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Contents

Thrice Monthly Volume 9 Number 20 July 16, 2021

EDITORIAL

- 5352 COVID-19: Considerations about immune suppression and biologicals at the time of SARS-CoV-2 pandemic

Costanzo G, Cordeddu W, Chessa L, Del Giacco S, Firinu D

REVIEW

- 5358 Obesity in people with diabetes in COVID-19 times: Important considerations and precautions to be taken

Alberti A, Schuelter-Trevisol F, Iser Betine PM, Traebert E, Freiburger V, Ventura L, Rezin GT, da Silva BB, Meneghetti Dallacosta F, Grigollo L, Dias P, Fin G, De Jesus JA, Pertille F, Rossoni C, Hur Soares B, Nodari Junior RJ, Comim CM

- 5372 Revisiting delayed appendectomy in patients with acute appendicitis

Li J

MINIREVIEWS

- 5391 Detection of short stature homeobox 2 and RAS-associated domain family 1 subtype A DNA methylation in interventional pulmonology

Wu J, Li P

- 5398 Borderline resectable pancreatic cancer and vascular resections in the era of neoadjuvant therapy

Mikulic D, Mrzljak A

- 5408 Esophageal manifestation in patients with scleroderma

Voulgaris TA, Karamanolis GP

- 5420 Exploration of transmission chain and prevention of the recurrence of coronavirus disease 2019 in Heilongjiang Province due to in-hospital transmission

Chen Q, Gao Y, Wang CS, Kang K, Yu H, Zhao MY, Yu KJ

- 5427 Role of gastrointestinal system on transmission and pathogenesis of SARS-CoV-2

Simsek C, Erul E, Balaban HY

ORIGINAL ARTICLE

Case Control Study

- 5435 Effects of nursing care in fast-track surgery on postoperative pain, psychological state, and patient satisfaction with nursing for glioma

Deng YH, Yang YM, Ruan J, Mu L, Wang SQ

Retrospective Study

- 5442 Risk factors related to postoperative recurrence of dermatofibrosarcoma protuberans: A retrospective study and literature review

Xiong JX, Cai T, Hu L, Chen XL, Huang K, Chen AJ, Wang P

- 5453** Prediction of presence and severity of coronary artery disease using prediction for atherosclerotic cardiovascular disease risk in China scoring system

Hong XL, Chen H, Li Y, Teeroovengadum HD, Fu GS, Zhang WB

- 5462** Effects of angiotensin receptor blockers and angiotensin-converting enzyme inhibitors on COVID-19

Li XL, Li T, Du QC, Yang L, He KL

- 5470** Prognostic factors and its predictive value in patients with metastatic spinal cancer

Gao QP, Yang DZ, Yuan ZB, Guo YX

Clinical Trials Study

- 5479** Prospective, randomized comparison of two supplemental oxygen methods during gastro-scopy with propofol mono-sedation in obese patients

Shao LJZ, Hong FX, Liu FK, Wan L, Xue FS

SYSTEMATIC REVIEWS

- 5490** Herb-induced liver injury: Systematic review and meta-analysis

Ballotin VR, Bigarella LG, Brandão ABM, Balbinot RA, Balbinot SS, Soldera J

META-ANALYSIS

- 5514** Type 2 diabetes mellitus increases liver transplant-free mortality in patients with cirrhosis: A systematic review and meta-analysis

Liu ZJ, Yan YJ, Weng HL, Ding HG

CASE REPORT

- 5526** Duplication of 19q (13.2-13.31) associated with comitant esotropia: A case report

Feng YL, Li ND

- 5535** Multiple left ventricular myxomas combined with severe rheumatic valvular lesions: A case report

Liu SZ, Hong Y, Huang KL, Li XP

- 5540** Complete pathological response in locally advanced non-small-cell lung cancer patient: A case report

Parisi E, Arpa D, Ghigi G, Micheletti S, Neri E, Tontini L, Pieri M, Romeo A

- 5547** Successful reversal of ostomy 13 years after Hartmann procedure in a patient with colon cancer: A case report

Huang W, Chen ZZ, Wei ZQ

- 5556** Delayed papillary muscle rupture after radiofrequency catheter ablation: A case report

