Case Report

A rare adrenal encounter: Non-secretory pheochromocytoma in a child with *SDHAF2* mutation

ABSTRACT

Pheochromocytoma is a catecholamine-producing tumor that originates from the chromaffin cells of the adrenal medulla and is rare in children. The clinical manifestations are usually variable and nonspecific, and patients might rarely be asymptomatic. Diagnosis requires urinary or plasma fractionated metanephrine measurement and radiological studies. The preferred treatment is surgical resection of the tumor. We report a case of a 4-year-old boy presenting with right-sided lower abdomen pain and multiple episodes of vomiting for 2 months and found to have hypertension. All the routine investigations, along with 24 h urine metanephrines, normetanephrines, overnight dexamethasone suppression test, serum dehydroepiandrostenedione, and midnight serum cortisol, were found to be normal. Contrast-enhanced computed tomography abdomen with adrenal protocol revealed a well-defined heterogeneously enhancing soft tissue lesion measuring 47 × 36 mm arising from the right adrenal region with a baseline Hounsfield Unit of +29. The child was taken up for exploratory laparotomy with right-sided adrenalectomy. Histopathological examination and immunohistochemistry were suggestive of pheochromocytoma. Whole exome sequencing detected a heterozygous variant of uncertain significance in exon 4 of the *SDHAF2* gene. This is the first report of non-secretory pheochromocytoma in a child with *SDHAF2* mutation.

Keywords: Adrenal incidentaloma, paraganglioma, pheochromocytoma, *SDHAF2* mutation

INTRODUCTION

Pheochromocytomas are catecholamine-secreting tumors that arise from the adrenal medulla. Secretory pheochromocytomas can produce epinephrine, norepinephrine, or less commonly dopamine and methoxytyramine.[1] The classical triad of presentation is episodic headache, palpitations, and profuse sweating. The disease presentation can vary from an asymptomatic incidentaloma to a hypertensive crisis.

It is rare to find pheochromocytoma in the pediatric age group, accounting for about 10% of all cases.[2] Most commonly, it presents as hypertension in children. The association with hereditary syndromes, like Von Hippel-Lindau disease, multiple endocrine neoplasia type 2A, and familial paragangliomas, might be seen more commonly in the pediatric age group.[3]

Here, we discuss a child who presented with pain abdomen, vomiting, and hypertension with a right adrenal incidentaloma, which was found to be biochemically silent. Post-adrenalectomy, it was confirmed by histopathological examination (HPE) and immunohistochemistry (IHC) to be a pheochromocytoma. Whole exome sequencing (WES)

Roohi Nanda, Soumik Goswami, Nilanjan Sengupta, Arjun Baidya, Vibhu Ranjan Khare, Sapan Shah

Department of Endocrinology, Nil Ratan Sircar Medical College and Hospital, Kolkata, West Bengal, India

Address for correspondence: Dr. Roohi Nanda, Department of Endocrinology, Nil Ratan Sircar Medical College and Hospital, Kolkata 700014, West Bengal, India.
E-mail: roohinanda@gmail.com

Submitted: 15-Feb-2025, **Revised:** 01-May-2025,
Accepted: 02-May-2025, **Published:** 23-Jun-2025.

Access this article online	
Website: https://journals.lww.com/jmcr	Quick Response Code
DOI: 10.4103/ijemcr.ijemcr_11_25	

How to cite this article: Nanda R, Goswami S, Sengupta N, Baidya A, Khare VR, Shah S. A rare adrenal encounter: Non-secretory pheochromocytoma in a child with *SDHAF2* mutation. IJEM Case Rep 2025;3:75-8.

detected a heterozygous variant of uncertain significance at chromosome 11, exon 4 of the *SDHAF2* gene.

