

Peer Review File

Article information: <https://dx.doi.org/10.21037/ls-23-12>

Reviewer A

The authors present a case of a giant adrenal cyst that was resected by laparoscopy. They have undertaken a thorough literature review on the clinical presentation and differential diagnosis of retroperitoneal cysts. The article is well written and the figures are clear and informative.

Comments

1. This report does not add much to the existing literature. A laparoscopic approach is well accepted to be a feasible option for large adrenal lesions, including for solid tumours or cysts.

Reply 1: While the laparoscopic approach has been documented for large adrenal lesions, the treatment of giant adrenal cysts (greater than 10 cm) specifically, has been scarcely reported and typically performed through an open approach (doi.org/10.1016/j.eucr.2021.101725; [doi:10.1016/j.ijscr.2011.05.007](https://doi.org/10.1016/j.ijscr.2011.05.007); Indian J Urol 2016;32:81-2; doi.org/10.1186/s13256-018-1876-8

). In the case presented, a comprehensive account of the employed surgical technique is provided, offering valuable visual guidance to surgeons who may encounter these pathologies infrequently. A clarification pertaining to this aspect has been included in the text (see Page 10, line 174 and Page 11 line 193).

Changes in the text:

-Laparoscopic partial adrenalectomy stands as the preferred procedure for the resection of adrenal cysts, since the adrenal gland is preserved. (7, 11) Nevertheless, a considerable number of giant adrenal cyst cases continue to be managed through open surgical procedures, even in specialized referral centers. (4-6, 8, 11) The presented case exemplifies the viability of employing a laparoscopic approach for managing such lesions, complemented by a visual elucidation of the procedure. (Page 10, line 174)

-Despite the most reported cases of giant adrenal cysts have been treated using open approaches, the appropriate diagnostic and therapeutic approach render laparoscopic resection safe and effective in these patients. (Page 11 line 193)

2. Highlight box (line 46). “The majority of these cysts have an average size of 5 centimeters.” This statement does not make any sense.

Reply 2: This statement pertains to the average size of adrenal cysts documented in the literature, which stands in contrast to the 15 centimeter lesion that we have reported. The correction has been made to enhance clarity in this line (see Page 4, line 46).

Changes in the text: The average size of adrenal cysts reported in the literature is 5 cm. (Page 4, line 46)

Reviewer B

Thank you for sharing your manuscript on giant adrenal cysts. While interesting to read, it is not novel. Other than size, why is this case unique? You have stated that the purpose of your report is to review the management and surgical approach of a giant adrenal cyst. What has changed since earlier reports? The case report can be significantly edited. At times, I felt like I was reading a patient chart. Normal vital signs

is not a sentence. I am not sure if your functional assessment was complete - you have not mentioned ARR.

Comment 1: Other than size, why is this case unique?

Reply 1: The comprehensive description of the laparoscopic approach in this particular case yields significant insights for future recommendations concerning the application of minimally invasive surgery in similar instances. Furthermore, while adrenal tumors are frequently encountered in medical literature, reports on adrenal cysts are scarce, and the occurrence of cysts larger than 10 centimeters is rare. A clarification pertaining to this aspect has been included in the text (Page 10, line 174).

Changes in the text: Laparoscopic partial adrenalectomy stands as the preferred procedure for the resection of adrenal cysts, since the adrenal gland is preserved. (7, 11) Nevertheless, a considerable number of giant adrenal cyst cases continue to be managed through open surgical procedures, even in specialized referral centers. (4-6, 8, 11) The presented case exemplifies the viability of employing a laparoscopic approach for managing such lesions, complemented by a visual elucidation of the procedure. (Page 10, line 174)

Comment 2: You have stated that the purpose of your report is to review the management and surgical approach of a giant adrenal cyst. What has changed since earlier reports?

