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Case Report of Patient with IgG4-Related Disease and Renal Cell Carcinoma

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Case report

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Abstract

Cases of immunoglobulin G4-related disease (IgG4-RD) along with renal cell carcinoma are extremely rare. In this study, we report on a 61-year-old male who was diagnosed with both IgG4-RD and renal cell carcinoma. We examined the period beginning 13 years before the renal cancer diagnosis to two months after surgical removal of the tumor.

IgG4-RD is an immune-mediated disease that leads to the formation of multi-system masses. It affects almost every organ and is challenging to diagnose and cure in clinical settings [1]. In this case, we report the clinical data, surgical methods, pathology, and immunohistochemical characteristics of a patient who was diagnosed with IgG4-RD 7 years ago and diagnosed with a tumor in the left kidney by our department in August 2020.

1 Clinical Data

The patient, a 61-year-old male, was admitted to the hospital after three months of the following symptoms: cough, dyspnea, and swelling of the double mandibular lymph nodes and both eyelids. A CT scan revealed a mass in the left kidney. The patient had undergone a submandibular lymph node biopsy 13 years ago due to bilateral submandibular tumors, which indicated reactive lymph node hyperplasia. However, there was no further diagnosis and the patient was not treated. Seven years ago, the patient experienced bilateral mandibular enlargement and bilateral eyelid enlargement and was subsequently diagnosed with IgG4-related sialadenitis at Peking University Stomatological Hospital. Examining the pathology results under a microscope showed the structure of the right submandibular lymph node. Typically, normally distributed lymphatic follicles and lymphatic sinuses are observed in the lymph nodes, but in this case, the lymphoid follicles were slightly increased. There were more lymphocytes, plasma cells, and scattered infiltration observed in the salivary glands of the right submandibular gland, with interstitial fibrosis. Immunohistochemistry was partially positive for IgG and net positive for IgG4NS and CD21FDC. A kidney color Doppler ultrasound prompt showed no obvious abnormalities in either kidney. Results from a blood test showed IgG levels of 19.38 g/L. The swelling of both jaws and bilateral lacrimal glands significantly decreased after six days of intravenous methylprednisolone treatment. After discharge, the patient regularly took hormonal drugs (prednisone acetate) for three years, and irregularly took Imulan for four years. Three years ago, the patient's IgG4 was measured at 3.11 g/L. The patient stopped taking Imulan of his own accord seven months prior to his most recent hospitalization, which was due to the recurrence of double mandibular swelling, bilateral eyelid swelling, coughing, and dyspnea which re-appeared three months ago. He was admitted to the rheumatology department of The First Hospital of Jilin University. A blood test showed 12.4 g/L IgG4, and the tumor markers showed no obvious abnormalities. Upon admission to the hospital, the patient was administered intravenous methylprednisolone for four days, significantly improving his symptoms. The patient was later transferred to the Department of Urology after a CT scan showed a tumor in his left kidney. We re-checked his IgG4 levels, which were 10.1 g/L, and administered 30 mg oral prednisone acetate each day.

Ultrasound examination of the kidney: A mixed mass of 2.0×1.8cm in the upper parenchyma of the left kidney was observed, with unclear boundaries. No obvious blood echo was observed inside or around the mass. The results of a kidney CT plain scan and three-phase enhancement detection showed a nodular, slightly low-density shadow on the posterior part of the upper pole of the left kidney (Figure 1.A), about 2.2×2.9cm in size, and an unevenly enhanced cortical phase (Figure 1.B). We observed reduced degrees of enhancement in both the medullary phase (Figure 1.C) and the secretory phase (Figure 1.D).

PET-CT results showed a convex nodule with a size of 1.6×2.1cm behind the upper pole of the left kidney (Figure 1.E), with a maximum SUV value of 1.5. This indicates that the nodule in the upper pole of the left kidney shows mild FDG uptake, meaning kidney cancer was not excluded.

Preoperative diagnosis: left kidney tumor.

The patient underwent retroperitoneal laparoscopic partial resection of the left nephron with the preserved nephron. Pathological results suggested clear cell renal cell carcinoma in the left kidney (grade 3 according to the WHO/ISUP nuclear grade standards, 2016 edition).

The tumor volume was 2.5×1.8×1.8cm. Vessels and nerves had no clear cancer infiltration. No cancer was observed on the margin of the surgically removed kidney tissue. A small amount of lymphocyte infiltration was observed in the renal parenchyma around the tumor. According to the 2017 AJCC, the patient's tumor stage was T1a.

