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Intra-adrenal Paraganglioma and Paraaortic Paraganglioma in 15 Years Old Boys

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ABSTRACT

Intra-adrenal paraganglioma (also called pheochromocytoma) is a chromaffin cell tumor that arises in the adrenal medulla and produces excess catecholamines. Paraganglioma can also be located in the extra-adrenal area. The incidence rate of intra-adrenal and extra-adrenal paraganglioma is about 1 case per 2.500-6.500 population, highest incidence at 40-50 years old, and distribution is the same in males and females. Intra-adrenal paraganglioma in pediatrics is more familial, bilateral, multifocal, and malignant. In children, the incidence rate of these tumors was 8.86%, the ratio of boys to girls was 2:1, and the average age of 11. This article reports a case, of a 15 years old boy with severe headaches, recurrent seizures, and a hypertension crisis (143/103-220/110 mmHg). MSCT scan of abdominal showed solid mass heterogeneous with central necrotic multiple in the supero-anterior of the left and right kidneys and on the right anterolateral aorta as high as CV L2, impressive adrenal gland mass and extra-adrenal, suspect pheochromocytoma. Performed surgery, routine histopathological examination, and Immunohistochemistry. Macroscopic examination showed an oval round shape mass of left and right adrenal tumors as well as the paraaortic, a smooth outer surface of the capsular, with yellowish brown color mass tumor at cut surface, supple consistency. Microscopic examination showing adrenal gland and paraaortic tissue with fibrous capsule contains proliferation of neoplastic cells forming a nested alveolar (Zellballen) pattern with a round oval to polygonal cells, granular eosinophilic cytoplasm, round oval nuclei, surrounded by sustentacular cells. Chromogranin A and S-100 are positive. The case was concluded by clinical findings, histopathological, and immunohistochemistry as intra-adrenal paraganglioma and paraganglioma of paraaortic.

Keywords: Adrenal, Paraaortic, Paraganglioma, Pheochromocytoma

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INTRODUCTION

The intra-adrenal paraganglioma is the primary neoplasm of chromaffin cells and is the essential sympathetic paraganglioma of the adrenal medulla.[1,2] The term extra-adrenal paraganglioma denotes a paraganglioma often related to the orthosympathetic system. Paragangliomas, such as normal chromaffin cells, produce and secrete catecholamines and sometimes peptide hormones.[1]

Intra-adrenal paraganglioma is a rare case, where the incidence rate is 1 case per 2,500-6,500 population, found mostly in the fourth or fifth decade of life with equal distribution in males and females. The causative factor of paraganglioma is suspected to be hereditary, with the most important clinical manifestation being hypertensive crisis due to catecholamine secretion.[3] In addition to hypertension, there are classic triad symptoms of headache, tachycardia/palpitations, and sweating seen in <25% of patients.[1]

Here is reported a case of intra-adrenal paraganglioma and paraaortic paraganglioma that occurred in a 15 years old boy with the main symptoms of seizures and hypertensive crisis. This case is a rare case in children, with simultaneous intra- and extra-adrenal neoplasm manifestations, making it interesting to report.

CASE REPORT

A 15 years old boy was referred to Prof. dr. IGNG Ngoerah Hospital on January 4th, 2021, with a referral letter from a pediatrician at RSUD Negara along with laboratory results. The patient was admitted to Negara Hospital on January 2nd, 2021 due to seizures with a blood pressure of 220/110 mmHg. On laboratory examination found hyponatremia and hypokalemia. The patient was referred to Prof. dr. IGNG Ngoerah Hospital with a diagnosis of recurrent hypertensive crisis and needed intensive care and follow-up examinations.

The patient came to the emergency room of Prof. dr. IGNG Ngoerah Hospital with the main complaint being headaches. The patient also complained of sudden blurred vision in both eyes 2 weeks before admission to the hospital and worsened after seizures (2 days before admission to Prof. dr. IGNG Ngoerah Hospital), vision is said to be covered by curtains. Seizures are said to be throughout the body for 5 minutes then followed by nausea and vomiting. The previous history of hypertension is denied, family history of the disease is absent. On physical examination, compos mentis consciousness (E4V5M6), respiration 18 times/minute, pulse 113x / minute, temperature 36.7 ^{0}C, body weight 36 kgs. On examination of the eyes found a picture of retinopathy, hypertension, and macular edema.

