

Received: 2018.03.28
Accepted: 2018.06.30
Published: 2018.09.15

e-ISSN 1941-5923
© Am J Case Rep, 2018; 19: 1096-1102
DOI: 10.12659/AJCR.910259

Laparoscopic Trans-Abdominal Right Adrenalectomy for a Large Primitive Adrenal Oncocytic Carcinoma: A Case Report and Review of Literature

Authors' Contribution:
Study Design A
Data Collection B
Statistical Analysis C
Data Interpretation D
Manuscript Preparation E
Literature Search F
Funds Collection G

ABCD 1 **Valerio Panizzo**
BC 2 **Barbara Rubino**
ABCDEF 3 **Guglielmo Niccolò Piozzi**
ABCD 4 **Paolo Ubiali**
ABCDEF 5 **Anna Morandi**
BCDF 6 **Marco Nencioni**
ABCDEF 1,7 **Giancarlo Micheletto**

1 Department of General Surgery, Istituto Clinico Sant'Ambrogio, Milan, Italy
2 Department of Pathology and Cytopathology, IRCCS Policlinico San Donato, Milan, Italy
3 General Surgery Residency Program, University of Milan, Milan, Italy
4 Department of General Surgery, Santa Maria degli Angeli Hospital, Pordenone, Italy
5 Department of Pediatric Surgery, Fondazione IRCCS Ca' Granda – Maggiore Policlinico Hospital, Milan, Italy
6 Department of General Surgery, San Raffaele Hospital, Milan, Italy
7 Department of Pathophysiology and Transplantation, University of Milan, Milan, Italy

Corresponding Author: Guglielmo Niccolò Piozzi; e-mail: guglielmopiozzi@gmail.com
Conflict of interest: None declared

Patient: Male, 48
Final Diagnosis: Adrenal oncocytic carcinoma
Symptoms: Asymptomatic
Medication: —
Clinical Procedure: Transabdominal laparoscopic right adrenalectomy
Specialty: Surgery

Objective: Rare disease
Background: Adrenocortical oncocytic neoplasms (AONs) are extremely rare tumors. AONs are classified as: oncocytoma (AO), oncocytic neoplasm of uncertain malignant potential (AONUMP), and oncocytic carcinoma (AOC). Among the 162 reported cases of AONs in the literature, 30 cases were classified as malignant. Adrenalectomy is the treatment of choice for AON.

Case Report: We report the case of a 48-year-old man with a primitive 12-cm mass affecting the right adrenal gland, detected by ultrasonography during follow-up for alcoholic liver cirrhosis. Computed tomography (CT) scan and magnetic resonance imaging (MRI) showed a mass of the right adrenal gland compressing the inferior vena cava (IVC) and displacing the right lobe of the liver, with no invasion of kidney, liver, or IVC. Preoperative blood tests showed mild transaminase increase. Laparoscopic right adrenalectomy with lateral transperitoneal approach was performed. The postoperative course was uneventful. The lesion was diagnosed as a primitive adrenal oncocytic carcinoma (AOC). No recurrence was evidenced during 24-month follow-up.

Conclusions: Although AONs are very rare, they must be considered in the differential diagnosis of adrenal masses due to their prognostic difference compared to non-oncocytic tumors. AOCs are a rare presentation of AONs. Only 30 cases are described in the literature. Laparoscopic adrenalectomy is the treatment of choice for AOC. We report the first case of laparoscopic lateral trans-abdominal adrenalectomy for a voluminous AOC (120×95×110 mm) and we review the literature regarding AOCs. Laparoscopy in experienced hands is safe and effective for the treatment of AONs. Despite the rarity of AOC, a case series should be performed to confirm the results of our case report.

MeSH Keywords: Adrenal Gland Neoplasms • Adrenalectomy • Adrenocortical Carcinoma • Laparoscopy

Full-text PDF: <https://www.amjcaserep.com/abstract/index/idArt/910259>



2856 2 2 1 89

Background

Oncocytic neoplasms (ONs), or oncocytomas, are tumors that are mainly composed of oncocytic cells. Oncocytic cells were described for the first time by Hamperl in 1931 as large, highly eosinophilic, granular cells with pyknotic nucleus, typically associated with a Hurtle cell tumor of the thyroid gland [1,2]. The cytoplasmic granularity is characterized by a striking accumulation of mitochondria, as demonstrated through electron microscopy in 1986, that can occupy up to 60% of the cytoplasm volume [3,4]. ONs arise in various organs, including kidney, thyroid, pancreas, parathyroid, salivary, lacrimal, pituitary glands, paraganglia, respiratory tract, paranasal sinuses, pleura, liver, pancreatobiliary system, stomach, colon, rectum, central nervous system, female and male genital tracts, skin, and soft tissues [5–21]. ONs arising from adrenal glands are extremely rare and were first described by Kakimoto et al. in 1986 [22]. Adrenocortical oncocytic neoplasms (AONs) are usually observed to be non-functional and mostly benign tumors. AONs are classified as: oncocytoma (AO), oncocytic neoplasm of uncertain malignant potential (AONUMP), and oncocytic carcinoma (AOC) [23]. Since the first description, a total of 162 cases of AONs have been reported, with 30 cases described as AOC [23,24]. Tumor size is considered to be a practical sign to differentiate benign from malign disease in adrenocortical carcinomas (diameter <4–5 cm suggests a benign mass). However, in case of AONs, the size of the mass and the imaging findings (through abdominal CT scan and MRI) are not pathognomonic or related to malignancy [24]. Because AONs are non-functional, differential diagnosis should be done with indeterminate adrenal tumors (incidentalomas). AONs are usually detected as a large mass with an average diameter of 8 cm (range 2–20 cm) [25]. Adrenalectomy is the treatment of choice for AONs. Surgical approaches to adrenal gland include laparotomy, combined thoraco-abdominal access, retroperitoneal posterior access, laparoscopy, and robotic surgery [27]. Since the first successfully laparoscopic adrenalectomy (LA) performed by Gagner in 1991 [28], the lateral trans-abdominal approach has become the most common therapeutic strategy for adrenal neoplasms [29–34]. To the best of our knowledge, this is the first case report of laparoscopic lateral trans-abdominal adrenalectomy for a large AOC (12 cm) (Supplementary Video 1).