Sun ZW, Wu BF, Ying X, Zhang BQ, Yao L, Zheng LR

- 5562** Temporary coronary sinus pacing to improve ventricular dyssynchrony with cardiogenic shock: A case report

Ju TR, Tseng H, Lin HT, Wang AL, Lee CC, Lai YC

- 5568** Hemoglobin Fukuoka caused unexpected hemoglobin A_{1c} results: A case report
Lin XP, Yuan QR, Niu SQ, Jiang X, Wu ZK, Luo ZF
- 5575** Giant androgen-producing adrenocortical carcinoma with atrial flutter: A case report and review of the literature
Costache MF, Arhirii RE, Mogos SJ, Lupascu-Ursulescu C, Litcanu CI, Ciunanghel AI, Cucu C, Ghiciuc CM, Petris AO, Danila N
- 5588** Can kissing cause paraquat poisoning: A case report and review of literature
Ly B, Han DF, Chen J, Zhao HB, Liu XL
- 5594** Spinal dural arteriovenous fistula 8 years after lumbar discectomy surgery: A case report and review of literature
Ouyang Y, Qu Y, Dong RP, Kang MY, Yu T, Cheng XL, Zhao JW
- 5605** Perianal superficial CD34-positive fibroblastic tumor: A case report
Long CY, Wang TL
- 5611** Low-dose clozapine-related seizure: A case report and literature review
Le DS, Su H, Liao ZL, Yu EY
- 5621** Rapid diagnosis of disseminated *Mycobacterium mucogenicum* infection in formalin-fixed, paraffin-embedded specimen using next-generation sequencing: A case report
Liu J, Lei ZY, Pang YH, Huang YX, Xu LJ, Zhu JY, Zheng JX, Yang XH, Lin BL, Gao ZL, Zhuo C
- 5631** Cytomegalovirus colitis induced segmental colonic hypoganglionosis in an immunocompetent patient: A case report
Kim BS, Park SY, Kim DH, Kim NI, Yoon JH, Ju JK, Park CH, Kim HS, Choi SK
- 5637** Primary extra-pancreatic pancreatic-type acinar cell carcinoma in the right perinephric space: A case report and review of literature
Wei YY, Li Y, Shi YJ, Li XT, Sun YS
- 5647** Muscular atrophy and weakness in the lower extremities in Behçet's disease: A case report and review of literature
Kim KW, Cho JH
- 5655** Novel technique of extracorporeal intrauterine morcellation after total laparoscopic hysterectomy: Three emblematic case reports
Macciò A, Sanna E, Lavra F, Calò P, Madeddu C
- 5661** Rare isolated extra-hepatic bile duct injury: A case report
Zhao J, Dang YL, Lin JM, Hu CH, Yu ZY
- 5668** Gelfoam embolization for distal, medium vessel injury during mechanical thrombectomy in acute stroke: A case report
Kang JY, Yi KS, Cha SH, Choi CH, Kim Y, Lee J, Cho BS

- 5675** Oncocytic adrenocortical tumor with uncertain malignant potential in pediatric population: A case report and review of literature
Chen XC, Tang YM, Mao Y, Qin DR
- 5683** Submucosal hematoma with a wide range of lesions, severe condition and atypical clinical symptoms: A case report
Liu L, Shen XJ, Xue LJ, Yao SK, Zhu JY
- 5689** Chorioamnionitis caused by *Serratia marcescens* in a healthcare worker: A case report
Park SY, Kim MJ, Park S, Kim NI, Oh HH, Kim J
- 5695** Endoscopic management of biliary ascariasis: A case report
Wang X, Lv YL, Cui SN, Zhu CH, Li Y, Pan YZ
- 5701** Role of ranulas in early diagnosis of Sjögren's syndrome: A case report
Chen N, Zeng DS, Su YT
- 5709** Sacral chondroblastoma — a rare location, a rare pathology: A case report and review of literature
Zheng BW, Niu HQ, Wang XB, Li J
- 5717** Primary liver actinomycosis in a pediatric patient: A case report and literature review
Liang ZJ, Liang JK, Chen YP, Chen Z, Wang Y
- 5724** Splenosis masquerading as gastric stromal tumor: A case report
Zheng HD, Xu JH, Sun YF
- 5730** Hemorrhagic transformation of ischemic cerebral proliferative angiopathy: A case report
Xia Y, Yu XF, Ma ZJ, Sun ZW
- 5737** Multidisciplinary team therapy for left giant adrenocortical carcinoma: A case report
Zhou Z, Luo HM, Tang J, Xu WJ, Wang BH, Peng XH, Tan H, Liu L, Long XY, Hong YD, Wu XB, Wang JP, Wang BQ, Xie HH, Fang Y, Luo Y, Li R, Wang Y
- 5744** Histopathology and immunophenotyping of late onset cutaneous manifestations of COVID-19 in elderly patients: Three case reports
Mazzitelli M, Dastoli S, Mignogna C, Bennardo L, Lio E, Pelle MC, Trecarichi EM, Pereira BI, Nisticò SP, Torti C

