catecholamines. Most of those that are called PGLs, which originate from the extra-adrenal gland, are nonfunctional [2]. The incidence of PGL/PHEO is estimated to be 0.3 cases per million on an annual scale, and about 20 percent of cases are diagnosed during childhood [3]. Contrary to adults, pediatric patients may present with atypical findings such as psychiatric disorders and orthostatic hypotension, aside from the classical triad (e.g episodic headaches, sweating, and tachycardia), and are therefore likely to be misleading [4]. Here, we present a 15-year-old patient diagnosed with PGL who presented with the complaint of blurred vision.

CASE PRESENTATION

A 15-year-old male patient was admitted with short-term palpitations after effort for the last year and blurred vision in the left eye for one month. In his physical examination, blood pressure was 170/100 mmHg, heart rate was 140 per min, and other examination findings were normal. Except for the high renin levels (4.75 ng/mL/h) in laboratory tests, other results were normal. There were signs of stage 4 hypertensive retinopathy in the eye examination. Abdominal ultrasonography revealed a 47×46×58 mm hypo-isoechoic solid mass in the para-aortic area, adjacent to the left kidney lower pole (Fig. 1). The normetanephrine level that was measured in the 24-hour urine for the diagnosis of the mass was as high as 15322.43 µg/day. In the echocardiography of the patient that was evaluated by pediatric cardiology, it was found that he had left

Received: **November 11, 2021;** *Accepted:* **February 21, 2022;** *Published Online:* **August 5, 2022**

How to cite this article: *Yılmaz İ, Özcan Sıkı F, Öztürk M, Buğrul F, Çelik ZE, Arslan Ş. Paraganglioma admitting with stage 4 hypertensive retinopathy. Eur Res J 2023;9(1):173-177. DOI: 10.18621/eurj.1022302*

e-ISSN: 2149-3189

Address for correspondence: *İsa Yılmaz, MD., Selçuk University School of Medicine, Department of Pediatric Nephrology, Konya, Turkey. E-mail: drisayilmaz@hotmail.com, Phone: +90 505 928 23 46, Fax: +90 332 237 60 25*

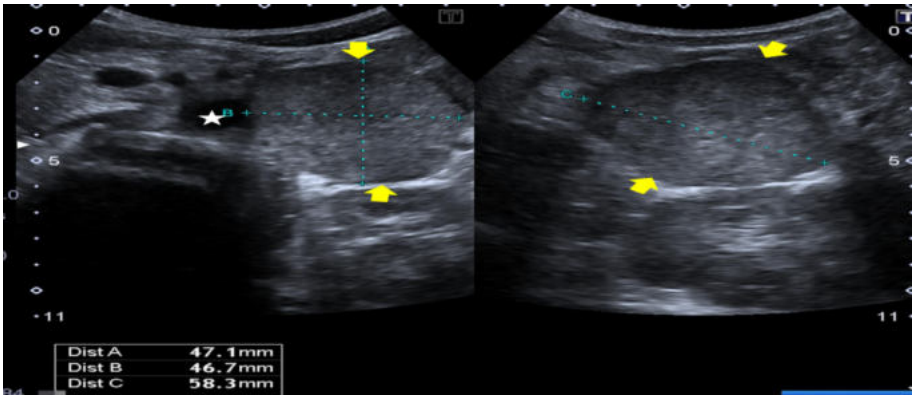

Fig. 1. Hypo-isoechoic solid mass image of 47×46×58 mm in the paraaortic area, adjacent to the left kidney lower pole in abdominal ultrasonography.

ventricular hypertrophy. The patient was initiated with nifedipine and enalapril for hypertension control.

Contrast-enhanced abdominal magnetic resonance imaging (MRI) revealed a mass lesion with homogeneous enhancement and smooth borders, adjacent to the lower pole of the left kidney, and the widest anterior-posterior diameter was 40 mm, the widest mediolateral diameter was 50 mm, and the widest craniocaudal length was 60 mm (Fig. 2). Oncological positron emission tomography (PET) scan (whole-body scan) showed a mass lesion that had dotatate in the left lower quadrant of the abdomen, adjacent to the kidney inferior area. The antihypertensive treatment was adjusted before the surgery as doxazosin and carvedilol. The patient, whose blood pressure measurements were examined, was operated on by the pediatric surgeon, after which blood pressure measurements were normal and antihypertensive treatment was not needed. Pathological examination of the mass revealed that it was compatible with PGL (Fig. 3).