CASE REPORT

A 4-year-old boy, born out of a non-consanguineous marriage, by normal vaginal delivery at term, presented to the hospital with complaints of right-sided, severe, dull aching lower abdomen pain and multiple episodes of non-projectile, non-bilious vomiting. He had no history of profuse sweating, episodic headache, palpitations, tremors, or loss of consciousness. There was no history of neck swelling, flushing, altered bowel habits, or the presence of pubic or axillary hair, hyperpigmented spots, or nodular skin lesions. There was no significant past, personal, or family history. On examination, the child was conscious and oriented to time, place, and person with a pulse rate of 102/min, respiratory rate of 14/min, systolic blood pressure of 110 mm Hg (between the 95th and 99th percentile according to age and sex), and diastolic pressure of 70 mm Hg (between the 95th and 99th percentile according to age and sex). On anthropometric assessment, his height was 102 cm (between 25th and 50th percentile for age and sex, height standard deviation score [SDS]: −0.25, height age of 4 years), and weight was 15 kg (25th percentile for age and sex, weight SDS: −0.5, weightage of 3.5 years). The mid-parental height was 169 cm, and target height was 169.8 cm (target height SDS of −0.44). The arm span was 104 cm, upper segment:lower segment (US:LS) ratio was 1.21, and BMI was 14.41 kg/m^2 (SDS: −0.74). The general examination was normal. Sexual maturity rating according to Tanner was G1P1A0, with bilateral testes 2 mL each, present in the scrotum, stretched penile length was 6 cm, and the urethral opening was present at the tip of the urethra. The systemic examination was unremarkable. Laboratory investigations revealed complete blood count, renal function test, liver function test, and electrolytes to be normal. The 8 AM basal serum cortisol was 13.7 mcg/dL, midnight serum cortisol (awake) was 2.5 mcg/dL, and post-overnight dexamethasone suppression test serum cortisol was 0.9 mcg/dL. The 24 h urine metanephrines and normetanephrines were 35.46 mcg/day (25–117 mcg/day) and 107.88 mcg/day (54–249 mcg/day), respectively. ECG showed T wave inversions in lead V1–V3, and no other significant changes were present. 2D Echocardiography was normal. Ultrasound abdomen showed a well-defined hypoechoic rounded space-occupying lesion of 52 × 34 mm size in the right supra renal region. Contrast-enhanced computed tomography abdomen with adrenal protocol revealed a well-defined heterogeneously enhancing soft tissue lesion measuring 47 × 36 mm arising from the right adrenal region with a baseline Hounsfield Unit of +29. Few in-homogenous lymph nodes at para-caval region with the largest measuring 1.9 × 1.2 cm were seen [Figure 1a]. The child was started on amlodipine 5 mg once a day for the management of hypertension. After 4–5 days of starting the oral anti-hypertensive medication, the blood pressure was controlled, SBP being 90 mm Hg (50th percentile) and diastolic pressure 52 mm Hg (50–90th percentile).

The child was then referred to the Department of Pediatric Surgery, and an exploratory laparotomy along with right-sided adrenalectomy was performed. Regular intra-operative and post-operative blood pressure monitoring was done, and amlodipine was stopped after the surgery, due to normalization of blood pressure. Grossly, the specimen was a single, irregular, gray-brown soft tissue piece measuring

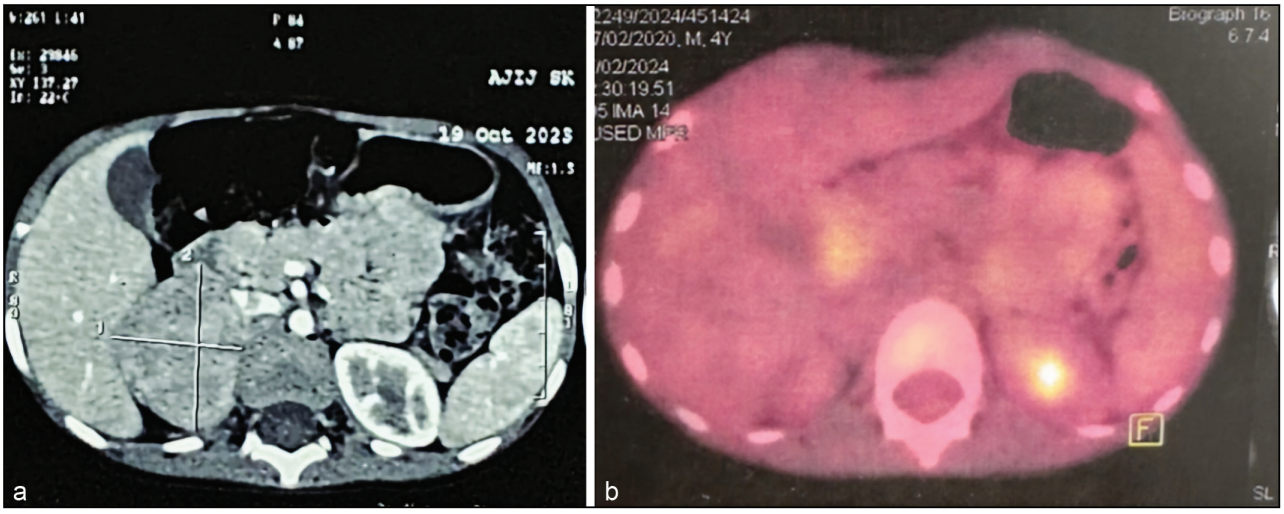

Figure 1: (a) Axial section of contrast- enhanced computed tomography (CECT) – abdomen showing a well-defined, heterogeneously enhancing right adrenal mass of 47 × 36 mm. (b) Fluorodeoxyglucose positron emission tomography/computed tomography showing mildly avid ill- defined retroperitoneal lymph nodes in aorto- caval and para- caval region