CORRECTION

- 5752** Corrigendum to "Probiotic mixture VSL#3: An overview of basic and clinical studies in chronic diseases"
Sang LX

ABOUT COVER

Editorial Board Member of *World Journal of Clinical Cases*, Fan-Zheng Meng, MD, PhD, Director, Professor, Department of Pediatrics, The First hospital of Jilin University, Changchun 130021, Jilin Province, China. mengfanzheng1972@163.com

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The primary aim of *World Journal of Clinical Cases* (WJCC, *World J Clin Cases*) is to provide scholars and readers from various fields of clinical medicine with a platform to publish high-quality clinical research articles and communicate their research findings online.

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Multidisciplinary team therapy for left giant adrenocortical carcinoma: A case report

Zheng Zhou, Hong-Mei Luo, Jian Tang, Wu-Jun Xu, Bin-Hui Wang, Xu-Hui Peng, Heng Tan, Li Liu, Xiang-Yang Long, Yu-De Hong, Xiao-Bin Wu, Jian-Ping Wang, Bai-Qi Wang, Hai-Hui Xie, Yong Fang, Yong Luo, Rong Li, Yi Wang

ORCID number: Zheng Zhou 0000-0002-4791-4841; Hong-Mei Luo 0000-0001-2345-6789; Jian Tang 0000-0002-6496-5376; Wu-Jun Xu 0000-0002-3391-471X; Bin-Hui Wang 0000-0002-2157-632X; Xu-Hui Peng 0000-0001-6384-6001; Heng Tan 0000-0002-0466-8599; Li Liu 0000-0003-1162-4516; Xiang-Yang Long 0000-0003-3234-2171; Yu-De Hong 0000-0002-9547-1950; Xiao-Bin Wu 0000-0002-3058-046X; Jian-Ping Wang 0000-0002-4920-8801; Bai-Qi Wang 0000-0002-4464-6247; Hai-Hui Xie 0000-0002-2685-4675; Yong Fang 0000-0002-2887-2607; Yong Luo 0000-0002-5747-3189; Rong Li 0000-0001-8566-1438; Yi Wang 0000-0003-2565-2948.

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Zheng Zhou, Jian Tang, Wu-Jun Xu, Bin-Hui Wang, Xu-Hui Peng, Heng Tan, Li Liu, Xiang-Yang Long, Yu-De Hong, Xiao-Bin Wu, Yi Wang, Department of Urology, The Second Affiliated Hospital, University of South China, Hengyang 421001, Hunan Province, China

Hong-Mei Luo, Department of Histology and Embryology, Clinical Anatomy and Reproductive Medicine Application Institute, University of South China, Hengyang 421001, Hunan Province, China

Jian-Ping Wang, Department of Endocrinology, The Second Affiliated Hospital of University of South China, Hengyang 421001, Hunan Province, China

Bai-Qi Wang, Department of Oncology, The Second Affiliated Hospital, University of South China, Hengyang 421001, Hunan Province, China

Hai-Hui Xie, Department of Radiotherapy, The Second Affiliated Hospital, University of South China, Hengyang 421001, Hunan Province, China

Yong Fang, Department of Pathology, The Second Affiliated Hospital, University of South China, Hengyang 421001, Hunan Province, China

Yong Luo, Department of ICU, The Second Affiliated Hospital, University of South China, Hengyang 421001, Hunan Province, China

