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Contents

Thrice Monthly Volume 10 Number 28 October 6, 2022

REVIEW

- 9970 COVID-19 and the heart

Xanthopoulos A, Bourazana A, Giamouzis G, Skoularigki E, Dimos A, Zagouras A, Papamichalis M, Leventis I, Magouliotis DE, Triposkiadis F, Skoularigis J

- 9985 Role of short chain fatty acids in gut health and possible therapeutic approaches in inflammatory bowel diseases

Caetano MAF, Castelucci P

MINIREVIEWS

- 10004 Review of the pharmacological effects of astragaloside IV and its autophagic mechanism in association with inflammation

Yang Y, Hong M, Lian WW, Chen Z

ORIGINAL ARTICLE

Clinical and Translational Research

- 10017 Effects of targeted-edited oncogenic insulin-like growth factor-1 receptor with specific-sgRNA on biological behaviors of HepG2 cells

Yao M, Cai Y, Wu ZJ, Zhou P, Sai WL, Wang DF, Wang L, Yao DF

Retrospective Study

- 10031 Analysis of the successful clinical treatment of 140 patients with parathyroid adenoma: A retrospective study

Peng ZX, Qin Y, Bai J, Yin JS, Wei BJ

- 10042 Efficacy of digital breast tomosynthesis combined with magnetic resonance imaging in the diagnosis of early breast cancer

Ren Y, Zhang J, Zhang JD, Xu JZ

- 10053 Prevention and management of adverse events following COVID-19 vaccination using traditional Korean medicine: An online survey of public health doctors

Kang B, Chu H, Youn BY, Leem J

- 10066 Clinical outcomes of targeted therapies in elderly patients aged
- ≥ 80
- years with metastatic colorectal cancer

Jang HR, Lee HY, Song SY, Lim KH

- 10077 Endovascular treatment vs drug therapy alone in patients with mild ischemic stroke and large infarct cores

Kou WH, Wang XQ, Yang JS, Qiao N, Nie XH, Yu AM, Song AX, Xue Q

Clinical Trials Study

- 10085** One hundred and ninety-two weeks treatment of entecavir maleate for Chinese chronic hepatitis B predominantly genotyped B or C

Xu JH, Wang S, Zhang DZ, Yu YY, Si CW, Zeng Z, Xu ZN, Li J, Mao Q, Tang H, Sheng JF, Chen XY, Ning Q, Shi GF, Xie Q, Zhang XQ, Dai J

Observational Study

- 10097** Dementia-related contact experience, attitudes, and the level of knowledge in medical vocational college students

Liu DM, Yan L, Wang L, Lin HH, Jiang XY

SYSTEMATIC REVIEWS

- 10109** Link between COVID-19 vaccines and myocardial infarction

Zafar U, Zafar H, Ahmed MS, Khattak M

CASE REPORT

- 10120** Successful treatment of disseminated nocardiosis diagnosed by metagenomic next-generation sequencing: A case report and review of literature

Li T, Chen YX, Lin JJ, Lin WX, Zhang WZ, Dong HM, Cai SX, Meng Y

- 10130** Multiple primary malignancies – hepatocellular carcinoma combined with splenic lymphoma: A case report

Wu FZ, Chen XX, Chen WY, Wu QH, Mao JT, Zhao ZW

- 10136** Metastatic multifocal melanoma of multiple organ systems: A case report

Maksimaityte V, Reivytyte R, Milaknyte G, Mickys U, Razanskiene G, Stundys D, Kazenaite E, Valantinas J, Stundiene I

- 10146** Cavernous hemangioma of the ileum in a young man: A case report and review of literature

Yao L, Li LW, Yu B, Meng XD, Liu SQ, Xie LH, Wei RF, Liang J, Ruan HQ, Zou J, Huang JA

- 10155** Successful management of a breastfeeding mother with severe eczema of the nipple beginning from puberty: A case report

Li R, Zhang LX, Tian C, Ma LK, Li Y

- 10162** Short benign ileocolonic anastomotic strictures - management with bi-flanged metal stents: Six case reports and review of literature

Kasapidis P, Mavrogenis G, Mandrekas D, Bazerbachi F

- 10172** Simultaneous bilateral floating knee: A case report

Wu CM, Liao HE, Lan SJ

- 10180** Chemotherapy, transarterial chemoembolization, and nephrectomy combined treated one giant renal cell carcinoma (T3aN1M1) associated with Xp11.2/TFE3: A case report