Case Report

A 48-year-old man was admitted to our Surgical Department for a primitive 12-cm mass affecting the right adrenal gland. The mass was detected by abdominal ultrasound during annual follow-up for liver cirrhosis (Child-Turcotte-Pugh score A). The patient was submitted to contrast-enhanced abdominal CT scan in our hospital (Figure 1) and contrast-enhanced abdominal MRI in another institute with evidence of a capsulated solid



Figure 1. Contrast-enhanced abdominal CT scan axial image showing the right adrenal mass (white arrow), the hepatic dislocation, and the inferior vena cava compression (white arrow head).

adrenal mass (diameters: 120×95×110 mm) with an irregular vascularization pattern, compressing the inferior vena cava, and dislocating the right lobe of the liver. A cleavage plane between the liver and the right kidney was evident with no lymphonodal or any other intra-abdominal neoplastic involvement. Preoperative laboratory tests (including cortisol, 17-ketosteroids, and 17-hydrocorticosteroids serum levels), dexamethasone test, complete blood count test results, and renal function were all normal, while liver enzyme levels were mildly elevated. The patient was a non-smoker, chronic alcohol abuser (1–2 bottles of wine per day). No endocrinopathy sign or symptoms were identified. Therefore, a non-functional adrenal mass was diagnosed, but no preoperative US- or CT-guided fine-needle aspiration cytology was performed because of the wide size of the mass, which made surgery mandatory. Considering the presence of a clear cleavage plane between the adrenal lesion and the liver, the kidney, and the surrounding vascular structures, and the absence of evident lymphonodal or other visceral involvement, a laparoscopic approach was attempted. In fact, despite the size of the lesion, no signs of malignancy or infiltration were found preoperatively, thus making the laparoscopic approach laborious but feasible and oncologically radical in skilled hands. The patient underwent lateral trans-abdominal laparoscopic right adrenalectomy with a standard 4-trocars technique in left lateral decubitus position. During the operation, the IVC was easily dissociated from the lesion, and en-bloc right adrenalectomy was completed with no capsule rupture. Extraction was performed *in toto*. No major bleeding and no major intraoperative complications were encountered. The patient remained hemodynamically stable during the procedure. The postoperative course was uneventful and the patient was discharged on the 5th postoperative day in good condition. Macroscopic examination of the specimen revealed

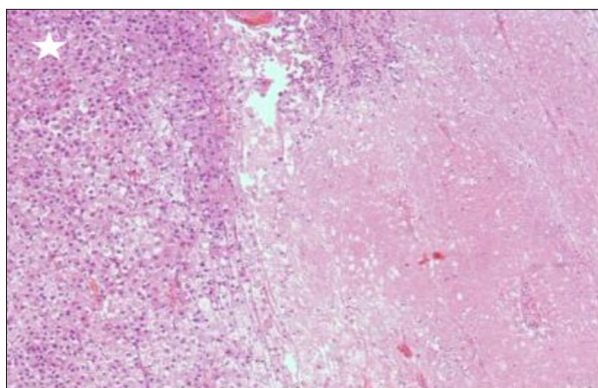


Figure 2. Adrenal cortical oncocytic carcinoma (left side area with the white star – 10×).

a solid mass, measuring 123×98×113 mm, weighting 300 g, with several necrotic areas. Microscopic examination reported a primitive oncocytic adrenal carcinoma (Figure 2). Several atypical mitotic figures and high mitotic index (10/50 HPFs) were observed, together with diffuse pattern of growth and venous invasion. The patient's Weiss score was 5 and, according to modified Weiss score, the patient had an AOC. The tumor cells were immunopositive for vimentin and presented typical oncocytic architecture. Ki-67 and MIB1 rate was 20%. The patient was not eligible for therapy with mitotane (*RS*)-1-chloro-2-[2,2-dichloro-1-(4-chlorophenyl)-ethyl]-benzene due to the chronic liver disease. He was submitted to follow-up with an abdominal CT scan performed every 6 months for the first year and once during the second year. No recurrence was evidenced during 24-month follow-up.