Rong Li, Department of Clinical Pharmacy, The Second Affiliated Hospital, University of South China, Hengyang 421001, Hunan Province, China

Corresponding author: Yi Wang, PhD, Chief Physician, Department of Urology, The Second Affiliated Hospital, University of South China, No. 35 Jiefang Avenue, Zhengxiang District, Hengyang 421001, Hunan Province, China. wangwang0906@163.com

Abstract

BACKGROUND

Adrenocortical carcinoma (ACC) is a rare malignant epithelial tumor originating from adrenocortical cells that carries a very poor prognosis. Metastatic or inoperable diseases are often considered incurable, and treatment remains a challenge. Especially for advanced cases such as ACC complicated with renal venous cancer thrombus, there are few cumulative cases in the literature.

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CASE SUMMARY

The patient in this case was a 39-year-old middle-aged male who was admitted to the hospital for more than half a month due to dizziness and chest tightness. Computed tomography (CT) findings after admission revealed a left retroperitoneal malignant space-occupying lesion, but the origin of the formation of the left renal vein cancer thrombus remained to be determined. It was speculated that it originated from the left adrenal gland, perhaps a retroperitoneal source, and left adrenal mass + left nephrectomy + left renal vein tumor thrombus removal + angioplasty were performed under general anesthesia. Postoperative pathology results indicated a diagnosis of ACC. Postoperative steroid therapy was administered. At 3 mo after surgery, abdominal CT reexamination revealed multiple enlarged retroperitoneal lymph nodes and multiple low-density shadows in the liver, and palliative radiotherapy and mitotane were administered, considering the possibility of metastasis. The patient is currently being followed up.

CONCLUSION

ACC is a highly malignant tumor. Even if the tumor is removed surgically, there is still the possibility of recurrence. Postoperative mitotane and adjuvant chemoradiotherapy have certain benefits for patients, but they cannot fully offset the poor prognosis of this disease.

Key Words: Adrenocortical carcinoma; Ki-67; Multidisciplinary team; Cancer thrombus; Mitotane; Case report

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Core Tip: Adrenocortical carcinoma (ACC) is a highly malignant tumor that is rarely seen in the clinic, especially with renal venous cancer thromboembolism, and the prognosis is very poor. In metastatic or locally advanced cases of ACC, there are a limited number of available treatments, and the curative effect is not significant. Priority is often given to surgical tumor reduction treatment, with mitotane as the basis of treatment. If the condition deteriorates, cytotoxic drugs should be added and radiotherapy taken into consideration.

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INTRODUCTION

Adrenocortical carcinoma (ACC) is a rare malignant epithelial tumor that originates from adrenocortical cells and is infrequently seen in the clinic. ACC can be divided into functional and nonfunctional types, with the latter accounting for approximately 40% of cases[1]. Its incidence in the population is 1-2 per million cases per year in North America and 4-12 cases per million cases per year worldwide[2]. The 5-year survival rate and median survival time reported by various medical centers vary to some extent[3-5], with 5-year survival ranging from 16%-47%[6]. The molecular mechanism of ACC is not completely clear at present and may be related to the inactivation of tumor suppressor genes (TP53, Men-1, p57Kip2, and H19), abnormal activation of proto-oncogenes (deletion of GAS, RAS, ACTH receptors), overexpression of growth factor IGF-2, and abnormal activation of the B-catenin gene[7]. In general[8], ACC patients have a poor prognosis and high recurrence rate, even if they actively undergo surgical resection. Ki-67 is a very important prognostic index for determining localized ACC immunohistochemically; if Ki-67 > 10%, the risk of

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recurrence is significantly increased. In this case, the patient underwent surgical resection of a large ACC from his left side. In a short period of time, the patient's weight had significantly decreased, and his clinical symptoms had improved. However, postoperative computed tomography (CT) reexamination showed obvious metastatic lesions. After describing this case in detail and providing a review of the literature, we further discuss the treatment and prognosis of ACC patients.

CASE PRESENTATION

Chief complaints

The patient was a 39-year-old middle-aged male who was admitted to the hospital for more than half a month due to dizziness and chest tightness, and he had gained approximately 30 kg in the past 3 mo. CT examination conducted in the local hospital 5 d before admission suggested a left retroperitoneal space-occupying lesion.