Reply 2: The laparoscopic approach has been documented in literature for managing cystic adrenal lesions; however, in all reported cases, cysts larger than 10 centimeters have been addressed through open surgical procedures. Our manuscript offers a comprehensive account of the laparoscopic approach for such lesions, enabling its replication by other surgeons. Moreover, we have included a succinct analysis on this subject to further enhance the understanding of the significance of our findings. (Page 10, line 174)

Changes in the text: Nevertheless, a considerable number of giant adrenal cyst cases continue to be managed through open surgical procedures, even in specialized referral centers. (4-6, 8, 11) The presented case exemplifies the viability of employing a laparoscopic approach for managing such lesions, complemented by a visual elucidation of the procedure. (Page 10, line 174)

Comment 3: The case report can be significantly edited. At times, I felt like I was reading a patient chart. Normal vital signs is not a sentence

Reply 3: We have modified our text as advised (Page 5, line 67, and page 6, line 81)

Changes in the text:

-The patient presented with vital signs within normal range, with a BMI of 33.7 Kg/m² (Grade I obesity). Abdomen with a palpable tumor on the left flank of approximately 10 x 10 centimeters, poorly defined borders, fixed to deep planes, with pain on palpation 4/10 on the Visual Analogue Scale of pain. (Page 5, line 67).

-Preoperative evaluation by Internal Medicine and anesthesiology with Goldman risk index class I and American Society of Anesthesiologists score class II. (Page 6, line 81)

Comment 4: I am not sure if your functional assessment was complete - you have not mentioned ARR.

Reply 4: The most recent guidelines on the evaluation of adrenal masses (doi.org/10.3803/EnM.2017.32.2.200; DOI: 10.1530/EJE-16-0467; doi: 10.1210/jc.2015-4061) recommend assessing primary aldosteronism with ARR measurement only in patients who present with hypertension and/or hypokalemia. The presented case demonstrated the absence of hypertension, and the patient's serum electrolyte levels were found to be within normal limits. Consequently, there was no indication to conduct tests to assess primary aldosteronism. In light of this information, additional details

regarding the patient's serum electrolyte levels and the rationale for not measuring the Aldosterone Renin Ratio (ARR) have been included. (Page 5, line 74, and Page 8, line 130)

Changes in the text:

-Serum electrolytes and coagulation times within normal parameters. (Page 5, line 74)

-The measurement of the aldosterone/renin ratio is warranted solely in patients exhibiting associated hypertension and/or hypokalemia; hence, there was no necessity to perform this assessment in the present case. (12-14) (Page 8, line 130)

Reviewer C

I am very grateful that I have the opportunity to revise this manuscript. Below is my peer-review report:

- General: The article concentrates on the laparoscopic removal of adrenal cyst which is a very rare condition in this anatomical localization.

- Specific:

1. Abstract

Correct

2. Introduction

Correct

3. Case description

Please in lines 70-72 introduce the reference values of parameters.

Reply 1: We have modified our text as advised (page 5, line 70).

Changes in the text: Laboratory test with leukocytes of 4.07 10³/L (reference value 4.6-10.4 10³/L), creatinine 0.74 mg/dL (reference value 0.50-1.20 mg/dL), dehydroepiandrosterone 73.7 mcg/dL (reference value 19-231 mcg/dL), serum metanephrines 134.6 pg/mL (reference value 33-190 pg/mL), morning cortisol 11.1 mcg/dL (reference value 3.7-19.4 mcg/dL), evening cortisol 3.35 mcg/dL (reference value 2.9-17.3 mcg/dL), testosterone 0.20 ng/mL (reference value 0.-0.81 ng/mL). Serum electrolytes and coagulation times within normal parameters. (page 5, line 70).

Do you check the immunological status (serologic tests) for *Echinococcus granulosus*? Without excluding parasitic infection, opening the cyst inside the abdomen may be dangerous.