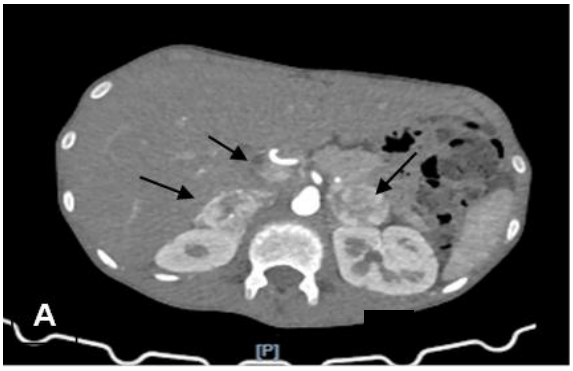

Figure 1. MSCT Scan of the abdomen. Heterogeneous solid masses with central necrotic multiple on the supero-anterior left right kidney and on the right anterolateral aorta as high as CV L2, impressive adrenal gland masses (adrenal and extra-adrenal).

The results of the MSCT (Multi Slice Computerized Tomography) abdominal scan and CTA with and without contrast on January 5th, 2021, suggest the presence of adrenal gland mass (adrenal and extra-adrenal) suspected pheochromocytoma. The results of a CT scan of the head on January 5th, 2021 showed vasogenic edema in the bilateral parieto-occipital region, according to the description of meningoencephalitis and cerebral edema.

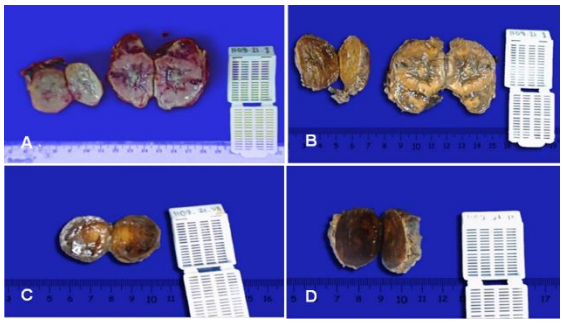

Figure 2. A and B. Right adrenal tumors before and after fixation with 10% formalin neutral buffer solution, C. Left adrenal tumors, and D. Paraoartic tumors

The patient underwent treatment from January 4th, 2021 to February 2nd, 2021. Hypertension begins to be controlled with a blood pressure of 100/70 mmHg and no seizures, so the patient is allowed to go home. However, on February 27th, 2021, the patient had a seizure again, recurrent seizures

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throughout the body for 2 minutes, accompanied by vomiting, with a blood pressure of 200/120 mmHg. The patient was referred to Prof. dr. IGNG Ngoerah Hospital on February 28th, 2021, for further treatment.

The patient underwent abdominal tumor removal surgery on March 12th, 2021. The tissue from surgery is examined in the Anatomical Pathology laboratory, in the form of 3 tissues, namely right adrenal tumor, left adrenal tumor, and paraaortic tumor. The right adrenal tumor consists of 2 pieces of tissue with a size of 3.7x3x2 cm and 5x3.5x3 cm respectively. The shape of the tissue is oval and encapsulated, the outer surface is slippery, the white-gray color is partially yellowish, the consistency is springy, and on the slice appears a mass of yellowish-brown color, with foci of necrosis. Left adrenal tumor, with a size of 3x2,7x2,5 cm oval round shape, and encapsulated, a slippery outer surface, white-gray partially yellowish color, supple consistency, on the slice appears a mass of yellowish-brown color filling the tissue. While paraaortic tumors with a size of 3.6x3x2.5 cm oval round shape, encapsulated, slippery outer surface partially rough, brownish color, in the slice appear brownish masses fill the tissue.