History of present illness

The patient presented with numbness of the hands and feet, increased nocturia, nocturia approximately 3-4 times/night, no obvious abdominal pain, abdominal distension, no frequent urination, no urgency, and no hematuria or other symptoms.

History of past illness

The patient was generally healthy and had no special disease history.

Personal and family history

His medical history and family history were unremarkable.

Physical examination

T: 36 °C, P: 78 times/min, R: 19 times/min, BP: 164/120 mmHg. There was no localized bulge in the bilateral kidney area, no tenderness at the bilateral costal ridge angles, no percussion pain the kidneys, and no obvious tenderness or rebound pain in the entire abdomen.

Laboratory examinations

The results of laboratory examination upon admission revealed the following: alanine aminotransferase: 115 U/L (reference < 40 U/L), uric acid: 526 μmol/L (reference < 420 μmol/L), brain natriuretic peptide: 14,157 pg/mL (reference < 400 pg/mL), aldosterone (sitting up): 616 pg/mL (reference 70-300 pg/mL), aldosterone (recumbent position) 610 pg/mL (reference 30-160 pg/mL), angiotensin II: 86 pg/mL (reference 25-60 pg/mL), K: 2.58 mmol/L (reference 3.5-5.5 mmol/L).

Imaging examinations

CT suggested malignant left retroperitoneal mass with left renal vein cancer thrombus, source to be determined: Left adrenal gland source? (Pheochromocytoma? Cortical cancer?) Retroperitoneal origin? (Leiomyolipoma? Sarcoma?) (Figure 1) and right adrenal atrophy.

FINAL DIAGNOSIS

The final diagnosis of the presented case is ACC complicated with renal venous cancer thrombus. Postoperative pathological results are shown in the (Figure 2).

TREATMENT

After admission, the patient was treated with symptomatic treatment to lower blood pressure, correct electrolyte imbalances, protect the liver and diuresis. At 2 d after admission, the patient experienced sudden chest pain and shortness of breath without obvious inducement and coughed up pink foam-like sputum. Considering acute left heart failure, the patient was transferred to the intensive care unit (ICU) for treatment to strengthen the heart, diuresis, protect the liver and stomach, lower blood pressure and correct electrolyte imbalances. After 1 wk of conservative treatment, multiple

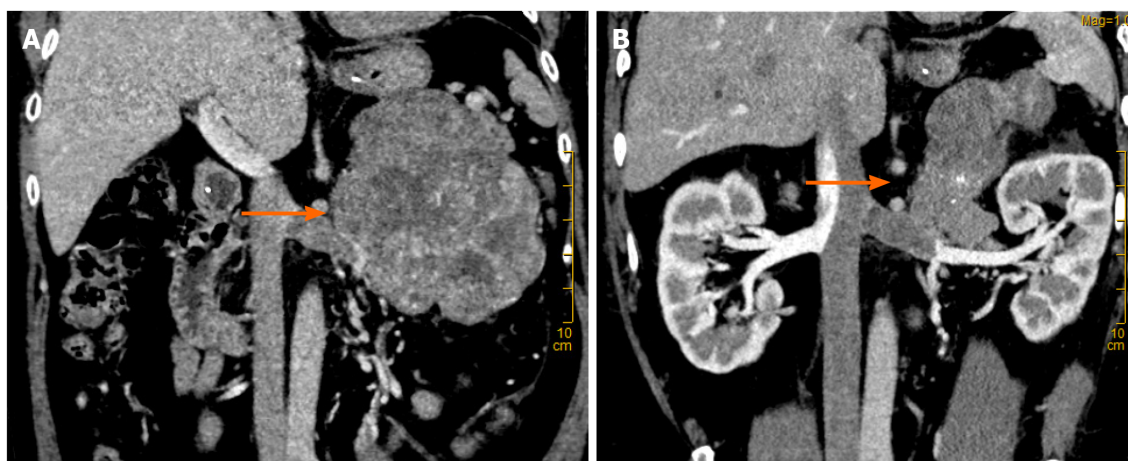


Figure 1 Computerized tomography scan after admission. A: Computer three-dimensional reconstruction (the arrow indicates a retroperitoneal mass); B: Uneven heterogeneous enhancement in the arterial phase.