DISCUSSION

Among hypertensive children, the incidence of surgically-confirmed catecholamine-secreting PGL/PHEO ranges between 0.8% and 1.7% [5]. However, it was reported in the case series that persistent or paroxysmal hypertension is the most common manifestation of PGL/ PHEO in children at a rate of 60-90% [6].

Our patient presented with hypertension that caused end-organ damage. Urinary metanephrine excretion, which was examined for the etiology, was elevated. Currently, the diagnostic test for PGL/ PHEO should reveal 87.5% and 99.7% specificity in a 24-hour urinary metanephrine and catecholamine excretion four-fold higher than the reference range [6, 7]. The tumor should be located with radiographic and nuclear imaging such as abdominal computerized tomography (CT) or MRI and 'iodine 131-metaiodobenzylguanidine scintigraphy after the biochemical diagnosis is made. Due to the predominant intra-abdominal location of PGL/PHEO, abdominal and

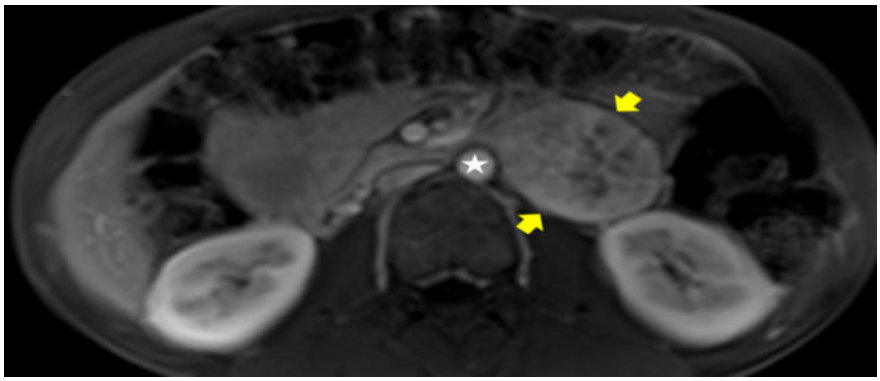

Fig. 2. In contrast-enhanced abdominal magnetic resonance imaging, a well-circumscribed mass lesion with homogeneous contrast, adjacent to the left kidney lower pole, has the widest anterior-posterior diameter 40 mm, the widest mediolateral diameter 50 mm, and the widest craniocaudal length 60 mm.

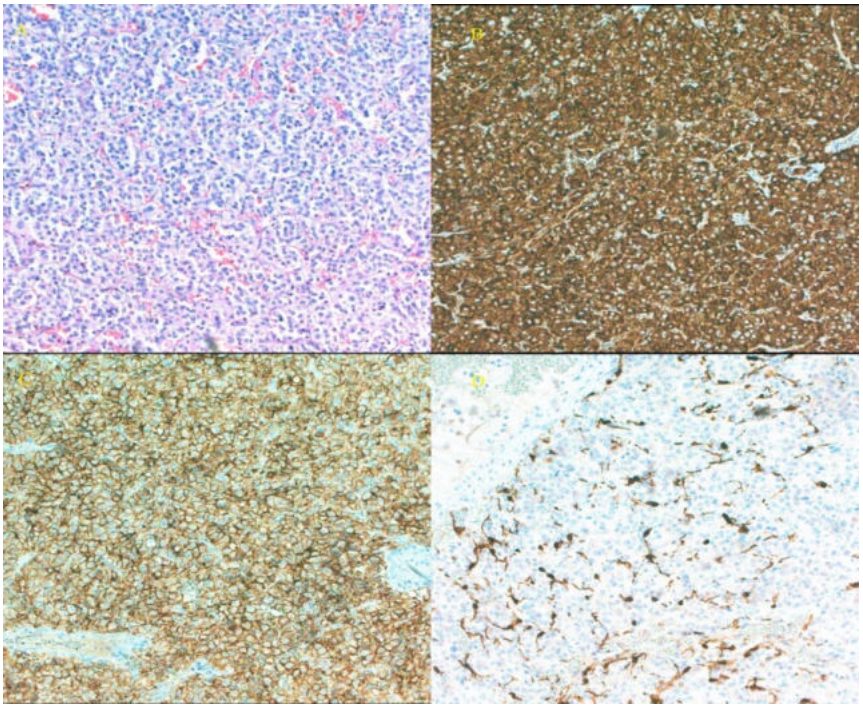

Fig. 3. Pathological examination. (A) Nests formed by tumor cells with oval, round, uniform nuclei and granular cytoplasm (HE×200), (B) Immunohistochemical synaptophysin positivity in tumor cells (×200), (C) Immunohistochemical CD56 positivity in tumor cells (×200), (D) Immunohistochemical S100 positivity in sustentacular cells surrounding tumor cells (×200).