Wang P, Zhang X, Shao SH, Wu F, Du FZ, Zhang JF, Zuo ZW, Jiang R

- 10186** Tislelizumab-related enteritis successfully treated with adalimumab: A case report

Chen N, Qian MJ, Zhang RH, Gao QQ, He CC, Yao YK, Zhou JY, Zhou H

- 10193** Treatment of refractory/relapsed extranodal NK/T cell lymphoma with decitabine plus anti-PD-1: A case report
Li LJ, Zhang JY
- 10201** Clinical analysis of pipeline dredging agent poisoning: A case report
Li YQ, Yu GC, Shi LK, Zhao LW, Wen ZX, Kan BT, Jian XD
- 10208** Follicular lymphoma with cardiac involvement in a 90-year-old patient: A case report
Sun YX, Wang J, Zhu JH, Yuan W, Wu L
- 10214** Twin reversed arterial perfusion sequence-a rare and dangerous complication form of monochorionic twins: A case report
Anh ND, Thu Ha NT, Sim NT, Toan NK, Thuong PTH, Duc NM
- 10220** Potential otogenic complications caused by cholesteatoma of the contralateral ear in patients with otogenic abscess secondary to middle ear cholesteatoma of one ear: A case report
Zhang L, Niu X, Zhang K, He T, Sun Y
- 10227** Myeloid sarcoma with ulnar nerve entrapment: A case report
Li DP, Liu CZ, Jeremy M, Li X, Wang JC, Nath Varma S, Gai TT, Tian WQ, Zou Q, Wei YM, Wang HY, Long CJ, Zhou Y
- 10236** Alpha-fetoprotein-producing hepatoid adenocarcinoma of the lung responsive to sorafenib after multiline treatment: A case report
Xu SZ, Zhang XC, Jiang Q, Chen M, He MY, Shen P
- 10244** Acute mesenteric ischemia due to percutaneous coronary intervention: A case report
Ding P, Zhou Y, Long KL, Zhang S, Gao PY
- 10252** Persistent diarrhea with petechial rash - unusual pattern of light chain amyloidosis deposition on skin and gastrointestinal biopsies: A case report
Bilton SE, Shah N, Dougherty D, Simpson S, Holliday A, Sahebjam F, Grider DJ
- 10260** Solitary splenic tuberculosis: A case report
Guo HW, Liu XQ, Cheng YL
- 10266** Coronary artery aneurysms caused by Kawasaki disease in an adult: A case report and literature review
He Y, Ji H, Xie JC, Zhou L
- 10273** Double filtration plasmapheresis for pregnancy with hyperlipidemia in glycogen storage disease type Ia: A case report
Wang J, Zhao Y, Chang P, Liu B, Yao R
- 10279** Treatment of primary tracheal schwannoma with endoscopic resection: A case report
Shen YS, Tian XD, Pan Y, Li H
- 10286** Concrecence of maxillary second molar and impacted third molar: A case report
Su J, Shao LM, Wang LC, He LJ, Pu YL, Li YB, Zhang WY

- 10293** Rare leptin in non-alcoholic fatty liver cirrhosis: A case report
Nong YB, Huang HN, Huang JJ, Du YQ, Song WX, Mao DW, Zhong YX, Zhu RH, Xiao XY, Zhong RX
- 10301** One-stage resection of four genotypes of bilateral multiple primary lung adenocarcinoma: A case report
Zhang DY, Liu J, Zhang Y, Ye JY, Hu S, Zhang WX, Yu DL, Wei YP
- 10310** Ectopic pregnancy and failed oocyte retrieval during *in vitro* fertilization stimulation: Two case reports
Zhou WJ, Xu BF, Niu ZH
- 10317** Malignant peritoneal mesothelioma with massive ascites as the first symptom: A case report
Huang X, Hong Y, Xie SY, Liao HL, Huang HM, Liu JH, Long WJ
- 10326** Subperiosteal orbital hematoma concomitant with abscess in a patient with sinusitis: A case report
Hu XH, Zhang C, Dong YK, Cong TC
- 10332** Postpartum posterior reversible encephalopathy syndrome secondary to preeclampsia and cerebrospinal fluid leakage: A case report and literature review
Wang Y, Zhang Q
- 10339** Sudden extramedullary and extranodal Philadelphia-positive anaplastic large-cell lymphoma transformation during imatinib treatment for CML: A case report
Wu Q, Kang Y, Xu J, Ye WC, Li ZJ, He WF, Song Y, Wang QM, Tang AP, Zhou T
- 10346** Relationship of familial cytochrome P450 4V2 gene mutation with liver cirrhosis: A case report and review of the literature
Jiang JL, Qian JF, Xiao DH, Liu X, Zhu F, Wang J, Xing ZX, Xu DL, Xue Y, He YH
- 10358** COVID-19-associated disseminated mucormycosis: An autopsy case report
Kyuno D, Kubo T, Tsujiwaki M, Sugita S, Hosaka M, Ito H, Harada K, Takasawa A, Kubota Y, Takasawa K, Ono Y, Magara K, Narimatsu E, Hasegawa T, Osanai M
- 10366** Thalidomide combined with endoscopy in the treatment of Cronkhite-Canada syndrome: A case report
Rong JM, Shi ML, Niu JK, Luo J, Miao YL
- 10375** Thoracolumbar surgery for degenerative spine diseases complicated with tethered cord syndrome: A case report
Wang YT, Mu GZ, Sun HL