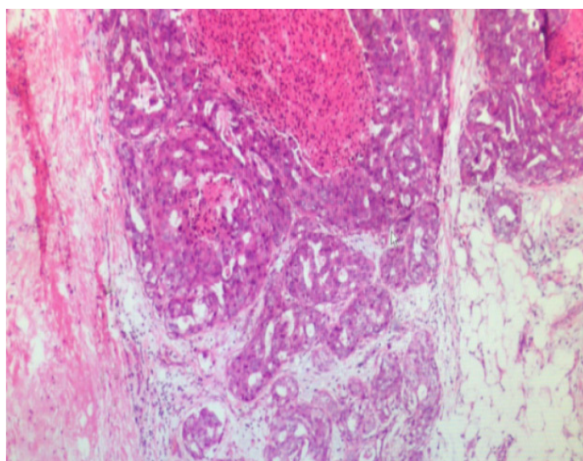


Figure 2 Postoperative pathological results: The tumor cells showed alveolar, solid, trabecular and other growth modes, and the tumor cells showed clear nucleoli and atypia. Some areas of mitotic phase > 20/50 high-power field showed focal necrosis and partial mucinous degeneration. Tumor thrombus could be seen in the vessel. The mass size was 20 cm × 10 cm × 7 cm and was consistent with adrenocortical carcinoma. No renal invasion was observed. Tumor thrombus was observed in the renal vein. Immunohistochemical results revealed the following: S100(-), HMB-45(-), Melan-A (weakly positive), Inhibin-α (weakly positive), CgA(-), CKpan (local focus+), Vimentin(+), Syn(+), TFE3 (nucleus individual+), PAX-8(-), P53 (20% nucleus+), CD34(+), and Ki-67 (15%).

departments within the hospital were consulted, and surgical treatment was considered based on the opinions of various departments. It was determined that preoperative vasodilation for 2 wk (prazosin 2 mg q8h + spiro lactone 80 mg q8h) would be administered. Under general anesthesia, the patient underwent laparoscopic resection of left renal retroperitoneal mass resection + left nephrectomy + left renal vein tumor thrombus removal + angioplasty. A large mass with a hard texture approximately 20 cm × 10 cm × 7 cm in size located in the adrenal region was observed intraoperatively (Figure 3), and the patient's blood pressure increased significantly when the mass was squeezed. Due to the difficult of laparoscopic separation of the renal pedicle and the inner and lower parts of the mass, a transabdominal laparoscopic approach was used to cut the left peritoneum, and the mass was found to be closely adhered to the pancreas. After careful separation, the pancreatic capsule was sutured with silk thread. After the pedicle was exposed, obvious varicose renal veins were observed, and thrombectomy became difficult under laparoscopic. Therefore, conversion to open surgery was decided for thrombectomy, which was performed by a vascular surgeon. The liver, pancreas, stomach, colon and adrenal gland were not invaded, and no lymph node metastasis was observed. After surgery, he was transferred to the intensive care unit for symptomatic supportive treatment such as correcting heart failure, improving cardiac function, controlling blood pressure, and maintaining homeostasis. In addition, based on the related problems arising from treatment, consultation with a multidisciplinary team was performed half a month