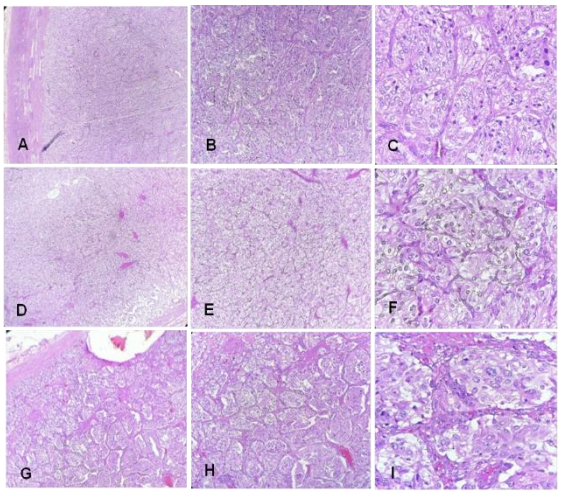

Figure 3. Right adrenal mass A. Tumor mass surrounded with connective tissue capsule (HE 40 times), B and C (HE 100 times and 400 times). Left adrenal mass D. Tumor mass coated with connective tissue capsule (HE 40 times), E, and F. (HE 100 times and 400 times). Paraaortic tumors G. Tumor mass coated with connective tissue capsule (HE 40 times), H and I. (HE 100 times and 400 times). C, F, I. The tumor mass consists of neoplastic cells with oval to polygonal spherical morphology with granulated eosinophilic cytoplasm and oval rounded nuclei forming a nested alveolar (Zellballen) pattern, surrounded by sustentacular cells.

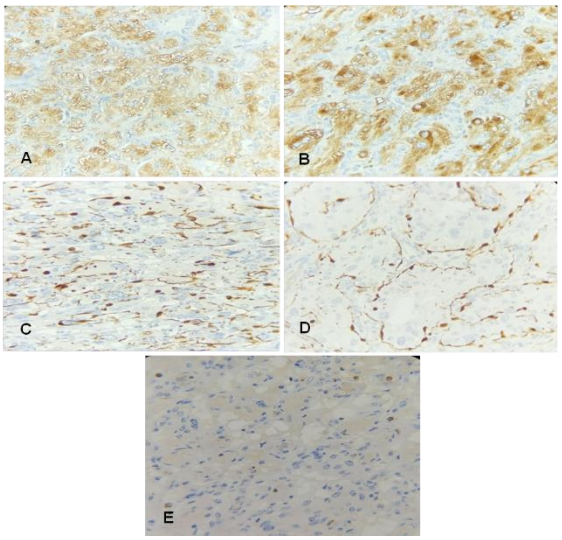

Figure 4. A. Chromogranin A stained diffusely positive in the cytoplasm of intra-adrenal paraganglioma tumor cells B. Chromogranin A stained diffusely positive in the cytoplasm of paraaortic paraganglioma tumor cells; C. S-100 stained in sustentacular cells in peripheral intra-adrenal paraganglioma tumor cells; D. S-100 stained in sustentacular cells in peripheral paraaortic paraganglioma tumor cells; E. Ki-67 expressed in <1% of paraaortic paraganglioma tumor cell nuclei (IHC, 400 times).

Microscopic examination of the right and left adrenal tissues showed adrenal gland tissue covered in fibrous connective tissue capsule containing a tumor mass consisting of a proliferation of neoplastic cells that form nested alveolar structures (Zellballen) surrounded by sustentacular cells. These cells are oval to polygonal spherical cell morphology, granulated eosinophilic cytoplasm, increased N/C ratio, oval round nucleus, relatively monotonous, irregular nuclear membrane, and rough chromatin with visible to prominent nucleoli. Mitosis 8/10 HPF. There is a picture of peripheral capillaries between neoplastic cells. There are also visible foci of necrotic and bleeding areas. There does not appear to be an invasion of the vascular and adrenal capsules.

Microscopic examination of paraaortic tumor tissue shows tumor tissue covered with fibrous connective tissue capsule, containing a tumor mass consisting of a proliferation of neoplastic cells that form nested alveolar structures (Zellballen) surrounded by sustentacular cells. These cells are oval to polygonal spherical cell morphology, granulated eosinophilic cytoplasm, increased N/C ratio, oval round nucleus, relatively monotonous, irregular nuclear membrane, and rough chromatin with visible to prominent nucleoli. Mitosis 9/10 HPF.

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Visible neoplastic cell foci with spindle shape. There is a picture of peripheral capillaries that are partially dilated. Hyaline globules and foci of necrosis and bleeding between neoplastic cells were also seen. There does not appear to be an invasion of the vascular and tumor capsule.

