Case Series

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Adrenalectomies for adrenal gland tumours-a retrospective study of 15 cases at a single center

Srinivas Kalabhavi, Revanasiddappa Kanagali, Pramod Makannavar, Sangamanth Benthur, Bhuvanesh Aradhya*

Department of Urology, SDM Medical college and Hospital, Dharwad, Karnataka, India

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*Correspondence:

Dr. Bhuvanesh Aradhya,

E-mail: bhuvanesh88@gmail.com

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ABSTRACT

We present our experience of 15 cases of adrenal tumours who underwent adrenalectomy procedure in last 5 years at our institute and analysed retrospectively clinical outcome. Pre-operative, intra-operative and post-operative data from 15 patients who underwent adrenalectomy between August2015 and July 2020 at our institution were retrospectively collected and reviewed. Diagnosis was obtained on the basis of clinical examination, laboratory values and imaging techniques. Prazosin was preoperatively administered in case of pheochromocytoma. All adrenalectomies were performed by team of urologists. A multidisciplinary management involving endocrinologists, urologists, onco-surgeons and anaesthesiologists was carried at our institute. Fifteen patients were evaluated retrospectively in our study. Functioning tumours were diagnosed in 08(53.3%) patients, 06 patients were affected by pheochromocytomas, 2 cases by adrenal cortical carcinoma (ACC). 3 (20%) patients had incidentalomas. 11 (73.3%) patients underwent open adrenalectomy and in 04 (26.6%) patients, laparoscopic adrenalectomy (LA) was performed. An accurate preoperative examination (radiological and biochemical evaluation) is mandatory to select eligible patients to LA or open adrenalectomy (OA). LA is safe and feasible for benign lesions up to 6 cm. A skilled operative team, composed by surgeons experienced in LA after adequate learning curve, is required. Preoperative alfa blockade does not prevent PCC hypertensive crises but, facilitating their pharmacological control, must be recommended.

Keywords: Adrenal tumours, Adrenalectomy, Pheochromocytoma, Incidentalomas, ACC, LA, OA

INTRODUCTION

An adrenal tumour or adrenal mass is any benign or malignant neoplasms of the adrenal gland which can be functional or non-functional.9 The common benign include adrenal masses benign pheochromocytomas (11%),adenomas myelolipomas (8%), ganglioneuromas (4%), adrenal cysts (5%) and rarely oncocytomas. The malignant adrenal masses include adrenal cortical carcinoma (ACC) 12%, neuroblastomas (common in paediatric age group), malignant pheochromocytomas and metastasis (2%) from other sites.³ In urologic practice, the evaluation of adrenal pathology is typically in the setting of patients referred with a diagnosis of a new adrenal mass or in existing patients in whom a new adrenal mass is discovered incidentally. Occasionally, patients are identified by clinicians based on clinical symptoms in the absence of prior radiographic identification of an adrenal lesion.9 Given the varied systemic adrenal functions and dysfunctions, evaluation and management of these multidisciplinary approach adrenal masses need involving endocrinologists, cardiologists, oncologists, surgeons. urologists. onco-surgeons, endocrine anaesthesiologists and general surgeons. With the urologist's advanced minimally invasive surgical skills,

comfort with both retroperitoneal anatomy and surgical approaches to retroperitoneal organs, and the close relationship between renal and adrenal pathophysiology, it is natural that the evaluation and surgical management of adrenal disorders remain firmly in the domain of practicing urologic surgeons.²

We evaluated retrospectively 15 cases of adrenal tumours operated in last 5 years at our institution. The presentation, evaluation, surgical treatment, histopathology report and post-operative outcomes were evaluated.

CASE SERIES

We evaluated retrospectively 15 cases of adrenal tumour patients who underwent adrenalectomy for variety of presentations and diagnosis in the last 5 years from august 2015 to July 2020. Diagnosis was obtained on the basis of clinical examination, laboratory values and imaging techniques (ultrasonography, computed tomography). Patient's evaluation included preoperative, intra-operative and post-operative data. Surgical procedures were all performed by team of urologists at our institute experienced in open and laparoscopic surgery.

Table 1: Patient demographics.