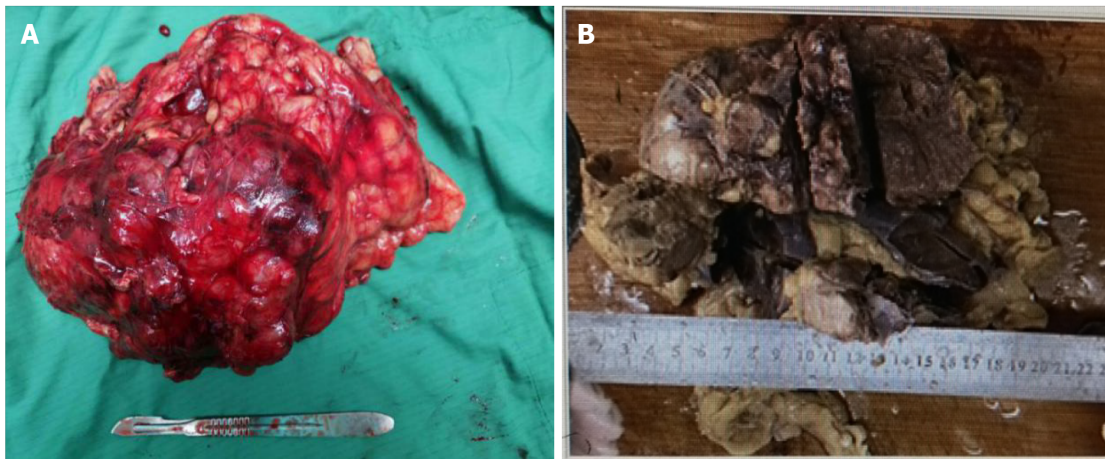


Figure 3 The 20 cm × 10 cm × 7 cm adrenal mass (A and B).

after the operation to provide supportive management such as anti-infection treatment, stomach and kidney support, hypotensive control, nutritional support, hemodialysis, and steroid therapy. During the first 3 d after surgery, the patient received hydrocortisone (100 mg q8h). The postoperative multidisciplinary team summary plan was as follows: intravenous hydrocortisone (100 mg q8h) with a gradual dose reduction (50 mg q8h). After 38 d, the prednisone dosage was changed to oral administration of 15 mg early and 5 mg late and hydrocortisone tablets at a dosage of 10 mg early and 5 mg late. After treatment, the general condition of the patient improved, his tolerance for activity increased, and the patient was discharged 48 d after surgery.

OUTCOME AND FOLLOW-UP

CT reexamination 3 mo after surgery indicated the following (Figure 4A): changes after left retroperitoneal mass resection + changes after left nephrectomy; multiple low-density shadows adjacent to enlarged retroperitoneal lymph nodes and the liver indicating a high possibility of metastasis; and right adrenal atrophy was the same as before. Palliative radiotherapy for metastatic left adrenal cortical carcinoma (PTV1: 30 Gy/10F, PTV2: 35 Gy/10F, PTV3: 35 Gy/10F 5 times/wk twice. Mitotane 500 mg q6h. CT reexamination 5 mo after surgery indicated (Figure 4B) local recurrence with invasion and metastasis of the spleen, along with multiple liver metastases and multiple retroperitoneal lymph node metastases that were more advanced than before. Metastases of the sacrum, chest, and lumbar vertebrae were also present. The patient was treated with amlotinib 12 mg qd × 12 d + mitotane 1 g qd + hydrocortisone 30 mg qd. The patient is currently being followed up.

DISCUSSION

ACC is a rare highly invasive endocrine tumor. The vast majority of ACC tumors are larger than 5 cm in diameter, but the size is not the only characteristic for the identification of benign and malignant tumors of the adrenal gland because some of the smaller adrenocortical tumors can shift[9]. Surgery is the main treatment for early metaphase ACC. Resection combined with postoperative adjuvant therapy provides the best possibility for long-term survival and a potential cure for local disease against a recurrent attack on tissues and organs. Interventional surgery, radiofrequency ablation or radiotherapy are options for oligometastases in parenchymal organs. In late ACC, operations cannot generally be performed, and patients may benefit from systemic treatment, including chemotherapy, radiotherapy, immunotherapy, and targeted therapy. Mitotane is now the most effective drug in the treatment of ACC and is applicable to cases that cannot be operated, have failed to shift or where surgery failed to completely resect the ACC. The pharmacological effects of mitotane can lead to adrenal cortical zona fasciculata and zona reticularis necrosis, and it is the only drug approved for use in the United States by the Food and Drug Administration for ACC