Immunohistochemical results showed that IgG4 protein/Ig protein>40% in the plasma cell. Mum-1 (+) histopathology showed that the tumor was a classic clear cell renal cell carcinoma and that the tumor cells had clear cytoplasm surrounded by a fine fiber vascular network (Figure 2.A). A focal lymphocyte aggregation area was observed outside the tumor capsule, which is composed of lymphocytes and plasma cells (Figure 2.B). Mum-1 immunohistochemical staining showed more plasma cells were scattered in the lymphocyte aggregation area (brown and nuclear positive, indicating plasma cells) (Figure 2.C). IgG4 immunohistochemical staining and lymphocyte aggregation areas are scattered in IgG4-positive cells (brown, cytoplasmic positive cells indicate IgG4 secreting plasma cells), while the ratio of IgG4 in IgG cells in the comparison section exceeded 40% (Figure 2.D).

The post-operative patient recovered without complications and was subsequently discharged. On the first day after the operation, the patient was given intravenous methylprednisolone for three days instead of oral prednisone acetate. At this point, the swelling of the patient’s jaws and eyelids was significantly relieved, and the symptoms of cough and dyspnea significantly subsided. Following the switch to oral prednisone acetate, the patient’s IgG4 was 5.92 g/L when rechecked four days after surgery. Methylprednisolone was subsequently changed to prednisone acetate. Following his discharge from the hospital, the patient was instructed to visit the rheumatology department for further treatment. The patient returned to our hospital two months after the operation, and we found that he recovered without postoperative complications.

2. Discussion

Patients with IgG4-RD and renal cell carcinoma are very rare. IgG4-RD are fibroinflammatory diseases of unknown etiology[2]. Histopathology of this disease consists of dense lymphoplasmic infiltration, a large number of IgG4-positive plasma cells, and typical fibrosis[3]. It can affect all organs of the body, enlarging organs, or appear as nodular/proliferative lesions[2]. Clinical symptoms are primarily observed as a mass effect[4], responding positively to glucocorticoid therapy[5]. IgG4-RD has special clinical, serological, and pathological characteristics, including the formation of tumor-like lesions involving organs (which usually form, but not always)[6]. It is unclear whether the occurrence of renal cell carcinoma is related to IgG4-RD in this patient. Kenji Hirano conducted a study on this relationship[7], including 113 IgG4-RD patients who were not diagnosed with malignant tumors at the onset of IgG4-RD. These patients were assessed for an average of 73 months and the incidence of their tumors was compared with the expected incidence in the general population for their age and sex, based on vital statistics. The study demonstrated that IgG4-RD is unrelated to increased incidences of malignant tumors. Motohisa Yamamoto conducted another study[8], with 106 cases of IgG4-RD patients. These patients were observed at the initial diagnosis of IgG4-RD or during subsequent checkups at an average follow-up period of 3.1 years. The National Cancer Registry was used to monitor the incidence of cancer data to assess the standardized incidence of IgG4-RD malignant tumors. The study showed that the incidence of malignant tumors in IgG4-RD patients is significantly higher than in the general population. However, the malignant tumors observed in patients with IgG4-related diseases are different from, and have no characteristics related to the development of, cancer[9]. Published studies are increasingly finding that the relationship between IgG4-RD and malignant tumors is complex[10]. In the case recounted here, the patient had an IgG4-related disease first. When the disease was discovered, the kidney color Doppler ultrasound examination did not identify any tumors, indicating that the kidney cancer was a new disease developed in recent years. However, we cannot be certain that no certain relationship with IgG4-related diseases exists. While it is unclear whether this relationship is related to long-term hormone use or whether the disease itself causes cancer, the cancer risk in such patients should be closely monitored. However, there are currently fewer clinical cases and additional study is needed to confirm this relationship.

3. Conclusion

IgG4-RD diseases are often associated with tumor-like lesions, which are typically benign. A clear diagnosis and timely treatment can improve patient prognosis. As such, doctors should consider malignant tumors as possible complications when diagnosing IgG4-RD patients.

Declarations

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Contributions

Z.H.Lcontributed to the manuscript writing and date collection. W.G.W.and M.S.J.contributed to analysis of data, Z.Y.Z.were involved in manuscript editing.W.G.W.contributed to the critical revision. All authors read and approved the final manuscript.