LETTER TO THE EDITOR

- 10384** Are pregnancy-associated hypertensive disorders so sweet?
Thomopoulos C, Ilias I
- 10387** Tumor invasion front in oral squamous cell carcinoma
Cuevas-González JC, Cuevas-González MV, Espinosa-Cristobal LF, Donohue Cornejo A

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Chemotherapy, transarterial chemoembolization, and nephrectomy combined treated one giant renal cell carcinoma (T3aN1M1) associated with Xp11.2/TFE3: A case report

Peng Wang, Xiao Zhang, Shuo-Han Shao, Fa Wu, Fei-Zhou Du, Jun-Feng Zhang, Zhi-Way Zuo, Rui Jiang

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Abstract

BACKGROUND

Renal cell carcinoma (RCC) with Xp11.2 translocation/TFE3 gene fusion is a rare and distinct subtype of RCC that is classified under tumors with translocation of the microphthalmia-associated transcriptional factor.

CASE SUMMARY

We report an adult case of Xp11.2 translocation advanced RCC with metastasis (T3aN1M1), after targeted treatment, alcohol ablation, and transarterial chemoembolization, who eventually underwent successful surgical excision. No recurrence or transfer was seen within one year, and the survival period was more than 3 years. A review of the relevant literature was conducted to improve our understanding of the pathogenesis, epidemiology, clinical manifestations, diagnosis, differential diagnosis, treatment, and other aspects of the disease.

CONCLUSION

Transarterial chemoembolization and ablation did not achieve the desired tumor reduction in this patient, but had a significant effect on reducing intraoperative bleeding and inhibiting tumor activity.

Key Words: Xp11.2/TFE3 Renal Cell Carcinoma; TACE; Axitinib; Zoledronic Acid; Targeted therapy; Multimodal imaging; Case report

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Core Tip: Under the guidance of multimodality imaging, surgical resection, targeted chemotherapy, alcohol ablation, and transarterial chemoembolization were used to treat a case of Xp11.2/TFE3 (T3aN1M1) advanced renal cell carcinoma with good results. No recurrence or metastasis occurred within 1 year, with a partial response over 3 years. By reviewing this case and related literature, we can improve our understanding of the diagnosis, differential diagnosis and treatment of the disease.

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INTRODUCTION

Renal cell carcinoma (RCC) with Xp11.2 translocation/TFE3 fusion is rare but highly malignant, and is associated with poor prognosis due to the lack of early diagnosis[1,2] and the difficulty in resecting advanced stage giant tumors[3]. It was classified into the microphthalmia-associated transcriptional factor translocation family of tumors as per the 2016 WHO criteria[4]. A break in the short arm of the X chromosome gene TFE3 and the subsequent translocation generates a novel TFE3 fusion gene that is overexpressed under the new promoter, resulting in abnormal cell proliferation and malignant transformation[5,6]. We present a case of Xp11.2/TFE3 RCC stage T3aN1M1 with a tumor diameter > 30 cm that was successfully resected after chemotherapy and transarterial chemoembolization (TACE), and eventually achieved a favorable prognosis.

CASE PRESENTATION

Chief complaints

The 18-year-old female patient had been experiencing occasional abdominal distension without abdominal pain, vomiting, constipation and other discomfort for over one year. There was no gross hematuria but the patient lost more than 10 kg, which unfortunately was ignored by the patient and her family members.

History of present illness

No special medical history.

