



Case Report

Single Stage Bilateral Adrenalectomy (Cortical-Sparing) and Pancreatectomy (Corpus-Sparing) in a Patient with Von Hippel-Lindau Disease

Mehmet Hacıyanlı,¹ Turan Acar,¹ Oguzhan Ozsay,² Nihan Acar,¹ Selda Gucek Hacıyanlı,¹
 Emine Ozlem Gur,¹ Osman Nuri Dilek¹

¹Department of General Surgery, Izmir Katip Celebi University, Atatürk Training and Research Hospital, Izmir, Türkiye

²Department of General Surgery, Samsun 19 Mayıs University Faculty of Medicine, Samsun, Türkiye

Abstract

Von Hippel–Lindau (VHL) disease is an autosomal dominant syndrome and affects many organs. We aim to report an adult patient with VHL disease having bilateral adrenal pheochromocytoma and multiple neuroendocrine tumors of the pancreas who was successfully treated with simultaneous function-preserving adrenalectomy and pancreatectomy.

A 27-year-old woman was admitted to hospital with hypertension. The computed tomography of the abdomen revealed a solid tumor in both adrenal glands with the sizes of 12x7 cm on the right and 4x4 cm on the left. She also had two pancreatic solid masses in the head and three in the tail with varying sizes. The laboratory tests are all within normal limits except elevated 24-hour urinary metanephrine and normetanephrine. I-123 MIBG scanning showed increased uptake in both adrenal glands.

Fine needle aspiration biopsy of the tumor on head of pancreas via endoscopic ultrasonography showed neuroendocrine tumor. Those findings were compatible with bilateral pheochromocytoma and multiple pancreatic neuroendocrine tumors and genetic tests revealed the mutation which confirmed the diagnosis of VHL disease.

After suppression with alpha-1 inhibitor, right total, left cortical-sparing adrenalectomy, Whipple procedure for the pancreatic head lesions and spleen-preserving distal pancreatectomy were performed and pancreatic corpus was preserved.

This case showed that multiple function-preserving procedures can be safely performed with oncological principles in patients with VHL disease.

Keywords: Adrenalectomy, cortical-sparing, pancreaticoduodenectomy, pheochromocytoma, VHL

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Von Hippel–Lindau (VHL) disease is a quite rare, systemic neoplastic syndrome with autosomal-dominant inheritance, characterized by benign and malignant tumors of central nervous system, kidney, reproductive organs, pancreatic lesions including pancreatic neuroendocrine tumors (PNETs) and pheochromocytoma.^[1]

Management of patients with VHL disease is complex and multidisciplinary. Although the surgical approach may vary from tumor enucleation to total radical resection and performing simultaneous or staged surgery^[2], it must cover both the elimination of the disease with oncological principles and preserving the function of vital organs if possible.

Address for correspondence: Turan Acar, MD. Department of General Surgery, Izmir Katip Celebi University, Atatürk Training and Research Hospital, Izmir, Türkiye

Phone: +90 507 215 31 04 **E-mail:** drturancar1982@gmail.com

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The present study reports an adult patient with adrenal and pancreatic manifestations of VHL disease who was treated by single-stage organ-sparing surgery in whom renal and pancreatic functions were preserved. To the best of the authors' knowledge, this is one of the first reports of single-stage successful cortical sparing adrenalectomy for bilateral pheochromocytoma, Whipple procedure, distal pancreatectomy (corpus and spleen preserving) and pancreatic tumor enucleation for multiple neuroendocrine tumors of pancreas in an adult patient with VHL disease in English literature.

Case Report

A 27-year-old woman presenting with dyspeptic and hypertensive symptoms was admitted to the hospital. Her initial abdominal examination was negative and laboratory tests revealed mildly elevated bilirubin and alkaline phosphatase levels. Since the ultrasonography showed cholelithiasis, dilated extrahepatic biliary ducts and multiple pancreatic small solid tumors and bilateral adrenal solid masses, further imaging was needed. Endoscopic ultrasonography showed small calculi in the distal common bile duct and multiple solid tumors in the pancreas and endoscopic retrograde cholangiopancreatography (ERCP), endoscopic sphincterotomy, stenting of the common bile duct and fine needle aspiration biopsy (FNAB) of a solid mass of pancreatic head was performed during the same procedure. Then triphasic contrast-enhanced computed tomography (CT) of the abdomen was done and revealed huge, solid masses in both adrenal glands with the sizes of 12x7 cm on the right and 4x4 cm on the left (Fig. 1a); she also had two pancreatic solid masses in the head and one in corpus and three in tail with varying size (Fig. 1b) which were compatible with bilateral pheochromocytoma and pancreatic neuroendocrine tumors.