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Ethics declarations

Ethics approval and consent to participate

This study was approved by the ethics committee of The First Hospital of Jilin University. Written informed consent was obtained from this patient.

Consent for publication

Written informed consent was obtained from this patient enrolled in the investigation. The study protocol conformed to the ethical guidelines of the 1975 Declaration of Helsinki and the guidelines of the regional ethical committees of The First Hospital of Jilin University.

Competing interests

No other conflict of interests.

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Figures

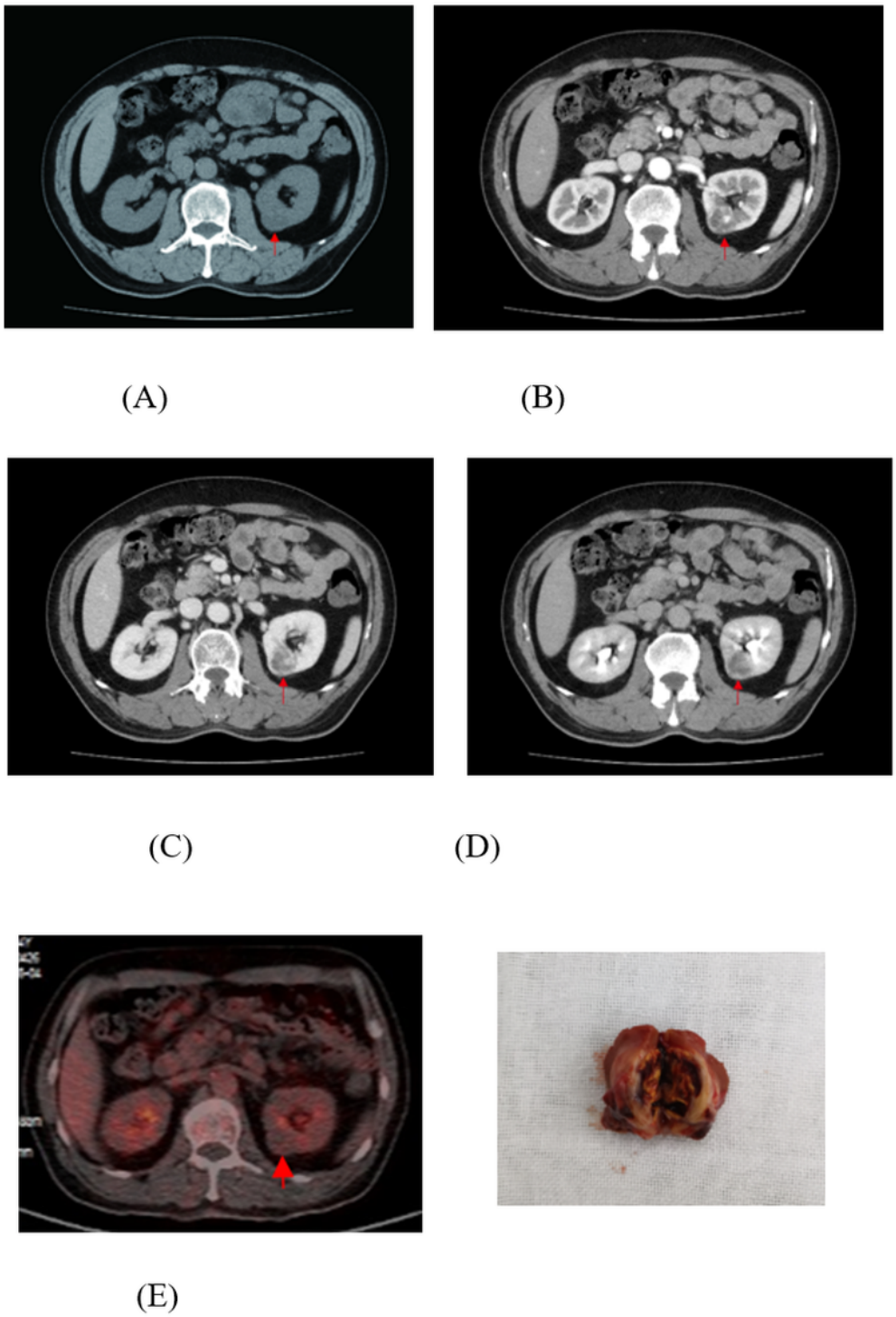

Figure 1

CT image: CT image: (A) computed tomography (CT) plain scan; (B) cortical phase; (C) medullary phase; (D) secretory phase; (E) PET-CT Physical tumor specimen