Reply 2: Adrenal localization of hydatid cysts is rare, even in endemic countries, estimated to be less than 1% of all hydatid cysts, and usually occurs in disseminated echinococcosis (doi.org/10.1016/j.radcr.2022.05.084; [doi:10.1186/1752-1947-1-61](https://doi.org/10.1186/1752-1947-1-61)). The case under our observation did not manifest computed tomography findings indicative of echinococcosis, such as the presence of a multiloculated cyst, daughter cysts, calcifications in septa or capsule, or membrane detachment (doi.org/10.2147/IDR.S331957; doi.org/10.1016/j.radcr.2022.05.084). Additionally, Mexico is not considered an endemic country for *E. granulosus* ([doi:10.1016/j.ijpara.2005.07.014](https://doi.org/10.1016/j.ijpara.2005.07.014)). Serological tests for *Echinococcus granulosus* were not considered necessary since the diagnostic probability was low. Relevant information was added (Page 7, lines 118).

Changes in the text: Adrenal hydatid cysts are infrequent (<1% of echinococcosis cases) and typically exhibit distinctive features on computed tomography, such as simple cysts with a double wall, multilocular cysts, the presence of the daughter cyst sign, calcifications in septa or capsule, and membrane detachment. (9, 10) The case presented did not show any past medical history or clinical manifestations, nor did the

imaging data indicate any evidence suggestive of an Echinococcus granulosus infection.. (Page 7, lines 118)

4. Discussion

Correct

5. References

Correct

6. Figures

Please in Figure 1 use arrows to indicate the described organs.

Reply 3: We have modified our text and figure as advised (page 12 and 15, lines 220, 237-240)

Changes in the text: Simple phase abdominal tomography, coronal section, showing left adrenal cyst (indicated with white asterisk) with homogeneous content, with thin and regular walls, without calcifications inside. There is evidence of displacement of spleen (indicated with black star), stomach (white star), pancreas (white triangle), and left kidney (black triangle). (Page 15 and 17, lines 266 y 283)

Figure 2-it is not clear where is the chest and where are the legs-problems with orientation for the potential reader

Reply 4: We have modified our figure as advised (page 15, line 268)

Changes in the text: Modifications in Figure 2, page 15, line 268.

7. Video

Correct

Conclusions

Correct

Summary

The article is well-written and in an accessible style. The work adds essential data to the possible techniques in adrenal surgery. Additionally, the article must be checked once again for the correctness of the English language.

With best regards

Reviewer D

It would include an assessment of malignancy by imaging and other clinical and laboratory signs prior to surgery. In this way, laparoscopy is safe with low risk of dissemination.

Reply 1: 60-80% of patients with adrenocortical carcinoma present autonomous hormonal production (doi.org/10.1210/jc.2013-3020; DOI: 10.1530/EJE-18-0608). Tomographic features indicative of malignancy in adrenal tumors include density >10-21 HU, heterogeneous image, size >4 cm, in addition to an excess of corticoadrenal hormones, rapid development of symptoms, or age younger than 40 years (DOI: 10.1530/EJE-14-0916; DOI: 10.1530/EJE-18-0608). The case presented demonstrated a lack of biochemical or imaging indicators suggestive of malignancy. Accordingly, revisions will be implemented in the discussion section to underscore this aspect. (page 8, line 133).

Changes in the text: Indicators pointing towards a malignant adrenal tumor encompass age younger than 40 years, rapid symptom development, excessive production of adrenocortical hormones, and tomographic findings suggestive of malignancy (density >10-21 HU, heterogeneous appearance, size >4 cm). (15, 16) In contrast, the patient under examination exhibited no abnormalities in adrenal hormones, and while the tumor size exceeded 4 cm, all other clinical, biochemical, and imaging characteristics pointed towards a benign tumor. (page 8, line 133).

"Other indications for surgery include cysts > 4 cm, functional, parasitic, 127 complicated cysts and those who present symptoms." Which way to surgically approach it? Is laparoscopy indicated as first option?

Reply 2: The definitive management of adrenal cysts will depend on the primary diagnostic suspicion. In cases of suspected malignancy, open surgery is the standard treatment, although tumors <6 cm without evidence of local invasion can be resected laparoscopically, provided it is performed by a surgeon experienced in this type of surgery (DOI: 10.1530/EJE-18-0608). Hydatid cysts can be resected either via laparoscopy or open surgery, considering the risk of cyst rupture and its consequences (anaphylactic shock and cyst dissemination). In cases not suitable for surgery, the PAIR method (Puncture, Aspiration, Injection, and Re-aspiration) can be considered. We have added relevant information to the text. (Page 9, line 146).