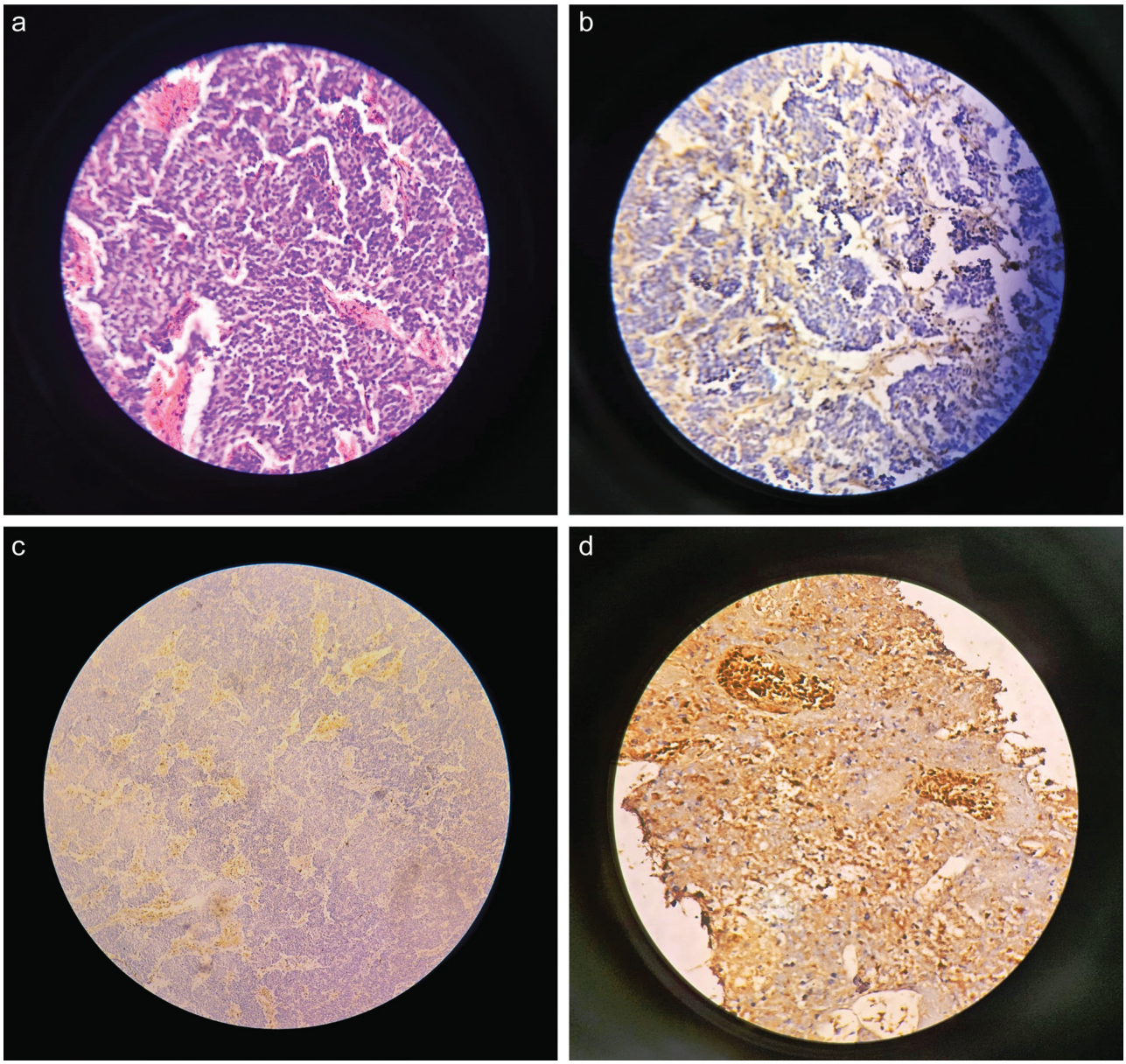

Figure 2: (a) Adrenal medulla section showing Zellballen pattern on histopathological examination. (b) Adrenal medulla section showing positive chromogranin stain. (c) Synaptophysin stain. (d) S-100 stain on immune-histochemistry

6 × 5 × 4.5 cm, appearing solid and focally hemorrhagic on cross-section. The HPE was suggestive of a well-circumscribed highly cellular tumor mass with cells arranged in nest pattern (Zellballen pattern) [Figure 2a]; the cells were uniform with granular cytoplasm and round nuclei. Capsular and vascular invasion was noted with increased mitotic activity (>4/10 high-power field) and a PASS score >4. The IHC was positive for chromogranin, synaptophysin, and S-100 [Figures 2b–d]. These findings were confirmative of right adrenal pheochromocytoma.