History of past illness

No special medical history.

Personal and family history

No special medical history.

Physical examination

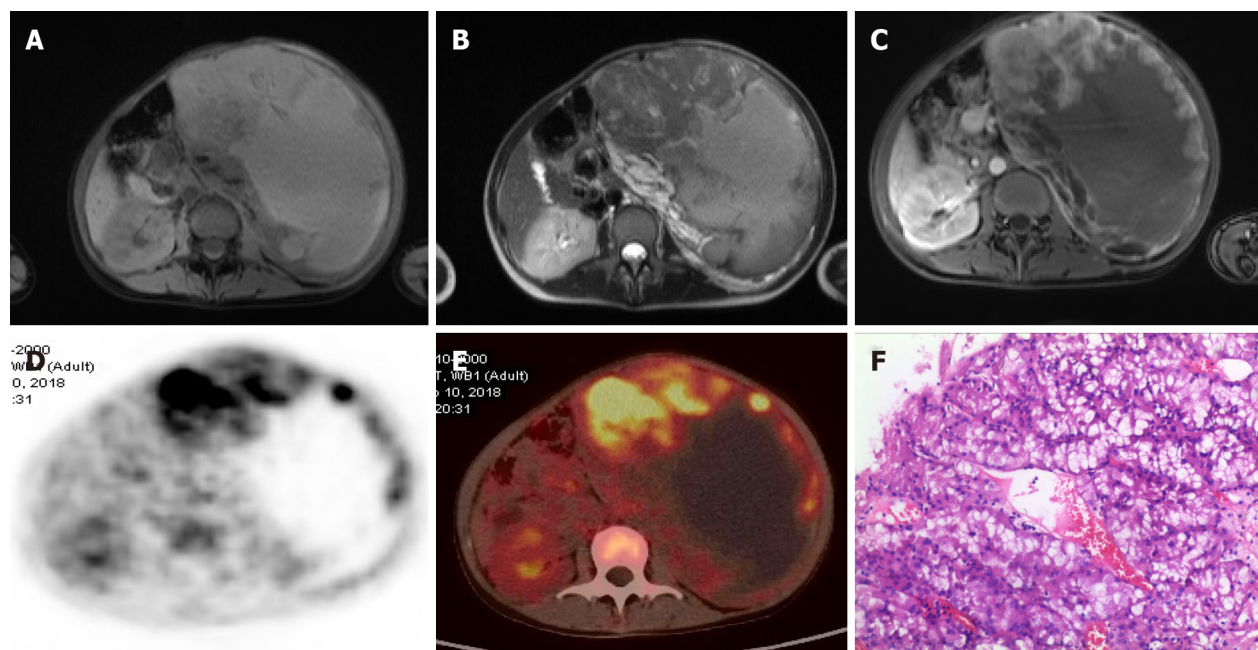
Physical examination indicated Zubrod-ECOG-WHO (ZPS) 2 points and Karnofsky (KPS) KPS 90 points. A tangible, immobile mass measuring approximately 30 cm in diameter was present in the middle and lower abdomen, and felt firm to the touch. There was no obvious tenderness, skin surface rupture or varicose vessels, and the skin temperature was normal.

Laboratory examinations

Routine laboratory test results indicated hemoglobin of 56 g/L, albumin of 30 g/L and a platelet count of 604×10^9 /L. Kidney and liver function indices were normal.

Imaging examinations

Multimodal imaging (Figure 1) revealed an elliptical mass measuring about 13.7 cm × 20 cm × 30.7 cm in the upper part of the left kidney with a distinct solid border, liquefaction in the center, and septa. Mural nodule blood flow was abundant with some spotty calcium. Computed tomography (CT) enhancement showed a solid margin with continuous uneven enhancement and high uptake of ¹⁸F-fluorodeoxyglucose (¹⁸F-FDG) (SUV_{max} - 6.1, SUV_{mean} - 4.2). Computed tomography angiography showed that the mass was fed by the left renal artery and vein, and the left renal vein was tortuously dilated.



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Figure 1 Tumor enhancement and metabolic imaging. A-C: Multiphase MR enhanced images; D-E: Positron emission tomography/computed tomography images, and F: Pathological sections of tumor (HE × 300).

The renal hilum of the left kidney was rotated due to hydronephrosis (Figure 2).