Discussion

Adrenocortical carcinoma (AC) is a rare and aggressive tumor of the adrenal cortex that accounts for 0.2% of all malignancies (prevalence 1–2 cases per million) [35]. AONs are an extremely rare subtype of AC, with 162 cases reported in the literature since the first description in 1986 [18]. AONs are usually incidental [36–41] with only 17% cases described as functional [42]. AONs do not have a precise peak incidence, with a mean age at diagnose of 47 years (range 27–72 years) [25]. AONs occurs more frequently in females (F/M: 2.5/1) and on the left side (L/R: 3.5/1) [25]. AONs are located in the adrenal cortex, with only 1 case reported within the adrenal medulla and 1 with in heterotopic adrenal tissue [43,44]. To date, no specific risk factors have been identified and the pathogenesis of oncocytosis is still unclear. Krech et al. [45] demonstrated the role of N-nitrosomorpholine, an airborne contaminant, as a chemical inducer of oncocytosis in renal tissue of Sprague-Dawley rats, managing to generate an *in vivo* model resembling human oncocytoma. However, no further experimental studies have been reported using this rat model. Oncocytes have characteristic

Table 1. Weiss criteria.

Weiss criteria	Score
High nuclear grade (III–IV)	1
Atypical mitotic figures	1
Mitotic rate >5/50 HPF	1
Eosinophilic tumor cell cytoplasm (>75% of tumor cells)	1
Diffuse architecture (>33% of tumor)	1
Necrosis	1
Venous invasion	1
Sinusoidal invasion (no smooth muscle in wall)	1
Capsular invasion	1

severe mitochondrial anomalies: mitochondria are numerous with an excess of cristae mitochondriales. The shape varies from round and oval to extremely elongated, slender, or cup-shaped, often piled up to form complex bodies; mitochondria can rarely form large ramifying organelles [45]. Some authors reported a role of mitochondrial genome mutation in oncocytosis pathogenesis [46,47]. Duregon et al. analyzed the presence of the mtDNA 4977 bp “common deletion”, present in 50% of AOCs, as a potential pathogenetic interest, but to date, it has no practical diagnostic value [47]. Macroscopically, AOCs are large, rounded, encapsulated, brown-yellow, and well-circumscribed masses with an average diameter of 8 cm (range 2–20 cm) and a thin rim of normal adrenal gland. The mean AOCs weight is 281 g (range 8–865 g) [48]. Microscopically, AOCs can appear with solid, trabecular, tubular, or papillary patterns. AOCs are characterized by: diffuse proliferation of polygonal cells with abundant granular and eosinophilic cytoplasm, large nuclei and prominent nucleoli, occasional mononuclear and binucleated giant cells, extracapsular extension with blood vessel invasion and necrosis, and variable atypia and mitotic figures [49]. The immunophenotypic profile of AONs is diffuse positivity for vimentin, melan-A, synaptophysin, and alpha-inhibin [50–52]. AONs are classified as oncocytoma (AO), oncocytic neoplasm of uncertain malignant potential (AONUMP) [48], and oncocytic carcinoma (AOC) [19,53–56]. The Weiss Criteria are considered the standard tool for diagnosis of AC [57]. This system considers 9 criteria (nuclear grade III–IV; mitotic rate >5/50 HPFs; atypical mitotic figures; eosinophilic tumor cell cytoplasm (>75% of tumor cells); diffuse architecture (>33% of tumor); necrosis; venous invasion, sinusoidal and capsular invasion) (Table 1). A 1-point score is given to each parameter. Malignancy can be suspected when 4 or more of the 9 criteria are met. However, care should be taken in applying these criteria during pathological evaluation of

Table 2. Modified Weiss criteria for AON.

AON subtypes	Criteria
AOC	One of the following 3 (major criteria)
	Mitotic rate >5/50 HPF
	Atypical mitotic figures
AONUMP	Venous Invasion
	At least one of the following 4 (minor criteria)
	Size >10 cm and/or weight >200 g
	Necrosis
AO	Capsular invasion
	Sinusoidal invasion
	Lack of major and minor criteria

the rare and peculiar AOC. Bisceglia et al. proposed a review of the Weiss Criteria, proposing major and minor criteria for AOC diagnosis (Table 2) [58]. AOC is characterized by the presence of 1 of the following 3 (major criteria): mitotic rate >5/50 HPF, atypical mitotic figures, and/or venous invasion. AONUMP is characterized by at least 1 of the following 4 (minor criteria): size >10 cm and/or weight >200 mg, necrosis, capsular invasion, and/or sinusoidal invasion. AO is characterized by the absence of both major and minor criteria. Several molecular and biological studies have been performed on AC to characterize the malignancy and establish new oncological parameters [59–64]. However, no established premalignant condition has been documented in the human adrenal cortex and no adrenocortical adenoma to AC transition has been described. Furthermore, there are very few cases of AOC described in the literature, with few molecular studies. In addition, ACs are markedly heterogeneous morphologically and functionally, even within the same tumor [65]. Among several molecular and/or cytological markers that may contribute to the differential diagnosis of adrenocortical carcinoma, the cell proliferation markers, such as Ki-67 and topoisomerase, and oncoprotein p53, can be of most value [59–64,66–69]. Unfortunately, the role of either Ki-67 or p53 as biomarkers remains uncertain due to the availability of so few of these tumors [70,71]. However, according to Mearini et al., MIB1 and Ki-67 are of practical value in order to achieve a differential diagnosis between benign mass and adenocarcinoma [25].