The laboratory tests for endocrine disorders are all within normal limits except a high metanephrine and normetanephrine concentration in the 24 h urine collection (normetanephrine level 9218 (>632) µg/day and metanephrine 641 (>276) µg/day). Tumor markers such as carbohydrate antigen (CA) 19-9, CA 125 and carcinoembryonic antigen (CEA) were normal. I-123 MIBG scanning showed increased uptake in both adrenal glands (Fig. 2).

The patient had the diagnosis of bilateral pheochromocytoma for the adrenal masses and neuroendocrine tumor of pancreas as a result of FNAB.

Preliminary diagnosis of VHL disease was suspected and further genetic tests revealed the mutation on VHL gene, Exon 3, c.500G>A which confirmed the diagnosis.

Fluorine 18-fluorodeoxyglucose PET was obtained for de-

tection of possible other organ tumors which was negative. After suppression therapy, right total, left cortical-sparing adrenalectomy, Whipple procedure for the pancreatic head lesions and spleen-preserving distal pancreatectomy for the others using intraoperative ultrasound were performed (Fig. 3). Frozen section analysis of the enucleated intraoperatively detected small tumor from the upper part of the corpus of the pancreas showed tumor-free margin. The postoperative course was uneventful. Adrenocorticotropic Hormone (ACTH)-stimulating test postoperatively revealed a normal cortisol response and no blood glucose abnormality occurred. All tumors were benign in the final examination.

She received no adjuvant treatment. 68Ga-DOTATATE positron emission tomography (PET/CT) was obtained for screening postoperatively and was completely normal. She is well and tumor-free 6 months postoperatively.

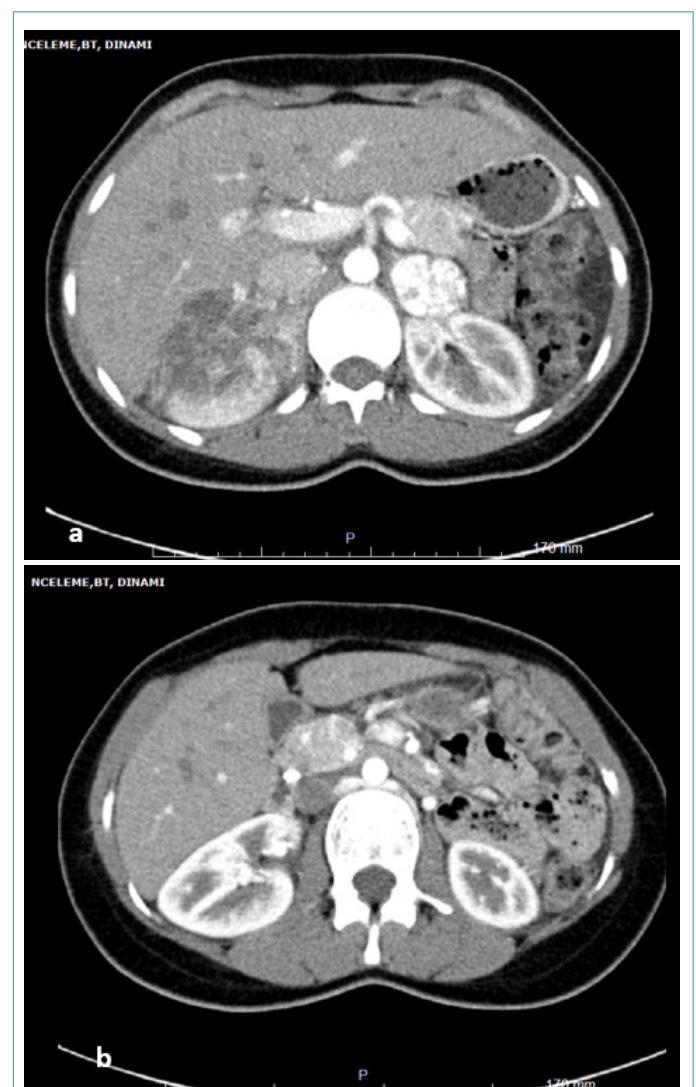


Figure 1. (a) Bilateral adrenal lesions on CT, (b) The pancreatic lesions on CT (Marked with an arrow and circles).



Figure 2. I-123 MIBG scintigraphy of the adrenal glands showed increased uptake bilaterally.