The child was followed up after 1 month at the Endocrine OPD and found to have normal blood pressure. WES was performed which revealed a heterozygous variant of uncertain significance at chromosome 11, exon 4 of the *SDHAF2* gene. Fluoro-deoxyglucose–positron emission tomography–computed tomography was done to look for any malignancy and showed mildly avid few ill-defined retroperitoneal lymph nodes in aorto-caval and para-caval region (1.82 × 1.42 cm) [Figure 1b]. Magnetic resonance imaging (MRI) abdomen showed enlarged upper retro-caval lymph node (1.5 × 1.2 cm). A follow-up MRI after 6 months did not show any enlarged intra-abdominal lymph nodes persisting suggesting the earlier finding to be of nonmalignant etiology.

DISCUSSION

Here, we present a case of a 4-year-old boy who presented with hypertension, abdomen pain, and vomiting. The biochemical parameters were normal, and on radiological investigation, a right suprarenal space-occupying lesion was seen. The post-adrenalectomy HPE and IHC were suggestive of pheochromocytoma. The WES revealed *SDHAF2* gene mutation.

The germline mutations associated with pheochromocytoma and paragangliomas have been classified into two major groups: hypoxic pathway: cluster 1 and the kinase signaling pathway: cluster 2. *SDHAF2*, SDHD, SDHC, SDHB, VHL, and HIF2A are part of cluster 1, while RET, NF1, MAX, and TMEM127 are part of cluster 2.[4,5] The cluster 2 paragangliomas have a low tumoral catecholamine content and lower rates of catecholamine secretion.[6]

Pediatric patients usually have a higher prevalence of hereditary, extra-adrenal, metastatic, recurring paragangliomas (PGL), and pheochromocytoma (PCC). There is usually a higher prevalence of cluster 1 mutation and more aggressive nature of PCC/PGLs in this age group. There is a more frequent occurrence of sustained hypertension (60–90%).[2]

SDHAF2 mutation, formerly known as PGL2 or SDH5, is known to be the causative gene in a small proportion of patients with head and neck paragangliomas. The phenotype of *SDHAF2* variant is characterized by the occurrence of non-metastatic and often multi-centeric head and neck paragangliomas.[7]

Non-secretory pheochromocytoma in association with *SDHAF2* mutation has not been reported in the pediatric age group earlier which makes our case report unique.

CONCLUSION

This case highlights that pheochromocytoma associated with *SDHAF2* mutation can be biochemically silent and present with pheochromocytoma in the pediatric age group. This showcases the importance of thorough evaluation of an adrenal mass in younger individuals.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form, the patient and his guardian have given their consent for his images and other clinical information to be reported in the journal. They understand that their names and initials will not be published and due efforts will be made to conceal their identity.

Financial support and sponsorship

Nil.

Conflicts of interest

There are no conflicts of interest.

REFERENCES

1. Bayley JP, Kunst HP, Cascon A, Sampietro ML, Gaal J, Korpershoek E, *et al*. SDHAF2 mutations in familial and sporadic paraganglioma and phaeochromocytoma. Lancet Oncol 2010;11:366-72.
2. Burnichon N, Rohmer V, Amar L, Herman P, Leboulleux S, Darrouzet V, *et al*.; PGL.NET Network. The succinate dehydrogenase genetic testing in a large prospective series of patients with paragangliomas. J Clin Endocrinol Metab 2009;94:2817-27.
3. Neumann HP, Erlic Z, Boedeker CC, Rybicki LA, Robledo M, Hermsen M, *et al*. Clinical predictors for germline mutations in head and neck paraganglioma patients: Cost reduction strategy in genetic diagnostic process as fall-out. Cancer Res 2009;69:3650-6.
4. Igaki J, Nishi A, Sato T, Hasegawa T. A pediatric case of pheochromocytoma without apparent hypertension associated with von Hippel-Lindau disease. Clin Pediatr Endocrinol 2018;27:87-93.
5. Januszewicz P, Wieteska-Klimczak A, Wyszyńska T. Pheochromocytoma in children: Difficulties in diagnosis and localization. Clin Exp Hypertens A 1990;12:571-9.
6. Pham TH, Moir C, Thompson GB, Zarroug AE, Hamner CE, Farley D, *et al*. Pheochromocytoma and paraganglioma in children: A review of medical and surgical management at a tertiary care center. Pediatrics 2006;118:1109-17.
7. Caty MG, Coran AG, Geagen M, Thompson NW. Current diagnosis and treatment of pheochromocytoma in children: Experience with 22 consecutive tumors in 14 patients. Arch Surg 1990;125:978-81.