The size and the function of the lesion are considered the most important factors in the diagnosis of an adrenal mass. In a report on 887 patients who had adrenal incidentalomas, a diameter greater than 4 cm was shown to have a 90% sensitivity for the detection of AC, but a low specificity (only 24%

of the lesions were malignant) [72]. Increase in size over time is another indication for surgery. Generally, resection is recommended for adrenal masses > 6 cm. Biochemical analyses should be undertaken to rule out the presence of a primary functioning mass, which requires resection despite the size.

Imaging has a major role during differential diagnosis between AC, included AONs, from adrenal adenomas. Fat concentration may be used as a tool to differentiate between benign and malignant adrenal lesions: with the first being lipid-rich. The CT criteria for the diagnosis of adrenal adenoma are unenhanced attenuation of 10 or fewer HUs [73] and absence of necrotic or cystic areas, which can be seen in some malignant lesions and adrenal cysts [74]. However, it has not been demonstrated to be a characteristic imaging for AON; therefore, CT imaging findings are generally nonspecific [75–77]. MRI with chemical shift subtraction [78] provides a high confidence level in distinguishing adrenal adenomas from other disease [79,80]. However, MRI is considered not specific for AON detection [81].

Although the use of contrast-enhanced ultrasound has shown an excellent sensitivity and specificity in the differential diagnosis between benign and malignant adrenal mass, no typical pattern has been described for AONs [82].

Fine-needle aspiration cytology and open biopsy are helpful during perioperative diagnosis of AC; however, they are not able to specifically characterize and define AONs [83,84].

Adrenalectomy is the treatment of choice for AON. Different surgical approaches are available to treat adrenal masses. The surgical approach choice depends on several parameters: tumor size, malignancy, patient condition, and surgical experience [85]. The surgical approach to adrenal gland includes laparotomy, combined thoraco-abdominal access, retroperitoneal posterior access, laparoscopy, and robotic surgery [86]. Since the first successfully laparoscopic adrenalectomy (LA) performed by Gagner in 1991 [28], the lateral trans-abdominal approach has become the most common therapeutic strategy for adrenal neoplasm [28–34]. LA is associated with lower postoperative pain, reduced ileus, shorter hospitalization, earlier return to work, and a better cosmetic result, guaranteeing a lower morbidity (5–20%) and mortality rate (below 0.5%) compared to open adrenalectomy [25,31,34]. In contrast, open adrenalectomy is associated with higher mortality (2–4%) and morbidity rates (bleeding, pulmonary and cardiac complications, pulmonary thromboembolism, and wound infections) and is reserved worldwide only for large tumors (diameter >6 cm) and primary malignancies, based on the radicality of resection, minor tumor local recurrence, and major survival [27,87,88]. The mainstay of the surgical procedure is to perform a complete resection of the adrenal gland without disruption of the adrenal capsule. Therefore, the presence of

capsular or vascular invasion, infiltration of surrounding tissues, and lymphonodal involvement represent the major contraindications to LA. Several different laparoscopic techniques have been proposed and are currently used for the resection of adrenal tumors [27]. Each technique has its own advantages and disadvantages. Lateral trans-abdominal adrenalectomy (LTA) is the most common adrenalectomy technique used by general surgeons. Compared with the retroperitoneal approach, LTA provides more working space, which can be beneficial for large tumors and morbidly obese patients. In addition, the lateral decubitus position used during this approach enables excellent exposure of the adrenal gland because of the effect of gravity on the abdominal organs. Posterior retroperitoneoscopic adrenalectomy (PRA) [27] is characterized by enhanced visualization following the use of higher insufflation pressures in the retroperitoneal cavity, as well as direct access to the adrenal gland (avoiding the intra-abdominal cavity), making it attractive in case of prior abdominal surgery. Additionally, the prone position facilitates equal access to the right and left sides, allowing bilateral procedures without the need for patient intra-operative repositioning. The disadvantages include lack of access to the intra-abdominal cavity for evaluation, difficult removal of large tumors, and increased difficulty with increasing body mass index (BMI). Anterior trans-abdominal adrenalectomy [27] is a sub-mesocolic approach and is the least common technique used for adrenalectomy; its main appeal is the conventional abdominal laparoscopic view, familiar to all general surgeons. However, the operating times are generally longer, and more ports are needed for a successful operation. Lateral retroperitoneoscopic adrenalectomy (LPA) [27] is the most common technique used by urologic surgeons for adrenalectomy, likely due to their familiarity with the anatomy of laparoscopic nephrectomy. Similar to PRA, LPA is advocated for patients with prior abdominal surgery.