Patient characteristics	Findings
Age (year)	Average 44.53 (range 23-63)
Sex	M:10, F:05
Laterality	Right:06, left:09, B/L:0
Symptomatic	12 (80%)
Incidentally detected	03 (20%)
Average size of tumour (cm)	7.97 (4.4-17)
Open adrenalectomy	11 (73.3%)
Laparoscopic adrenalectomy	04 (26.6%)
Conversion to open procedure	01 (6.6%)
Average weight of tumour (gm)	201 (45-1156)

Most of the symptomatic patients presented with symptoms like vague abdominal pain or discomfort, headache, palpitations, sweating, nausea, flushing, weight loss, tiredness, sustained hypertension, paroxysmal hypertension, orthostatic hypotension, hyperglycaemia. Patients with hypertension were already on one or 2 antihypertensive drugs. Other symptoms included chronic diarrhoea, psychologic symptoms (anxiety, panic). Most of these patients were evaluated by physicians and ultrasound abdomen was done for evaluation of pain abdomen revealed adrenal mass. These patients were then referred to urology department for further evaluation for adrenal masses. 3 patients were incidentally detected to have adrenal masses while evaluating for other diseases

(one patient had concomitant somatostatinoma, one patient had endometriosis, other patient had hydatid cyst of the liver).

Table 2: Clinical symptoms.

Symptoms	Number (%)
Pain abdomen/discomfort	12 (80)
Headache	08 (53.3)
Palpitations	06 (40)
Nausea/vomiting	09 (60)
Flushing	08 (53.3)
Weight loss	02 (13.3)
Hypertension	08 (53.3)
Hyperglycaemia	01 (6.6)
Chronic diarrhoea	01 (6.6)
Anxiety/panic	08 (53.3)
Asymptomatic	03 (20)

All patients were evaluated to assess both morphologic and functional features of adrenal masses. All patients underwent CT scan of abdomen and pelvis (unenhanced, contrast enhanced, delayed CT wash out study) to evaluate morphologic features of the adrenal masses.

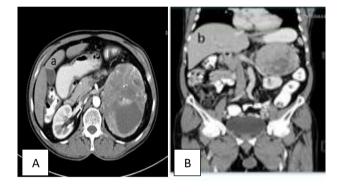


Figure 1: Large herogenously enhancing mass measuring 11.6x9.7x11 cm arising from left adrenal gland of necrotic and cystic areas (A) Axial section, (B) Coronal section.

All patients underwent metabolic evaluation. Current practice is to test all new adrenal masses for cortisol and catecholamine hypersecretion. In patients with a history of hypertension, aldosterone hypersecretion was also be assessed.

Table 3: Metabolic evaluation.

Metabolic marker	Number (%)
Elevated cortisol level	02 (13.3)
Raised urinary VMA	08 (53.3)
Raised 24 hr urinary	
metanephrines/nor	08 (53.3)
metanephrines	
Raised free plasma	08 (53.3)
metanephrines	06 (33.3)
Raised aldosterone levels	0

Before surgery, all patients underwent laboratory tests, chest X-ray, HRCT chest, ECG, ECHO cardiograph and cardiac evaluation. All patients were administered antithrombotic prophylaxis (LMWH Clexane 20 mg SC). patients suspected or diagnosed to have pheochromocytoma and an abnormal metabolic preoperative evaluation underwent catecholamine blockade. Tablet Prazosin was started 7 to 14 days prior to surgery on outpatient basis. Oral dosing of 2.5 mg twice daily was initiated and titrated by increases of 2.5 mg to a blood pressure of 120 to 130/80 mmHg in a seated position. Mild postural hypotension with systolic pressures greater than 80 mmHg was acceptable. Once adequate alpha blockade was achieved beta blockers like atenolol 25 mg PO BID or metoprolol 25-50 mg PO TID dose was started to prevent tachycardia/arrhythmias. Last dose of alpha blocker was given on night prior to surgery (no morning dose, to avoid post-op hypotension). Calcium channel blockers like amlodipine 10-20 mg PO daily was added in patients who had poor control of BP with alpha blockers alone. Adequate hydration achieved using 1-2 L of NS/RL was administered a night before surgery. Blood grouping and cross match was done and blood was reserved in all cases. All patients received general anaesthesia with endotracheal intubation and antibiotic prophylaxis (cefotaxime 1 g I.V.) was given. Systolic blood pressure (SBP) levels ≥180 mmHg was considered hypertensive crises, while SBP levels <90 mmHg was considered as hypotensive crisis. Operative decision regarding surgical approach was made based on tumour size on CT scan findings. Generally, patients with tumour size <6 cm size were planned for laparoscopic approach and tumours >6 cm size for open approach.