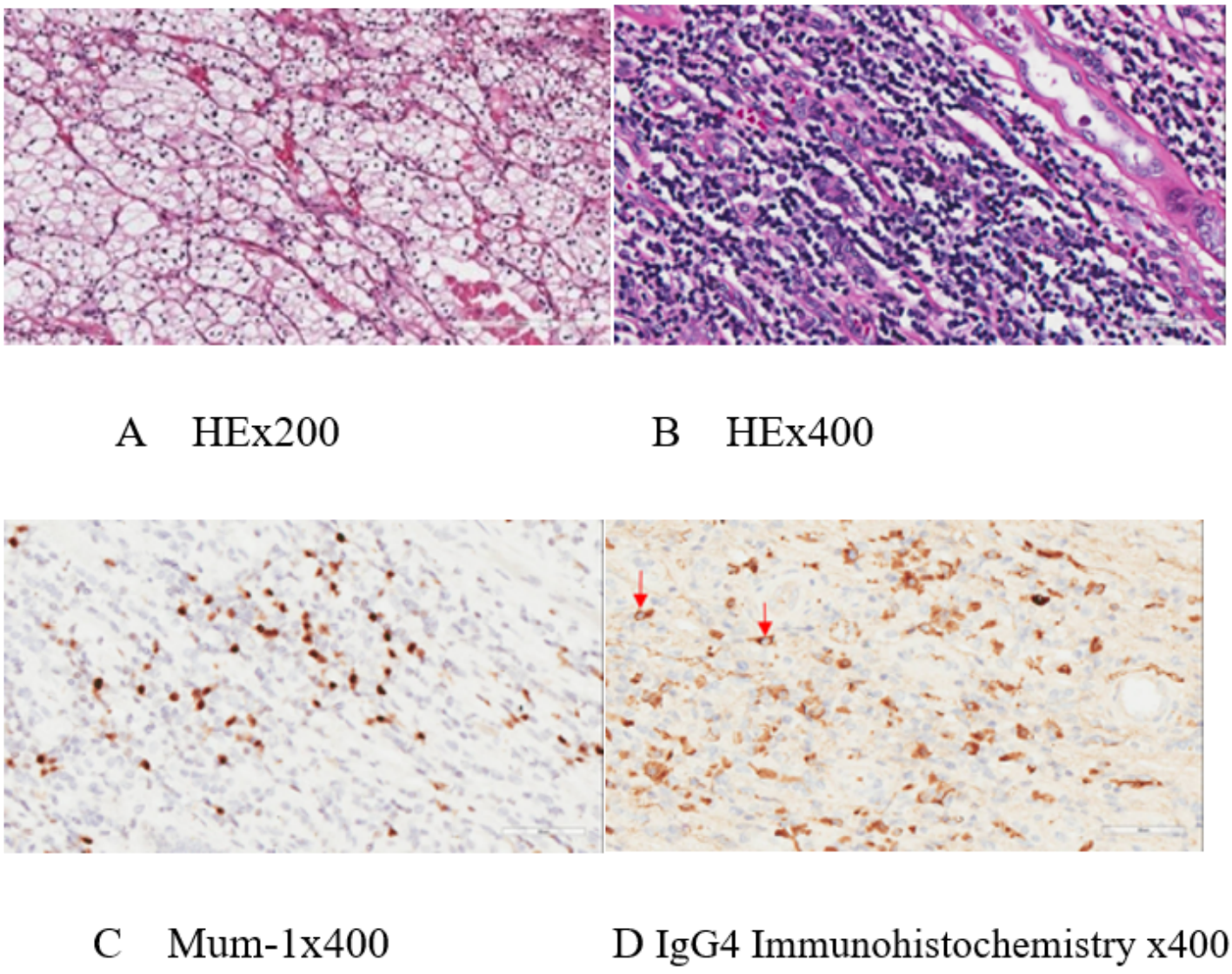

Figure 2

Histopathological examination: Histopathological examination: (A) hematoxylin-eosin staining (H□E 200x); (B)hematoxylin-eosin staining (H□E 400x); (C)Mum-1 Immunohistochemistry 400x; (D) IgG4 Immunohistochemistry 400x