AONs are very rare lesions, with 162 reported cases in the literature and only 30 cases reported as AOCs. To the best of our knowledge, this is the first reported case of laparoscopic adrenalectomy for a voluminous AOC (120×95×110 mm). Following CT and MRI imaging, a well-encapsulated tumor, with no evidence of invasion of the surrounding tissues and no regional adenopathy, was detected. In our case, laparoscopic approach with 4-trocar placement was chosen. The patient was positioned in left lateral decubitus position at a 60° angle. The table was flexed for space widening between the 12th rib and the iliac crest. Four ports were used. The procedural steps included: mobilization of the right triangular ligament of the liver, incision between the retroperitoneal attachments of the right hepatic lobe and the lateral border of the

inferior vena cava (IVC), dissection of the lateral edge of the IVC, and taking of the right adrenal vein at the takeoff from the IVC. Mobilization of the gland was performed with an inferior-to-superior and medial-to-lateral approach. The surgical procedure was safe and effective and the postoperative period was uneventful. The 24-month follow up was negative for disease recurrence. Macroscopic examination of the specimen revealed a solid mass weighting 300 g, with several necrotic areas. Microscopic examination showed a primitive oncocytic adrenal carcinoma. Several atypical mitotic figures and high mitotic index (10/50 HPFs) were observed, together with diffuse pattern of growth and venous invasion. The specimen was evaluated with a final Weiss score of 5 (necrosis, high mitotic rate >5/50 HPF, atypical mitotic figures, diffuse architecture, and venous invasion). According to modified Weiss score, an AOC was diagnosed (mitotic rate >5/50 HPF, atypical mitotic figures, and venous invasion). The tumor cells were immunopositive for vimentin and presented typical oncocytic architecture. In our case, the neoplastic cells had a KI-67 and MIB1 rate of 20%.

In 2013, the Society of American Gastrointestinal and Endoscopic Surgeons (SAGES) presented guidelines for minimally invasive treatment of adrenal pathology [27]. However, these guidelines are limited to a retrospective analysis of published case series, with no specificity for AONs. In our case, we performed an effective laparoscopic approach to a voluminous AOC, with 24-month follow-up negative for recurrence. In light of our result, a prospective multicentric observational study should be performed to better define the aims and limits of minimally invasive surgery for AON. Due to the scarcity of cases, it is difficult to establish precise guidelines on the management of adrenal oncocytic neoplasms. Our case report is fully compliant with SCARE criteria [89].

Conclusions

Adrenocortical oncocytic tumors must be taken into account in the differential diagnosis of adrenal masses due to their different prognosis compared to non-oncocytic tumors. Adrenocortical oncocytic carcinoma are a rare presentation of AONs. Only 30 cases are described in the literature. Laparotomic adrenalectomy is the treatment of choice for AOC. We report the first case of laparoscopic lateral trans-abdominal adrenalectomy for AOC, despite the large size of the mass (120×95×110 mm). Laparoscopy performed by an experienced surgeon is safe and effective for AOC. Despite the rarity of AOC, a case series should be performed to confirm the results of our case report.

Supplementary Video



Video 1. Laparoscopic transabdominal right adrenalectomy for a large oncocytic carcinoma.

References:

1. Hamperl H: Beiträge zur normalen und pathologischen histologic menschlicher speicheldrüsen. *Z Microanat Forsch*, 1931; 27: 1 [in German]
2. Hamperl H: Oncocytes and the so-called Hürthle Cell Tumor. *Arch Pathol*, 1950; 49: 563–67
3. Smirnova EA, Mikhailov IG: Electron microscopic characteristics of oncocytoma of the lung, small intestine and adrenal gland. *Arkh Patol*, 1986; 48: 79–81
4. Sun CN, White HJ, Thompson BW: Oncocytoma (mitochondrioma) of the parotid gland. An electron microscopical study. *Arch Pathol*, 1975; 99(4): 208–14
5. Chang A, Harawi SJ: Oncocytes, oncocytosis and oncocytic tumors. *Pathol Annu*, 1992; 27: 263–304
6. Baloch ZW, LiVolsi VA: Oncocytic lesions of the neuroendocrine system. *Semin Diagn Pathol*, 1999; 16: 190–99
7. Rosai J: *Rosai and Ackerman's surgical pathology*. 2004, Mosby: Elsevier Inc.
8. Sironi M, Spinelli M: Oncocytic angiomyolipoma of the kidney: A case report. *Int J Surg Pathol*, 2003; 11: 229–34
9. Ritter JH, Nappi O: Oxyphilic proliferations of the respiratory tract and paranasal sinuses. *Semin Diagn Pathol*, 1999; 16: 105–16
10. Sugihara A, Nakasho K, Ikuta S et al: Oncocytic non-functioning endocrine tumor of the pancreas. *Pathol Int*, 2006; 56: 755–59
11. Radi MJ, Fenoglio-Preiser CM, Chiffelle T: Functioning oncocytic islet-cell carcinoma. Report of a case with electron-microscopic and immunohistochemical confirmation. *Am J Surg Pathol*, 1985; 9: 517–24
12. Itatsu K, Fujii T, Sasaki M et al: Intraductal papillary cholangiocarcinoma and atypical biliary epithelial lesions confused with intrabiliary extension of metastatic colorectal carcinoma. *Hepatogastroenterology*, 2007; 54: 677–80
13. Rouzbahman M, Serra S, Chetty R: Rectal adenocarcinoma with oncocytic features: Possible relationship with preoperative chemoradiotherapy. *J Clin Pathol*, 2006; 59: 1039–43
14. Piana S, Asioli S, Foroni M: Oncocytic adenocarcinoma of the rectum arising on a villous adenoma with oncocytic features. *Virchows Arch*, 2006; 448: 228–31
15. Giangaspero F, Cenacchi G: Oncocytic and granular cell neoplasms of the central nervous system and pituitary gland. *Semin Diagn Pathol*, 1999; 16: 91–97
16. Young RH, Scully RE: Oxyphilic tumors of the female and male genital tracts. *Semin Diagn Pathol*, 1999; 16: 146–61
17. Vancura RW, Thomas JH, Jewell WR, Damjanov I: Bilateral oncocytic malignant melanoma in axillary lymph nodes without evidence of an extranodal primary. *Ultrastruct Pathol*, 2005; 29: 399–404
18. Coburn V, Radfar A, Snook D, Mahalingam M: Cutaneous oncocytoma – a report of three cases and review of the literature. *J Cutan Pathol*, 2007; 34: 355–59
19. Sav A, Scheithauer BW, Mazzola CA et al: Oncocytic choroid plexus carcinoma: case report. *Clin Neuropathol*, 2010; 29(1): 14–20
20. Kozakiewicz J1, Teodorowicz E, Haczyńska-Partyka A et al: Adenoma oxyphilicum an extremely rare case of tumour of the larynx end cancer lungs which are going together. *Otolaryngol Pol*, 2007; 61(3): 311–14
21. Tsuta K, Kalhor N, Raso MG et al: Oncocytic neuroendocrine tumors of the lung: Histopathologic spectrum and immunohistochemical analysis of 15 cases. *Hum Pathol*, 2011; 42(4): 578–85
22. Kakimoto S, Yushita Y, Sanefuji T et al: Non-hormonal adrenocortical adenoma with oncocytoma-like appearances. *Hinyokika Kyo*, 1986; 32(5): 757–63
23. Baloch ZW, LiVolsi VA: Oncocytic lesions of the neuroendocrine system. *Semin Diagn Pathol*, 1999; 16: 190–99
24. Corrales JJ, Robles-Lázaro C, Sánchez-Marcos AI et al: Plurihormonal cosecretion by a case of adrenocortical oncocytic neoplasm. *Case Rep Endocrinol*, 2016; 2016: 6785925
25. Mearini L, Del Sordo R, Costantini E et al: Adrenal oncocytic neoplasm: A systematic review. *Urol Int*, 2013; 91: 125–33
26. Shah VN, Premkumar A, Walia R et al: Large but benign adrenal mass: Adrenal oncocytoma. *Indian J Endocrinol Metab*, 2012; 16(3): 469–71
27. Stefanidis D, Goldfarb M, Kercher KW et al: SAGES guidelines for minimally invasive treatment of adrenal pathology. *Surg Endosc*, 2013; 27: 3960–80
28. Gagner M, Lacroix A, Prinz RA et al: Laparoscopic adrenalectomy in Cushing's syndrome and pheochromocytoma. *Surgery*, 1993; 114(6): 1120–24
29. Gagner M, Lacroix A, Bolté E: Laparoscopic adrenalectomy in Cushing's syndrome and pheochromocytoma. *N Engl J Med*, 1992; 327: 1033
30. Brunt LM: The positive impact of laparoscopic adrenalectomy on complications of adrenal surgery. *Surg Endosc*, 2002; 16: 252–57
31. Agrusa A, Romano G, Frazzetta G et al: Laparoscopic adrenalectomy for large adrenal masses: single team experience. *Int J Surg*, 2014; 12(Suppl. 1): S72–74
32. Assalia A, Gagner M: Laparoscopic adrenalectomy. *Br J Surg*, 2004; 91: 1259–74
33. Pędziwiatr M, Wierdak M, Ostachowski M et al: Single center outcomes of laparoscopic transperitoneal lateral adrenalectomy – lessons learned after 500 cases: A retrospective cohort study. *Int J Surg*, 2015; 20: 88–94
34. Coste T, Caiazzo R, Torres F et al: Laparoscopic adrenalectomy by transabdominal lateral approach: 20 years of experience. *Surg Endosc*, 2017; 31(7): 2743–51
35. Armignacco R, Cantini G, Canu L et al: Adrenocortical carcinoma: The dawn of a new era of genomic and molecular biology analysis. *J Endocrinol Invest*, 2018; 41(5): 499–507
36. Lee R, Al-Ahmadie HA, Boorjian SA et al: A case of incidental adrenocortical oncocytoma. *Nat Clin Pract Urol*, 2006; 3: 618–21
37. Vara Castrodeza A, Ablanado Ablanado P, García García J et al: Adrenal oncocytoma. *Arch Esp Urol*, 1999; 52: 525–28