Patients who underwent open adrenalectomy (OA) the choice of incision was made prior based on tumour size, benign or malignant. Subcoastal transperitoneal or roof top (bilateral subcostal) approach was used in open adrenalectomy patients. The anterior subcostal approach affords excellent exposure of the great vessels, in the event that lymph nodes or venous tumour thrombus needs to be addressed. For left side tumours, the patient was placed supine on the surgical table. If needed, a body roll was placed under the back at the level of the costal margin to accentuate the costal margin. A skin incision was made approximately two fingerbreadths below the costal margin. This incision is extended medially to the midline or beyond, depending on the degree of exposure needed. The external oblique, internal oblique, and transverse abdominal muscles, and their corresponding fasciae, are divided laterally; the rectus muscle and the rectus sheath divided medially. The peritoneum was entered sharply, and the falciform ligament is divided after it was clamped and ligated with a large-gauge vascular tie (no. 0 or 1 silk). The line of Toldt was incised, and the left colon was mobilized medially. The splenic flexure was taken down by dividing the splenocolic ligament. Division of the lienorenal ligament would allow medial mobilization of the spleen. The left

adrenal vein was identified on dissecting out the left renal vein. After ligation and division of the left adrenal vein, medial attachments to the aorta were taken with careful dissection and ligation of small arterial vessels while gentle lateral traction was placed on the gland. The lateral and inferior attachments to the kidney was taken by blunt and sharp dissection off of the renal capsule. Intra operative hypertensive/hypotensive crisis was managed by appropriate inotropes, nitroprusside infusion and I. V. crystalloids by experienced anaesthesiologists. After removal of the left adrenal gland, closure of the incision is performed with a running no. 1 polydioxanone suture in two layers. The deep layer consists of the transverse abdominal muscle, transverse fascia, internal oblique muscle and fascia, and posterior rectus sheath, and the superficial layer consists of the external oblique muscle and fascia, and the anterior rectus sheath. For right-sided tumours, the dissection was similar except for the need to dissect the duodenum medially by the Kocher manoeuvre. 24 F drain was kept for drainage in all cases for a day or two. Regional lymph node dissection was carried out in ACC cases. Figure 2 shows right open adrenalectomy procedure steps.

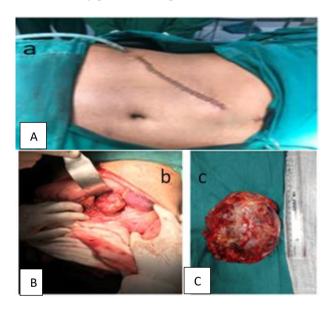


Figure 2: (A) Right subcostal incision, (B) Intraoperative right adrenal mass, (C) resected large adrenal pheochromocytoma specimen.

Laparoscopic adrenalectomy (LA) was performed using a standard transperitoneal lateral approach. The patients were placed in the left position (30° angle) for right LA, while they were placed in right position (90° angle) for left LA. LA was approached using 4 trocars. Pneumoperitoneum was maintained at 12-14 mmHg by insufflation of carbon dioxide (CO₂). Dissection done using Harmonic scalpel[™] (Ethicon endo surgery INC-Johnson and Johnson, NJ, USA). The first step consisted of vascular control of the main adrenal vein by clips. Whenever necessary, the lateral and posterior connections of the right hepatic lobe were incised and the liver was superiorly and medially retracted, adrenal gland was

mobilized on both the upper and medial sides, in order to have a safer access to the inferior cava vein and the ipsilateral renal vein. In left LA, a wide left colon mobilization was routinely carried out. The surgical specimens were extracted in retrieval bags through a mini-laparotomy of the trocars. A 20 Fr drainage was routinely placed. Figure 3 shows right laparoscopic adrenalectomy procedure steps.