Changes in the text: Although minimally invasive adrenalectomy serves as the gold standard for managing most benign adrenal lesions, particularly tumors with a diameter of up to 6 cm, the definitive approach should be selected based on diagnostic suspicion, cyst characteristics, and the surgeon's experience. In instances where malignancy is suspected, open surgery represents the standard treatment, although tumors smaller than 6 cm lacking evidence of local invasion can be effectively resected laparoscopically, provided the procedure is performed by an experienced surgeon in this field. (15). In the case of hydatid cysts, both laparoscopic and open surgical methods can be considered, with careful consideration of the risk of cyst rupture and the potential consequences of anaphylactic shock and cyst dissemination. In situations where surgical intervention is not feasible, the PAIR method (Puncture, Aspiration, Injection, and Re-aspiration) can be regarded as an alternative option. (18) This technique entails image-guided puncture and aspiration of the cyst, followed by irrigation with a hypertonic solution or alcohol, and re-aspiration of the cyst's contents. (Page 9, line 146).

Reviewer E

The clinical case is well presented and I believe it is evaluable for publication.

Just a few comments:

- page 5, line 67: please add Kg/m²;

Reply 1: We have modified our text as advised (see Page 5, line 67)

Changes in the text: BMI of 33.7 Kg/m² (Grade I obesity) (Page 5, line 67)

- please note in the discussion that minimally-invasive adrenalectomy is the gold standard treatment for most benign adrenal lesions, especially <= 6 cm;

Reply 2: We have modified our text as advised (Page 9, line 146).

Changes in the text: Although minimally invasive adrenalectomy serves as the gold standard for managing most benign adrenal lesions, particularly tumors with a diameter of up to 6 cm, the definitive approach

should be selected based on diagnostic suspicion, cyst characteristics, and the surgeon's experience. (Page 9, line 146).

-page 8, line 138, please use the term "partial adrenalectomy" instead of "enucleation."

Reply 3: We have modified our text as advised (see Page 10, line 174)

Changes in the text: Laparoscopic partial adrenalectomy stands as the preferred procedure for the resection of adrenal cysts, since the adrenal gland is preserved. (7, 11) (see Page 10, line 174)

- please add other important articles on the topic, e.g., 10.1007/BF03350324; 10.21037/gs.2020.03.44; 10.1007/s00464-022-09663-3; 10.23736/S1824-4785.22.03449-5; 10.3390/life13020425

Reply 4: We have incorporated additional data from the suggested articles. (Page 7, line 104, 111-110)

Changes in the text:

-Adrenal cysts represent a rare disease, with a reported incidence of 0.06 – 0.18%. Generally, these cysts present in the fourth/fifth decades of life. (3-5) (Page 7, line 106)

-Benign adrenal cysts are classified into four categories: vascular (45%), pseudocysts (39%), epithelial (9%), and parasitic (7%). Furthermore, adrenal cysts can be classified as functioning and non-functioning. (3,8) (Page 7, line 111)

-In cases of patients with adrenal tumors exhibiting borderline features on imaging studies, functional imaging modalities like single photon emission tomography (SPET) or positron emission tomography (PET) can be employed to assess laterality (unilateral or bilateral tumors) in functioning masses, as well as to differentiate between benign nodules and malignant adrenal disease in non-functioning tumors. (17) (Page 8-9, line 142)

-Robot-assisted approaches present a potential alternative for the management of adrenal cysts. Comparable outcomes have been documented when comparing laparoscopic adrenalectomy with robot-assisted adrenalectomy in terms of postoperative hospitalization, intraoperative complications, postoperative complications within 30 days, and cost-effectiveness. Substantial benefits have been noted in high-volume medical centers, specifically among patients with functional tumors and/or those presenting tumors larger than 6 cm. (19, 20) (Page 10, line 168)