Histomorphologically it was concluded to be suitable for intra-adrenal paraganglioma in the left-right adrenal with a PASS Score of 6, pT2, and paraganglioma in the paraaortic, pT2. The results of immunohistochemical examinations that have been carried out on intra and extra-adrenal paraganglioma tumor masses show immunohistochemical reviews of Chromogranin A stained diffusely positive, S-100 positive in sustentacular cells in peripheral tumor cell nests, Ki67 expressed in <1% in the cell nucleus of paraganglioma tumor masses. Based on immunohistochemical examination supports a diagnosis of paraganglioma.

DISCUSSION

Paraganglioma is a tumor that originates from chromaffin cells and secretes catecholamines. The most frequent location is the adrenal medulla; however, it may arise anywhere in the body along the sympathetic chain.[1-4] Tumors that arise from the adrenal medulla are referred to as intra-adrenal paragangliomas or pheochromocytomas, and those of extra-adrenal origin are called paragangliomas.[1,3,4] Eighty-five percent (85%) of sympathetic paraganglioma cases appear below the diaphragm, of which 42% are around the adrenal glands (hilus or renal pedicle), 28% around the Zuckerkandl organ, 10% in the bladder, about 12% in the thorax, and the rest in other locations.

Cases of intra- and extra-adrenal paraganglioma are rare cases with an incidence rate of 1 case per 2,500-6,500 population, found mostly in the fourth or fifth decade of life, the distribution is the same in males and females and can occur in children and adults at any age.[1.3] In children, the incidence of these tumors reached 8.86% of the total cohort with the ratio of boys to girls being 2:1.[6] This case occurred in a 15 years old boy with intra-adrenal paraganglioma and paraaortic paraganglioma appearing simultaneously. In terms of age, this case is still in accordance with the literature where it is said that the average age of intra-adrenal and extra-adrenal paraganglioma cases in children is classically 11 years old, while other studies are between 12 and 14 years old.[4.6] The prevalence of intra-adrenal paraganglioma at the initial presentation was 20.75% and overall 33%. The prevalence of extra-adrenal paraganglioma varies from 18 to 61.1%.[6]

At least 20-40% of intra-adrenal paragangliomas are known to be hereditary,[1,3,7,8] with bilateral localization, and 10% of these cases are malignant.[3] Intra-adrenal paraganglioma often occurs sporadically but can be inherited as an autosomal dominant trait.[1,5] Pediatric paraganglioma is almost always hereditary so genetic testing should be offered to all pediatric patients. In this case, bilateral intra-adrenal paraganglioma is found to occur together with paraaortic paraganglioma, this can be possible if it is influenced by hereditary conditions, but this needs further proof. Hereditary, intra-adrenal paraganglioma is associated with other syndromes such as Von Hippel Lindau syndrome (VHL), multiple endocrine neoplasias (MEN) 2A and 2B, familial paraganglioma syndrome and neurofibromatosis-1 (NF-1), MEN1 and tuberous sclerosis.[1,4,5] More than one-third of intra-adrenal paragangliomas are associated with germline mutations *of* the succinate complex dehydrogenase *gene (*SDHA, SDHB, SDHC, SDHD), Multiple endocrine neoplasia type 2 (RET), SDHAF2, TMEM 127 and MAX.[1,5,9,10]

The majority of intra-adrenal paragangliomas are benign, only about 10-12% are malignant mainly in the pediatric population.[5] Malignancy is defined as the presence of metastases in nonchromaffin tissue; prevalence varies between 10% and 17%. The most common metastatic locations include the liver, lymph nodes, lungs, and bones. Other rare locations include the peritoneum, pleura, ovaries, and testes.[1,7,9] Metastases sometimes develop years or decades after primary tumor resection.[1] Intra-adrenal paragangliomas tend to be more malignant in certain patient groups, such as carriers of SDHB gene mutations, extra-adrenal paragangliomas (35% malignant), and large tumors (>5 cm more likely to be malignant). Mutations in the gene coding for SDH subunit B (SDHB) can cause metastatic disease in more than 40% of patients.[9] SDHB mutations, adrenal gland scale (PASS) scores >6, and a high Ki-67 index are risk factors assigned to the malignant category.[7.9]