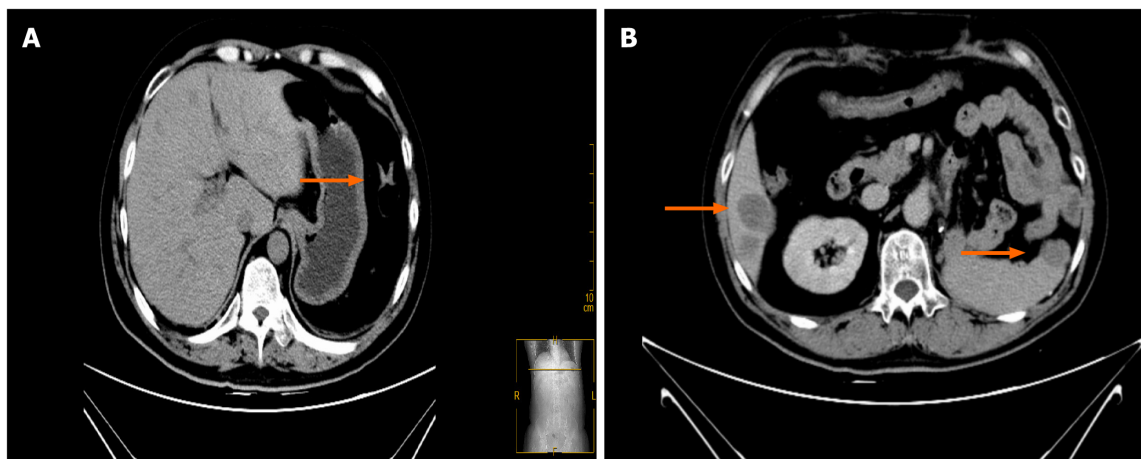


Figure 4 Multiple retroperitoneal lymph node metastases increased (the arrow on the left indicates hepatic metastases, the arrow on the right indicates spleen metastases). A: After the peritoneum was visible in the operative area, a nodular soft tissue density shadow with a size of approximately 15 mm × 19 mm could be seen. Multiple patchy slightly low-density shadows could be seen scattered in the liver parenchyma with fuzzy boundaries (the arrow indicates a nodular soft tissue density shadow in the retroperitoneal area); B: Local recurrence and invasion of the spleen were observed, with near-elliptical low-density foci of approximately 17 mm × 24 mm in the leading edge of the spleen. The number of multiple metastases in the liver increased.

clinical stages. It was listed as a rare disease drug by the European Medicines Agency in 2004[10]. To avoid drug-induced adrenal insufficiency, appropriate glucocorticoid supplementation can be considered[11]. A total of 177 ACC patients in Italy and Germany were treated with mitotane after radical resection[12], and the results showed that the duration of recurrence-free survival (RFS) in the mitotane group was significantly longer (42 mo) than that in the two control groups (10 mo and 25 mo), and the overall survival rate increased. Other foreign studies have shown that adjuvant therapy with mitotane can prolong the time of RFS (but cannot improve the overall survival rate), especially in combination with radiotherapy. Some patients diagnosed with advanced ACC and low tumor load benefit from monotherapy with mitotane. In patients with metastatic disease, mitotane monotherapy may not be an option. In such patients, the opportunity to combine mitotane with cytotoxic agents should be evaluated. Fassnacht *et al*[13] conducted a randomized study (including 304 patients) that confirmed that patients treated with mitotane combined with EDP (etoposide + cisplatin + epirubicin) had a significantly higher response and longer median progression-free survival than those treated with mitotane combined with streptocin. Mitotane in combination with EDP is also considered to be the preferred therapy in cases requiring a more aggressive treatment approach. Immunotherapy for ACC is still in the preliminary research stage. Studies have shown that adjuvant radiotherapy for ACC patients shows no significant improvement in overall survival and disease-free survival, but it can reduce the possibility of local tumor recurrence [14]. High tumor load, high tumor grade, high Ki-67 index and uncontrollable symptoms are the main factors affecting the prognosis of patients with advanced disease[15].

CONCLUSION

ACC is a rare disease that has a very poor prognosis, with a 5-year survival rate of less than 50%. Surgical treatment can be used for patients with early-/mid-stage disease confined to the adrenal gland. If the tumor is already in an advanced stage and has metastasized, tumor reduction surgery combined with radiotherapy and chemotherapy is the main treatment, and the overall prognosis of these patients is poor. We report the case of a patient with a large left adrenal mass and tumor thrombus in the left renal vein. The patient experienced recurrence 3 mo after surgery and is currently undergoing radiotherapy and chemotherapy and receiving regular follow-up.

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