pelvic CT/MRI are the first-choice imaging modalities [8]. Magnetic resonance imaging is recommended for (pregnant women, aged below 25 with metastatic PGL) with a contraindication of radiation exposure. Especially in patients with PGL, anatomical imaging is insufficient and further evaluation is required. Further assessment of localization may require functional investigation with scintigraphy (e.g.i. nuclear medicine modalities) or PET canning [9]. Functional imaging is recommended for the baseline evaluation of patients with large-size PHEOs or PGLs because it is associated with the risk of metastatic disease. Therefore, PET CT imaging was performed because the mass of our patient was located in the extra-adrenal gland.

Paraganglioma /pheochromocytoma is symptomatic in almost half of patients. These symptoms are typically paroxysmal [10]. We considered that our patient had longer hypertensive periods as he was admitted with stage 4 hypertensive retinopathy. However, echocardiography of our patient also revealed left ventricular hypertrophy that was secondary to hypertension. However, in the literature, patients with myocardiopathy secondary to catecholamine discharge were described in patients with pheochromocytoma, as was reported in the cases of Molaei *et al*. [11].

The mean age of diagnosis in children is 11-13 years. It is known that most of the cases are detected in males. In this age group, PGL/ PHEO tend to be bilateral, extra-adrenal, and benign [12]. The findings of our patient were compatible with the literature data since the tumor was in a 15-year-old male and was localized in the extra-adrenal area.

Surgery is the gold treatment for the treatment of PGL/ PHEO. However, as benign and non-functional tumors < 4-6 cm may rarely transform into malignant or become hormonally active, such tumors must be followed up with appropriate radiological imaging and hormonal evaluation. The purpose of surgery is complete resection. Pham *et al*. showed that survival was significantly increased in patients with radical resections that had macro and microscopic negative margins [13]. Medical treatment must be initiated 7-10 days before the surgery in PGL/PHEO cases to check hypertension as well as correct catecholamine-induced extracellular fluid volume contraction. Basically, alpha-adrenoreceptor blockers are used to control blood pressure; and phenoxybenzamine, which is a long-acting, irreversible, non-specific alpha-adrener-

gic antagonist, is the usual choice. Selective alpha-1-antagonists (e.g. prazosin, doxazocin or terazosin) can be used instead of phenoxybenzamine. Both phenoxybenzamine and doxazosin can effectively control perioperative blood pressure and prevent hemodynamic instability in patients of PGL. However, more often, beta adrenergic antagonist (e.g. metaprolol) or combined alpha and beta adrenergic antagonist (e.g. carvedilol, labetalol) are added to the treatment to control reflex tachycardia [14]. We applied premedication to our patient by using doxazosin and carvedilol. It is necessary during the surgery to avoid stimuli and drugs which may cause catecholamine release and to provide hemodynamic stabilization in anesthesia. Our patient, who had normal blood pressure after the surgery, did not require medication.

The surgical approach was adequate because our patient presented with a unilateral and single mass, and it was found that the pathology result was benign. There are controversial data on the malignant potential of PGL/PHEO in children between 3% and 47%. Despite this, overall 5-year survival is better in children than in adults in reported malignancy cases [11]. Long-term clinical and biochemical follow-up should be performed in all PGL/PHEO cases regarding increased recurrence and metastasis risk.

CONCLUSION

Paragangliomas and pheochromocytomas is one of the rare and important causes of secondary hypertension in pediatric patients. As the symptoms may have atypical progression in children, it may appear for the first time with end-organ damage. Even if there is no family history, it must be considered in hypertension cases that have an aggressive progression.

Authors' Contribution

Study Conception: İY; Study Design: ŞA; Supervision: FB; Funding: N/A; Materials: N/A; Data Collection and/or Processing: ZEÇ; Statistical Analysis and/or Data Interpretation: MÖ; Literature Review: FÖS; Manuscript Preparation: İY and Critical Review: ŞA.

Informed consent

Informed consent form was not obtained as this was a patient followed up in the past.

Conflict of interest

The authors disclosed no conflict of interest during the preparation or publication of this manuscript.

Financing

The authors disclosed that they did not receive any grant during conduction or writing of this study.

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