Intra-adrenal paraganglioma patients present with severe hypertension symptoms and various other symptoms such as palpitations, sweating, and headaches due to excessive secretion of catecholamines (norepinephrine, epinephrine, or dopamine) into the circulation.[1,3,4] The classic manifestations of intra-adrenal paraganglioma include hypertensive crises such as those experienced by

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this patient, where severe attacks of hypertension are associated with symptoms of hypertensive encephalopathy (such as altered states of consciousness and seizures). The effects of severe hypertension are seen in the end organs, especially the eyes, kidneys, central nervous system, and heart with acute myocardial ischemia due to increased oxygen demand.[3] In these patients, symptoms of hypertensive crisis with blood pressure reaching 220/110 mmHg and accompanied by recurrent seizures. Patients also feel headaches, nausea, vomiting, and visual disturbances. According to research, children are less likely to experience classic triads such as tachycardia, headaches, and diaphoresis. Symptoms that can arise include visual changes, nausea, vomiting, constipation, diarrhea, orthostatic hypotension, urinary tract symptoms, psychiatric disorders, and weight loss.[11]

The pathophysiological mechanism of intra-adrenal paraganglioma is based on an increased release of catecholamine hormones, secreted by tumors, continuously or episodically. These hormones include epinephrine, norepinephrine, and dopamine, excessively stimulating alpha and beta-adrenergic receptors, giving rise to various clinical manifestations.[1-3] Symptoms of intra-adrenal paraganglioma appear due to predominantly catecholaminergic secretions. Epinephrine stimulates beta-1 and beta-2 adrenergic receptors and causes vasodilation in striated muscles. Epinephrine also has a metabolic effect, stimulating liver glycogenolysis and gluconeogenesis, thereby causing hyperglycemia. Norepinephrine stimulates alpha-1, alpha-2, and beta-2 adrenergic receptors, which cause vasoconstriction and increased blood pressure. Dopamine stimulates dopaminergic receptors D1 and D2. In the case of intra-adrenal paraganglioma, dopamine concentrations increase, thereby causing vasoconstriction and increased heart rate. In addition, paraganglioma is characterized by the release of other substances, such as special neuronal enolases, vasoactive intestinal peptides, or adrenocorticotropic hormone (ACTH), which causes various other clinical manifestations.[3]

Intra-adrenal paraganglioma sometimes causes paraneoplastic syndromes by producing peptides with ectopic regulation. Cushing's syndrome is the most common, caused by the secretion of ACTH or CRH.[1] A clear understanding of the clinical and behavioral characteristics of this tumor is essential for clinicians to distinguish it from more common childhood neoplasms such as neuroblastoma and Wilms' tumor.[11]

Intra-adrenal paraganglioma is a well-defined tumor but usually a non-capsulated tumor that appears in the adrenal medulla. With increasing size and extending to the capsule of the adrenal glands so that it compresses or obliterates the cortex. The adrenal capsule thus becomes the tumor capsule. The surface of the cut is reddish-gray to brown (as opposed to bright yellow cortex tumors) but may turn yellow slightly after exposure to air or after administration of formalin. Hemorrhage, central degenerative changes, fibrosis, and cystic changes vary, the diameter of the tumor is usually about 3-5 cm but can be >10 cm or <1 cm. Sympathetic paragangliomas are usually well-defined, dense, soft, and brown in color. Hemorrhagic or cystic degeneration may be seen in larger tumors. Tumors can attach strongly and sometimes invade adjacent tissues such as blood vessels and nerves.[1]

Intra-adrenal paraganglioma shows an alveolar nest (Zellballen) pattern, which consists of a nest of polygonal tumor cells separated by peripheral capillaries. Architectural variations include trabecular and diffuse growth patterns as well as prominent vascularization resembling angiomas. Architectural variations include irregular combinations of Zellballen patterns and large and small pseudorosettes. The pseudorosette pattern indicates tumor-associated SDHB mutations.[1]

Malignancy in paragangliomas is difficult to determine only by histology.[12,13] Malignant paraganglioma is initially defined only by the presence of metastases.[1,13,14] However, according to the 2017 update on WHO endocrine tumors all paragangliomas can have metastatic potential due to the lack of a supportive histological system for the biological aggressiveness of paragangliomas. The term "metastatic" is used, replacing "malignant" in this group of tumors.[1.15] The European Clinical Guideline decides that all patients with paraganglioma should be followed up for at least 10 years and high-risk patients (young, genetic diseases, large tumors, and paragangliomas) should be offered follow-up annually for life.