There was residual normal tissue in the lower left kidney. The pancreas, liver, stomach and spleen were displaced by compression, although no obvious ascites were observed. Magnetic resonance imaging (MRI) showed equal or high T1 signal in the liquefied center, suggesting necrosis with hemorrhage and no definite adipose composition. The left adrenal gland was indistinguishable. The mesentery around the mass was partially thickened and swollen, and retroperitoneal lymph nodes were enlarged. ^{18}F -FDG metabolism increased in both cases ($\text{SUV}_{\text{max}} - 10.5$ and $\text{SUV}_{\text{mean}} - 7$). Hematoxylin-eosin staining of the biopsied samples (10×30) showed extensive hemorrhage and necrosis involving the renal pelvis, along with lymph node metastasis (3/10). Immunohistochemical staining indicated that the mass was TFE3+, CD8/18+, CD10+, PAX-2+, CK+ and Ki-67+ (1%).

CT showed a single small nodule (Figure 3; orange arrow) in the middle lobe of the right lung and digital subtraction angiography showed obvious staining of the tumor (Figure 3; black arrow). The feeding artery of the tumor was almost completely embolized after TACE, while that of the normal renal tissue was preserved.

FINAL DIAGNOSIS

Xp11.2 translocation/TFE3 gene fusion associated renal cell carcinoma with metastasis (T3aN1M1).

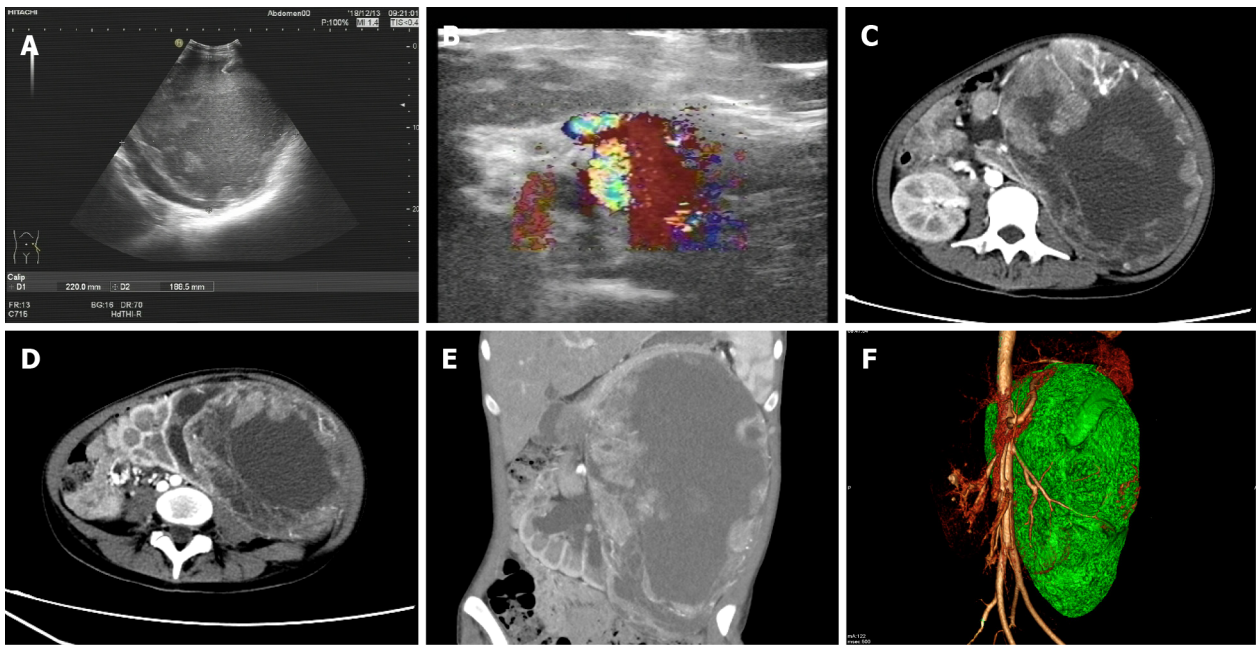
TREATMENT

The patient had a large tumor (T3aN1M1) along with distant metastases and severe anemia. In this setting, direct surgical resection can be extremely risky, and its long-term effect is unknown.

Nevertheless, the age of the patient, presence of a single metastatic focus in the right lung and the intact tumor capsule were consistent with the indication of abdominal tumor removal. Following a multidisciplinary consultation among the departments of urology, radiology, general surgery and oncology, we devised a therapeutic regimen consisting of targeted drugs, alcohol-mediated ablation and TACE, followed by surgical resection and post-surgery targeted drug therapy.