Discussion

The VHL gene was localized to the short arm of chromosome 3 which is a tumor suppressor gene.^[1] Approximately 20% of cases are found in individuals without any family history, known as de novo mutations.^[1] It may affect many organs such as central nervous system, retina, adrenal, kidney, epididymis, over and pancreas, and may cause development of various benign and malignant tumors.

Pheochromocytomas of patients with VHL disease are rarely malignant and usually are suspected during radiological examination.^[1] In case of bilateral adrenal mass in pheochromocytoma patients, I-123 MIBG-scintigraphy can help to identify the hormone-active gland to eliminate the nonfunctional tumors since the bilateral total adrenalectomy carries a significant morbidity. Bilateral total adrenalectomy has serious complications such as adrenal insufficiency and/or a need for lifelong steroid replacement therapy. Thus function-preserving surgical resections have been recommended due to low malignancy incidence especially for young patients to rescue them from the development of adrenal insufficiency, life-long steroid and hospital dependency in patients with VHL disease.^[3,4]

Bilateral cortical sparing surgery can be done but unilateral such type of surgery is usually enough to maintain cortical activity. Thus we preferred total adrenalectomy for huge vascular tumor on the right but cortical sparing surgery for the smaller tumor on the left side which might be sufficient for hormonal activity.



Figure 3. (a) Resected adrenal glands (b) Resected pancreatic head and tail (c) Remained corpus of pancreas (Corpus-Sparing).

About 35-70 % of patients with VHL disease have pancreatic tumors including simple cysts, serous cystadenomas, neuroendocrine tumors (PNETs) (9–17%) and combined lesions.^[1, 5] PNETs can be malignant and may invade and/or metastasize but mostly, the progression of PNETs with VHL is slow and they have a good prognosis. If the tumor is larger than 3 cm or larger than 2 cm and located in the head of pancreas, it is recommended that firstly enucleation should be considered and then when it is not suitable resection should be preferred.^[6] In our case, two large tumors in the head and close relation with the main pancreatic duct warranted the resection. Multiple tumors on the tail of pancreas were removed with spleen-sparing distal pancreatectomy and one small tumor on the upper border of the corpus was enucleated to preserve corpus to maintain the insulin secretion.

Fluorine 18-fluorodeoxyglucose PET was obtained for detection of possible other organ tumors which was negative. Its use in patients with VHL disease has some limitations which successfully identifies adrenal and pancreatic neuroendocrine tumors but failed to show renal cell cancer.^[7]

The single-stage bilateral adrenal resective surgery, Whipple operation and distal pancreatectomy need to be discussed since both operations carry their own morbidity and mortal-

ity. Matsubuyashi et al.^[8] reported pancreatoduodenectomy and distal pancreatectomy in a patient with VHL disease who previously had bilateral total adrenalectomy for pheochromocytoma. Langrehr et al.^[9] reported organ-sparing enucleation of bilateral pheochromocytoma and pancreatoduodenectomy in children with VHL disease. Laparoscopic unilateral cortical sparing adrenalectomy and enucleation of pancreatic tumors have also been reported recently.^[10]

In general, hypertension of pheochromocytoma in patients having VHL disease is interestingly not severe and the hemodynamic stability doesn't change during the surgery.^[3] The situation was the same in our patient and after the completion of adrenal resections and we were sure about the stable hemodynamic condition of her, we decided to proceed with the pancreatectomy. We thought if possible single-stage surgery offered the best option for the patient because a significant risk of scarring around the pancreatic region just near the adrenal surgical site was possible which might cause difficulty in dissection in the second operation. Although the preferred resection of pancreatic neuroendocrine tumors is enucleation or limited resection, it was obligatory to do the Whipple procedure because of the close relation of the two tumors in the head of the pancreas and main pancreatic duct.

In our case, the postoperative course has been uneventful with no symptoms of pancreatic or adrenal insufficiency. So she is free of medications on follow-up.

To the best of our knowledge, no adult case of simultaneous bilateral adrenalectomy (left cortical-sparing), pancreatoduodenectomy and partial distal pancreatectomy (corpus-sparing) with the diagnosis of VHL was reported in the literature. Both adrenal glands and pancreas maintain to secrete endocrine hormones and additionally pancreas secretes exocrine hormones which are essential for life.

Conclusion

In conclusion, a single-stage function-preserving surgery for multiple intraabdominal organ tumors is a considerable option for patients with VHL disease. With careful patient selection and surgical planning, combined major procedures can be safely performed simultaneously thus reducing surgical trauma and preserving organ function.

Disclosures

Informed consent: Informed consent of the patient was obtained.

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