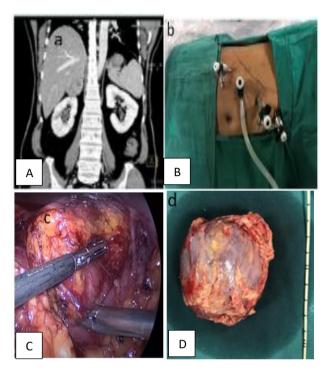


Figure 3: (A) CT scan (contrast study) in coronal view of mass arising from right adrenal gland measuring 5.5x4.3x4 cm, (B) Laparoscopic port placement for right adrenalectomy, (C) Intr-operative picture of clipping of right adrenal vein, (D) Resected right adrenal pheochromocytoma specimen.

Post-operative management

After surgery all patients were managed for a day in intensive care unit. All patients were administered with fluids (1000 ml of saline solution NaCl 0.9% and 500 ml of glucose solution 5% I. V.) and antithrombotic therapy (LMWH clexane 20 mg. S. C.) until discharge. Postoperative hypotensive crises were treated by Crystalloid's hydrocortisone and infusions. Hypoglycaemia was managed using 5% dextrose infusion and sugar levels were monitored. Early mobilization and feeding were recommended on the first postoperative day. Drainage was removed on the first or second postoperative day. Major and minor complications were recorded. Patients follow up consisted of clinical evaluation and blood examination at 1 month after discharge, followed by half-yearly later. The histopathological report of adrenalectomies is shown in the Table 4:

Table 4: Histopathological report.

HPE report	Number (%)
Adrenal adenoma	06 (40)
Pheochromocytoma (benign)	06 (40)
ACC	02 (13.3)
Adrenal cyst (endothelial)	01 (6.6)

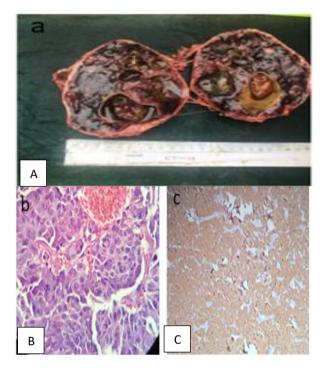


Figure 4: (A) Gross cut specimen of large pheochromocytoma specimen, (B) Microscopic appearance of pheochromocytoma (Zellballen appearance- "group of cells"), (C) Microscopic appearance of IHC synaptophysin positive staining.

Intraoperative hypertensive crisis was reported in 08 (53.3%) cases (06 in PCC patients,2 cases in ACC) during tumour manipulation while hypotensive crises were reported in 4 (26.6%) cases (one severe hypotension), but they were promptly and successfully treated. Bleeding requiring transfusions occurred in 2 (13.3%) cases (one ACC case and in one case of large pheo), no adjacent visceral injury, pulmonary or cardiac complications seen. No post op DVT in any case seen. Post op adrenal was crisis seen in 1 (6.6%) case of large ACC which was promptly managed by steroid replacement (100 mg hydrocortisone iv QID) was maintained until oral foods restarted and then converted to oral steroids (hydrocortisone, 20-20-10 mg/day, aiming to decrease by 5 mg/day every 3-5 days). Conversion to open procedure happened in 1 (6.6%) case of pheochromocytoma due to inadvertent bleeding during surgery. No significant morbidity or mortality was observed in any of the patients. Mean hospital stay was 4.3 days (2-10 days). Mean operative time was 3.2 hours in open adrenalectomy cases and 2.7 hours in lap adrenalectomy cases.

Table 5: Post-operative complications.