The chemotherapy regimen included oral axitinib 5 mg twice a day for 2 wk, and the treatment was repeated after 2 mo. In order to accelerate tumor shrinkage, we extracted liquid necrotic substances from the tumor and injected anhydrous alcohol for ablation. This was followed by infusion of red blood cells (RBCs), antibiotics and other symptomatic support treatment.

For TACE, 30 mg pirarubicin and 30 mg recombinant human endostatin were infused through the left renal artery trunk. The grade 2-3 branches of the tumor-feeding artery were preserved, and the remaining branches were embolized with polyvinyl alcohol foam embolic particles (PVA-100). There



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Figure 2 Tumor blood supply and vascular imaging. A and B: Ultrasonography and color Doppler flow imaging; C-E: Multiphase computed tomography enhanced images; F: Vascular and tumor volume reconstruction.



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Figure 3 Tumor metastasis and transarterial chemoembolization images. A: Metastases in the middle lobe of the right lung (orange arrow); B: DSA showed tumor vascular mass staining; C: Digital subtraction angiography showed disappearance of tumor vascular mass staining after transarterial chemoembolization (black arrow).

was 18% reduction in the tumor after TACE in conformity with the RECIST criteria.

Radical resection of left renal carcinoma, celiac lymph node dissection and intestinal adhesion lysis were performed under general anesthesia by the urological surgery team after two courses of axitinib treatment. The surgery was successful, and the intraoperative blood loss was only about 400 mL. Postoperative anti-infection, hemostasis and nutritional support were given as symptomatic treatment, along with 3U RBCs and 430 mL plasma. Oral axitinib therapy was continued after surgery.

OUTCOME AND FOLLOW-UP

Compensatory hyperplasia of the right kidney was detected 4 mo after surgery. SPECT and pelvic enhanced MRI scans revealed sacral bone metastases 14 mo after surgery, and zoledronic acid chemotherapy was initiated. Abdominal lymph node metastasis was detected 18 mo after surgery. Chemotherapy drugs included axitinib, karelizumab (Erica), and zoledronic acid (Elan). Radiotherapy

was performed with linear accelerator 15 MV X-rays, and the enlarged lymph nodes received local and conventional irradiation with a total dose of 40–60 Gy. Partial response was achieved, and the patient survived with the tumor for more than 46 mo and her overall condition is good.

DISCUSSION

Xp11.2/TFE3 RCC is more common in children and adolescents, and accounts for roughly one-third of pediatric RCC and 0.5% of adult RCC cases[7]. Our patient was 18 years old at the time of diagnosis, and thus belonged to the age group that is predisposed to RCC.

Although surgical resection is an effective first-line treatment for RCC, it is not a feasible option for advanced or large tumors. TACE is often performed to reduce the size of the tumor before surgery. Some studies have shown that TACE can inhibit intra-tumor blood flow, accelerate tumor tissue necrosis, reduce tumor volume before surgery, and reduce intra-operative blood transfusion. The combination of embolic agents with high doses of chemotherapeutic drugs can improve the clinical outcomes of systemic chemotherapy and minimize side effects[8].

The effective clinical management of tumors is incumbent on imaging, regular re-examination and timely modification of the treatment plan[9]. Ultrasound and CT should be the primary screening methods for suspected renal neoplasms. The differential diagnosis of Xp11.2/TFE3 RCC should include MRI enhancement, fat suppression sequence, diffusion sequence and MRS to enhance understanding of tumor components. In addition, preoperative CT/MR enhancement can detect lymph node metastasis, distant metastasis or vascular invasion. PET/CT and SPECT scans are recommended for postoperative follow-up; while PET/CT can supplement focus metabolism, and SPECT can detect lesions related to bone metabolism.

CONCLUSION

In summary, the sequential application of multimodal imaging can be used for the early detection of Xp11.2/TFE3 RCC, and assist in surgical planning and postoperative follow-up. TACE and ablation did not achieve the desired tumor reduction in this patient, but had a significant effect on reducing intraoperative bleeding and inhibiting tumor activity.

FOOTNOTES

Author contributions: Wang P and Jiang R designed the research study; Zhang X, Shao SH, Wu F, and Du FZ performed the research; Zhang JF and Zuo ZW collected clinical data and radiation images; Wang P analyzed the data and wrote the manuscript; all authors have read and approved the final manuscript.

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