Oncology

Multiple Recurrent Paraganglioma in a Pediatric Patient with Germline SDH-B Mutation

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Abstract

Magnetic Resonance Imaging (MRI) and fluorodeoxyglucose positron emission tomography (FDG-PET) are recognized approaches for locating paragangliomas. Recently, gallium-68 DOTA-octreotate (DOTATATE) scans have shown promise detecting neuroendocrine tumors missed by FDG-PET and MRI. 13-year-old male with SDH-B mutation presented with symptoms of paraganglioma and elevated catecholamines. MRI did not demonstrate the T2 hyper intense signal typical of paraganglioma and pheochromocytoma; FDG-PET scan did not reveal increased foci of uptake. DOTATATE scan revealed a signal consistent only with residual adrenal tissue. Resection of the right adrenal bed revealed paraganglioma. Following surgery, no further symptoms were reported and biochemical tests normalized.

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Introduction

Succinate Dehydrogenase B (SDHB) is part of a family of genes that codes for the Krebs cycle enzyme succinate dehydrogenase. Mutations in these genes are associated with development of paragangliomas, pheochromocytomas, and renal cell carcinoma (RCC). Paragangliomas are extra-adrenal tumors of sympathetic and parasympathetic ganglion that, like pheochromocytomas, are derived from neural crest cells and have the ability to secrete catecholamines. This may cause symptoms including headaches, sweating, palpitations, hypertension, and behavior changes. Approximately 10–20% of cases are diagnosed during childhood, and most cases are functional in nature with clinical symptoms related to catecholamine hypersecretion and/or tumor mass effect. Both MRI and computed tomography (CT) can identify tumor location after biochemical diagnosis. Functional imaging, such as fluorodeoxyglucose (FDG) positron emission tomography (PET) scans, are highly sensitive and specific for detecting metastatic disease in patients who have biochemically confirmed paraganglioma. Gallium-68 DOTA-octreotate (DOTATATE) scans are superior in detecting somatostatin-avid malignancies, including neuroendocrine tumors. Surgical resection, with long term surveillance is standard treatment for these tumors.

Case presentation

A 13-year-old boy presented to the National Institutes of Health (NIH) with recurrent headaches, occasional chest pain, and hypertension. His past medical history was significant for a previous right total adrenalectomy at age 11 at an outside institution for biochemically active pheochromocytoma associated with germline SDHB alteration. His presenting symptoms at that time were consistent hypertension of 155/115, episodic headaches, and non-exertional chest pain. Elevated serum and urine catecholamines were found; and an MRI revealed a 2.5 cm right adrenal mass with no evidence of metastatic disease. He underwent an uncomplicated laparoscopic right radical adrenalectomy.

After surgery, his symptoms and catecholamines normalized until age 13, when he re-presented with headaches and chest pain similar to his previous episode. Laboratory testing again revealed...
elevated catecholamines. He underwent a full-body CT, and an MRI
of the abdomen and pelvis which revealed an enhancing soft-tissue
artifact in the right adrenal bed and a 1.6 cm renal cortical mass
(Fig. 1A). DOTATATE scan revealed signal in the right adrenal bed
suggestive of residual right adrenal tissue rather than recurrent
tumor (Fig. 1B). DOTATATE scan demonstrated increased uptake in
the right renal mass seen on CT and MRI. He elected to undergo a
robotically assisted right partial nephrectomy and resection of the
right adrenal site at the Urologic Oncology Branch at the NIH.

The patient underwent alpha blockade and catecholamine-
synthesis inhibition for 2 weeks prior to the procedure. Intra-
operatively, suspicious nodular lesions were found along the
inferior vena cava, underneath the liver, and in the right adrenal
bed. Frozen section of the paracaval tissue revealed multiple small
neuroendocrine tumors. The paracaval lesions were not identi-
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fied on any of the preoperative imaging. Additional nodules were
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fied and resected between anterior Gerota’s fascia and the
liver capsule as well as throughout the right adrenal fossa.

Final pathology revealed paraganglioma in the right residual
adrenal tissue and multiple nodules of hyperplastic paraganglia
along the periaortal and adjacent renal fibroadipose tissue (Fig. 2).
Interestingly, the right renal mass was also a paraganglioma with no
invasion to renal parenchyma. The renal tumor and hyperplastic
paraganglia were positive for synaptophysin and chromogranin
immunohistochemistry staining which are markers for neuroen-
docrine tumors. Ki67 proliferation index was higher than 5%
(intermediate).

Discussion

This patient’s FDG PET scan did not identify the paragangliomas
in this patient. However, it was noted that there was extensive
brown fat present, which may have obscured the detection of the
paraganglioma using this imaging modality. However, the DOTA-
TATE scan also failed to conclusively demonstrate any of the para-
ganglioma, except for some equivocal findings in the right adrenal
fossa. The paracaval lesions were essentially invisible on all the
imaging modalities; This illustrates the need a low threshold of
suspicions when evaluating equivocal soft tissue lesions in symp-
tomatic SDHB patients. It also highlights the shortcomings of
current imaging techniques in children where brown fat may
obscure small paragangliomas.

The renal mass identified on MRI (Fig. 1A) was initially suspected
to be renal cell carcinoma (RCC). Patients affected with germline
mutations of the SDHB gene are at risk for the development of RCC
and, it is recommended that patients with this mutation undergo
annual surveillance in order to identify and treat these lesions early.
Germline SDHB mutation may result in aggressive RCC and early
surgical resection of solid renal masses is recommended. Active
surveillance for SDHB-related renal masses is not recommended.

Since it was suspected the artifact embedded within the right
adrenal bed would be a remnant chromaffin tumor, the therapeutic
goal was to achieve definitive treatment with complete surgical
resection. Surprisingly, the pathology of the surgically removed
kidney lesion also demonstrated paraganglioma with no invasion
outside of the tumor capsule or into the renal parenchyma. This
case demonstrates a rare location of a paraganglioma, occurring
adjacent to the renal parenchyma. Partial adrenalectomy is often
recommended for other hereditary adrenal tumors, such as VHL-
related pheochromocytomas. However, given this local recurrence
after a radical adrenalectomy, this approach may not be
suitable for SDH-related pheochromocytomas and paragangliomas.

On 3-month follow up, the patient was normotensive and
reported no headaches or chest pain. Additionally, his serum and
urine catecholamines and metanephrines were within normal
limits. The clinical improvement and biochemical normalization,
along with an uncomplicated surgical course. Lifelong surveillance is recommended for SDHB-related tumors.

To our knowledge, this is the first case report on the management of a symptomatic pediatric SDHB patient with robotically-assisted partial nephrectomy and local resection of a paraganglioma. Furthermore, this case highlights the significance of thorough intraoperative inspection for suspicious tissue in a previously treated SDHB patient with biochemical and symptomatic recurrence, despite an MRI or FDG PET scan failing to conclusively identify recurrent paraganglioma.

Conflict of interest

No competing financial interests exist.

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