Complications	Number (%)
Hypertensive crisis	08 (53.3)
Hypotensive crisis	04 (26.6)
Adrenal crisis	01 (6.6)
Conversion to open	01 (6.6)
Bleeding requiring transfusion	02 (13.3)
Wound infection	01 (6.6)
Pulmonary/cardiac adverse events	00
DVT	00

DISCUSSION

Since the first successfully performed LA by Gagner in 1991, the transperitoneal approach has become the most common therapeutic strategy for adrenal neoplasm.^{1,2} Thanks to the minimal invasive approach, LA allowed a decreased postoperative pain, a reduced ileus, a shorter hospitalization, an earlier return to work and a better cosmetic result, guarantying a lower morbidity (5 to 20%) and mortality rates (below 0.5%).³⁻⁸

In 1889, Knowsley-Thornton reported the removal of a large adrenal tumour and in 1926, Roux in Lausanne, Switzerland, and Charles Mayo in Rochester, Minnesota, successfully removed a phaeochromocytoma.9 The anterior approach was initially advocated by Cahill, one of the pioneers of adrenal surgery. 10 The posterior approach was originally described by Young and offered the technical advantage of being extraperitoneal, extra pleural, and subdiaphragmatic and the clinical advantage of being associated with low postoperative morbidity.¹¹ In current day surgical practice, the posterior approach has become obsolete, as all patients who in the past were deemed to benefit from this procedure are currently being laparoscopic retroperitoneoscopic offered adrenalectomy.

Open adrenalectomy (OA) is associated with higher mortality (2-4%) and morbidity rates (bleeding, cardiac pulmonary and issues. pulmonary thromboembolism, wound infections), is worldwide reserved only for large tumours (diameter >6 cm) and primary malignancies. Suspected primary malignant adrenal tumours should be considered as contraindication to minimal invasive approach, for the poor oncological outcome and the high risk of peritoneal dissemination of primary adrenal cancer. Nevertheless, the best surgical approach is still a matter of debate. 12-15 Patients with large adrenocortical tumours (>6-8 cm) and those with CT suspicion of locally invasive tumours expected to have an adrenocortical cancer should have an open operation.^{20,21} According to literature data, LA is indicated in patients affected by PCC up to 8 cm, incidentalomas up to 6 cm and metastases <6 cm size. 16-18 Currently indication to LA for lesions >6 cm is still a matter of debate and experienced endocrine surgeons are divided between supporters (6-8) and detractors.¹⁹

Surgical approach in all 15 cases was effective, safe and well tolerated, with a negligible morbidity rate. We had only one case of conversion to open surgery due to excess intra op bleeding. A preoperative selective adrenergic blockade with prazosin, routinely performed, did not prevent intraoperative hypertensive episodes, occurring principally during tumour manipulation was seen in 8 (53.3%) out of 15 cases, and were promptly treated by anaesthesiologists. Major intraoperative cardiovascular complications-cerebral vascular accident, pulmonary oedema, myocardial infarction or ischemia, cardiac arrhythmias and multiorgan failure-were not observed, although it is reported that laparoscopic treatment for metastases or PCCs present high risk for hemodynamic disorders. Post-operative adrenal crisis seen in one (6.6%) case of large ACC which was promptly managed by steroid replacement (100 mg hydrocortisone iv QID) was maintained until oral foods restarted and then converted to oral steroids (hydrocortisone, 20-20-10 mg/day, aiming to decrease by 5 mg/day every 3-5 days). Mean hospital stay was 4.3 days (2-10 days). Mean operative time was 3.2 hours in open adrenalectomy cases and 2.7 hours in lap adrenalectomy cases.

The presented retrospective study has several limitations. The study design was retrospective and a comparison with an "open surgery" series was not carried out. The sample size in our present study is considerably less. Nevertheless, it is possible to drawn some conclusions.

CONCLUSION

A multidisciplinary management involving endocrinologists, urologists, oncologists, onco-surgeons and anaesthesiologists-is recommended in referral high volume units for the treatment of adrenal pathology. An accurate preoperative examination (radiological and biochemical evaluation) is mandatory to select eligible patients to LA or open adrenalectomy. LA is safe and feasible for benign lesions up to 6 cm. A skilled operative team, composed by surgeons experienced in LA after adequate learning curve, is required. Preoperative alfa blockade does not prevent PCC hypertensive crises but, facilitating their pharmacological control, must be recommended.

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