For the pathological diagnosis of intra-adrenal paraganglioma, in 2002 Thompson introduced the Pheochromocytoma of the Adrenal Gland Scaled Score (PASS) scoring system, consisting of 12 parameters and a score of up to 20 points (can be seen in Table 1). Tumors with a PASS score of >4 were defined as having an increased metastatic potential, while those with a score of <4 were

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considered to have no metastatic potential.[13,14,15] Recent studies show values of <4 for benign tumors and ≥6 for malignant tumors, while values between 4 and 6 indicate intermediate risk.[14] PASS is not used in extra-adrenal paraganglioma and provides only one threshold for predicting the risk of metastasis. The original PASS system consisted of only overgrown and complex histopathological indicators, and some of them was not specific for paragangliomas.[15]

Table 1. Pheochromocytoma of the Adrenal Gland Scaled Score (PASS).[14]

Histomorphology parameter	Score
Hyperchromatic nuclei	1
Marked pleomorphism of the nucleus	1
Capsular invasion	1
Vascula invasion	1
Expansion into periadrenal fatty tissue	2
Atypical Mitosis	2
Mitosis >3/ 10 HPF	2
Spindling cell	2
Cellular monotony	2
High Cellularity	2
Confluent and central necrosis	2
Large nest or growth diffuse (>10 % tumor volume)	2
Total	20

Table 2. Grading System for Adrenal Phaeochromocytoma and Paraganglioma (GAPP).[13]

Parameter	Score
Histology Pattern	
Zellballen	0
Large and irregular tumor nests	1
Pseudorosette (can be focal)	1
Cellularity	
Low (<150 cell/U*)	0
Moderate (150-250sel/U*)	1
High (>250 cell/U*)	2
Comedonecrosis	
No	0
Seen	2
Capsular and vascular invasion	
No	0
Seen	1
Ki67 Index	
<1%	0
1-3%	1
>3%	2
Type Of Catecholamines	
Adrenaline type (A or A +NA)	0
Noradrenaline Type (NA or NA +DA)	1
Non-functioning Type	0
Maximum total score	10

Description: U* → cells with units of 10x10 mm (400 times magnification), NA (noradrenaline), A (adrenaline), DA (Dopamine)

The grading system for Adrenal Phaeochromocytoma and Paraganglioma (GAPP), developed by Kimura in 2014 in Japan for intra- and extra-adrenal paraganglioma, histological assessment is based on a scoring system consisting of six parameters (metastatic risk factors): Histological, cellular, comedo necrosis, capsular/vascular invasion, Ki67 index, and catecholamine phenotype, for a total of 10 points. GAPP scores of 0-2 are low risk, 3-6 are medium risk and 7-10 are high risk.[1.13]

Although the PASS scoring system was created only for intra-adrenal paraganglioma (pheochromocytoma), another study classified extra-adrenal paraganglioma according to the PASS system, and the results showed that the PASS system also had the same ability to predict malignant paraganglioma behavior.[15] It was also found that the GAPP system assessment had the same high sensitivity, low specificity, low predictive accuracy rate against tumor metastasis, and excellent prediction for non-metastatic paraganglioma compared to the PASS system.[15] In this patient the PASS score in intra-adrenal paraganglioma is 6, including mitosis >3/10 LPB with a score of 2, cells tend to be monotonous with a score of 2, and the presence of necrosis with a score of 2, while other histomorphological parameters of PASS are not found. In paraaortic tumors, GAPP scoring should be used, but it cannot be done because in these patients there is no catecholamine-type examination (GAPP scoring can be seen in Table 2). If paraaortic tumors are scored with a PASS score, a PASS score of 8 is obtained which includes mitosis >3/10 LPB with a score of 2, cells tend to be monotonous with a score of 2, necrosis with a score of 2 and the presence of spindle cells with a score of 2. With a total PASS score of more than 4, the tumor in this case has an increased potential for metastasis. While staging is determined from the AJCC Cancer Staging Manual, where intra-adrenal paraganglioma with pT2 staging (with an adrenal mass of 5 cm or more), while paraganglioma tumors in the paraaortic of any size with pT2 staging *(*see Table 3).