38. Kitching PA, Patel V, Harach HR: Adrenocortical oncocytoma. *J Clin Pathol*, 1999; 52: 151–53
39. Macchi C, Rebuffat P, Blandamura S et al: Adrenocortical oncocytoma: Case report and review of the literature. *Tumori*, 1998; 84: 403–7
40. Bégin LR: Adrenocortical oncocytoma: Case report with immunocytochemical and ultrastructural study. *Virchows Arch A Pathol Anat Histopathol*, 1992; 421: 533–37
41. Sasano H, Suzuki T, Sano T et al: Adrenocortical oncocytoma. A true non-functioning adrenocortical tumor. *Am J Surg Pathol*, 1991; 15: 949–56
42. Wong DD, Spagnolo DV, Bisceglia M et al: Oncocytic adrenocortical neoplasms – a clinicopathologic study of 13 new cases emphasizing the importance of their recognition. *Hum Pathol*, 2011; 42: 489–99
43. Corsi A, Riminucci M, Petrozza V et al: Incidentally detected giant oncocytoma arising in retroperitoneal heterotopic adrenal tissue. *Arch Pathol Lab Med*, 2002; 126: 1118–22
44. Nguyen GK, Vriend R, Ronaghan D, Lakey WH: Heterotopic adrenocortical oncocytoma. A case report with light and electron microscopic studies. *Cancer*, 1992; 70: 2681–84
45. Krech R, Zerbán H, Bannasch P: Mitochondrial anomalies in renal oncocytes induced in rat by N-nitrosomorpholine. *Eur J Cell Biol*, 1981; 25(2): 331–39
46. Sun CN, White HV, Thompson BW: Oncocytoma (mitochondrioma) of the parotid gland. *Arch Pathol*, 1975; 99: 208–14
47. Duregon E, Volante M, Cappia S et al: Oncocytic adrenocortical tumors: Diagnostic algorithm and mitochondrial DNA profile in 27 cases. *Am J Surg Pathol*, 2011; 35: 1882–93
48. Botsios D, Blouhos K, Vasiliadis K et al: Adrenocortical oncocytoma – a rare tumor of undefined malignant potential: Report of a case. *Surg Today*, 2007; 37(7): 612–17
49. Gupta P: Adrenocortical carcinoma – oncocytic variant. *PathologyOutlines.com website*. 2017 <http://www.pathologyoutlines.com/topic/adrenocorticalcarcinomaoncocytic.html>
50. Hoang MP, Ayala AG, Albores-Saavedra J: Oncocytic adrenocortical carcinoma: A morphologic, immunohistochemical and ultrastructural study of four cases. *Mod Pathol*, 2002; 15: 973–78
51. Ohtake H, Kawamura H, Matsuzaki M et al: Oncocytic adrenocortical carcinoma. *Ann Diagn Pathol*, 2010; 14: 204–8
52. Lázaro Santander R, Andrés Gozalbo C, Cortés Vizcaíno V, Vera Román JM: Lowgrade oncocytic adrenal carcinoma. *Arch Esp Urol*, 2001; 54: 1123–26
53. el-Naggar AK, Evans DB, Mackay B: Oncocytic adrenal cortical carcinoma. *Ultrastruct Pathol*, 1991; 15: 549–56
54. Argyriou P, Zisis C, Alevizopoulos N et al: Adrenocortical oncocytic carcinoma with recurrent metastases: A case report and review of the literature. *World J Surg Oncol*, 2008; 6: 134–39
55. Juliano JJ, Cody RL, Suh JH: Metastatic adrenocortical oncocytoma: A case report. *Urol Oncol*, 2008; 26: 198–201
56. Song SY, Park S, Kim SR, Suh YL: Oncocytic adrenocortical carcinomas: A pathological and immunohistochemical study of four cases in comparison with conventional adrenocortical carcinomas. *Pathol Int*, 2004; 54: 603–10
57. Weiss LM: Comparative histologic study of 43 metastasizing and nonmetastasizing adrenocortical tumors. *Am J Surg Pathol*, 1984; 8: 163–69
58. Bisceglia M, Ludovico O, Di Mattia A et al: Adrenocortical oncocytic tumors: Report of 10 cases and review of the literature. *Int J Surg Pathol*, 2004; 12: 231–43
59. Iino K, Sasano H, Yabuki N et al: DNA topoisomerase II alpha and Ki-67 in human adrenocortical neoplasms: A possible marker of differentiation between adenomas and carcinomas. *Mod Pathol*, 1997; 10: 901–7
60. Nakazumi H, Sasano H, Iino K et al: Expression of cell cycle inhibitor p27 and Ki-67 in human adrenocortical neoplasms. *Mod Pathol*, 1998; 11: 1165–70
61. Martins ACP, Cologna AJ, Tucci S et al: Clinical features and immunoeexpression of p53, MIB-1 and proliferating cell nuclear antigen in adrenal neoplasms. *J Urol*, 2005; 173: 2138–42
62. Bernini GP, Moretti A, Viacava P et al: Apoptosis control and proliferation marker in human normal and neoplastic adrenocortical tissues. *Br J Cancer*, 2002; 86: 1561–65
63. Wachenfeld C, Beuschlein F, Zwermann O et al: Discerning malignancy in adrenocortical tumors: Are molecular markers useful? *Eur J Endocrinol*, 2001; 145: 335–41