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Table 3. Staging TNM medulla adrenal tumor and ekstra-adrenal paraganglia (pheochromocytoma dan paraganglioma).

T- Tumor Primer		M- Distant metastases		
Tx	Primary tumors cannot be assessed	M0	No distant metastases	
T0	No evidence of primary tumor	M1	Distant metastases	
T1	*Pheochromocytoma* of the adrenal glands with the largest size less than 5cm, no extra-adrenal invasion	Stage		
T2	*Pheochromocytoma* of the adrenal glands of the largest size of 5 cm or more, or functional paraganglioma of any size, there is no extra-adrenal invasion	Stage I	T1	N0 M0
T3	Tumors of any size with the invasion of surrounding tissues (liver, pancreas, kidney)	Stage II	T2	N0 M0
		Stage III	T1	N1 M0
			T2	N1 M0
			T3	*Any* N M0
N- Regional Lymph node		Stage IV	*Any* T	*Any* N M1
NX	Regional lymph nodes cannot be assessed			
N0	No metastasis at the regional lymph node			
N1	Metastasis at the regional lymph node			

Confirmation of the diagnosis requires an immunohistochemical review. The main differential diagnosis is adrenocortical neoplasia. To distinguish from adrenocortical neoplasia, renal cell carcinoma, and metastasis of a non-endocrine tumor by staining with Chromogranin A. Chromogranin A must be stained in the cytoplasm with strong intensity and diffuse in a paraganglioma. The expression of tyrosine hydroxylase and dopamine beta-hydroxylase, which are necessary for catecholamine synthesis, can help get rid of neuroendocrine tumors metastatic to the adrenal glands.[1] Another immunohistochemical review is S100 stained in the nucleus and cytoplasm of sustentacular cells, which can be found in peripheral Zellballen or among tumor cells. There has been a remarkable decrease in the immunoreactivity of the S100 protein in malignant cases.[1,14] SDHB mutations are the only factor indicating the possibility of future metastasis.[13] This new immunohistochemistry is associated with SDH mutations, which result in the loss of the SDHB protein.[1] Therefore, it is important to perform SDHB immunohistochemistry for all paragangliomas except the adrenaline-producing type. Patients with SDHB-negative tumors should be carefully monitored for long periods of time because of the high likelihood of metastasis.[13] In this case, the diagnosis was confirmed by histochemical reviews of Chromogranin A and S100, both of which gave positive results. Diffuse stained chromogranin A in 80% of the cytoplasm of intra-adrenal and paraaortic paraganglioma tumor cells. S-100 is stained diffusely in the cell nucleus and cytoplasm of sustentacular cells located in the peripheral part of Chromaffin tumor cells.

The prognosis for paraganglioma is closely related to genetic profile and resectability,[1] with a high metastatic potential documented in SDHB and MAX mutated paraganglionic tumors. However, SDHB germline mutations account for only 55% of metastatic paragangliomas; 45% of patients appear to have sporadic tumors. Other factors that may be associated with the potential for metastasis include larger tumor size, older patient age at initial diagnosis, and noradrenergic and/or dopaminergic biochemical phenotypes.[1] In this case, judging from the PASS score value, the possibility of metastasis is high and has a tendency to moderate to high malignancy, but there are no other tests that can determine the possibility of metastasis such as SDHB and catecholamine reviews, so the prognosis of this patient cannot be determined more precisely and further observation is needed.

SUMMARY

Intra-adrenal paraganglioma and paraaortic paraganglioma that occur together in pediatrics are rare cases but require special treatment. This disease has the main symptoms of a hypertensive crisis even accompanied by hypertensive encephalopathy (loss of consciousness and seizures) which can be fatal for patients, so the initial assessment of this case must be done carefully. In addition, paraganglioma in pediatrics has a potential malignancy of 10-12%, especially if it is related to carriers of SDHB gene mutations, extra-adrenal paragangliomas, and tumors with large sizes. Determination of prognosis is also required using PASS and GAPP scores where tumors with a PASS score of >4 are defined as having an increased metastatic potential, and GAPP scores of 7-10 are at high risk of metastasis.

A clear understanding of the clinical characteristics and biochemical behavior of tumors as well as the determination of diagnosis assisted by supporting examinations such as radiology and anatomical pathology are essential for doctors to provide appropriate treatment for patients.

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