64. Terzolo M, Boccuzzi A, Bovio S et al: Immunohistochemical assessment of Ki-67 in the differential diagnosis of adrenocortical tumors. *Urology*, 2001; 57: 176–82
65. Stojadinovic A, Ghossein RA, Hoos A et al: Adrenocortical carcinoma: Clinical, morphologic, and molecular characterization. *J Clin Oncol*, 2002; 15: 941–50
66. Kirschner LS: Emerging treatment strategies for adrenocortical carcinoma: A new hope. *J Clin Endocrinol Metab*, 2006; 91: 14–21
67. Vargas MP, Vargas HI, Kleiner DE, Merino MJ: Adrenocortical neoplasms: Role of prognostic markers MIB-1, p53 and RB. *Am J Surg Pathol*, 1997; 21: 556–62
68. Billimoria KY, Shen WT, Elaraj D et al: Adrenocortical carcinoma in the United States: Treatment utilization and prognostic factors. *Cancer*, 2008; 113: 3130–36
69. Goldblum JR, Shannon R, Kaldjian EP et al: Immunohistochemical assessment of proliferative activity in adrenocortical neoplasms. *Mod Pathol*, 1993; 6: 663–68
70. Krishnamurthy S, Ordonez NG, Shelton TO et al: Fine-needle aspiration cytology of a case of oncocytic adrenocortical carcinoma. *Diagn Cytopathol*, 2000; 22: 299–303
71. Lin BTY, Bonsib SM, Mierau GW et al: Oncocytic adrenocortical neoplasms: A report of seven cases and review of the literature. *Am J Surg Pathol*, 1998; 22: 603–14
72. Angeli A, Osella G, Ali A, Terzolo M: Adrenal incidentaloma: An overview of clinical and epidemiological data from the National Italian Study Group. *Horm Res*, 1997; 47: 279–83
73. Tirkos T, Gokaslan T, McCrea J et al: Oncocytic neoplasms of the adrenal gland. *Am J Roentgenol*, 2011; 196: 592–96
74. Boland GWL: Adrenal imaging. *Abdom Imaging*, 2011; 36: 472–82
75. Shah RK, Oto A, Ozkan OS et al: Adrenal oncocytoma: US and CT findings. *JBR-BTR*, 2004; 87: 180–82
76. Poretti D, Mazzarol G, Bonomo G et al: Adrenocortical oncocytoma: Case report. *Clin Imaging*, 2003; 27: 426–30
77. Park BK, Kim B, Ko K et al: Adrenal masses falsely diagnosed as adenomas on unenhanced and delayed contrast-enhanced computed tomography: Pathological correlation. *Eur Radiol*, 2006; 16: 642–47
78. Haider MA, Ghai S, Jhaveri K, Lockwood G: Chemical shift MR imaging of hyperattenuating (110 HU) adrenal masses: does it still have a role? *Radiology*, 2004; 231: 711–16
79. Savci G, Yazici Z, Sahin N et al: Value of chemical shift subtraction MRI in characterization of adrenal masses. *Am J Roentgenol*, 2006; 186: 130–35
80. Monk IP, Lahiri R, Sivaprakasam R et al: Adrenocortical oncocytoma: Review of imaging and histopathological implications. *Int J Surg Case Rep*, 2010; 1: 30–32
81. Kekis P, Seretis C, Lagoudianakis E et al: Laparoscopic approach to a large adrenocortical oncocytoma: A case report and review of the literature. *Int J Surg Case Rep*, 2012; 3: 279–82
82. Friedrich-Rust M, Glasemann T, Polta A et al: Differentiation between benign and malignant adrenal mass using contrast-enhanced ultrasound. *Ultraschall Med*, 2011; 32: 460–71
83. Krishnamurthy S, Ordonez NG, Shelton TO et al: Fine-needle aspiration cytology of a case of oncocytic adrenocortical carcinoma. *Diagn Cytopathol*, 2000; 22: 299–303
84. Lee CK, Choi KH, Cha YJ et al: Large oncocytic adrenocortical tumor with uncertain malignant potential. *Korean J Urol*, 2011; 52: 650–52
85. Lombardi CP, Raffaelli M, Boniardi M et al: Adrenocortical carcinoma: Effect of hospital volume on patient outcome. *Langenbeck's Arch Surg*, 2012; 397: 201–7
86. Young JA, Chapman WH 3rd, Kim VB et al: Robotic-assisted adrenalectomy for adrenal incidentaloma: Case and review of the technique. *Surg Laparosc Endosc Percutan Tech*, 2002; 12: 126–30
87. Miller BS, Gauger PG, Hammer GD, Doherty GM: Resection of adrenocortical carcinoma is less complete and local recurrence occurs sooner and more often after laparoscopic adrenalectomy than after open adrenalectomy. *Surgery*, 2012; 152: 1150–57
88. Cooper AB, Habra MA, Grubbs EG et al: Does laparoscopic adrenalectomy jeopardize oncologic outcomes for patients with adrenocortical carcinoma? *Surg Endosc*, 2013; 27: 4026–32
89. Agha RA, Fowler AJ, Saetta A et al., SCARE Group: The SCARE statement: Consensus-based surgical case report guidelines. *Int J Surg*, 2016; 34: 180–86