acta medica

Case 7: Immunoglobulin G4-Related Disease (IgG4-RD)

Professor Ayten Yazici, MD
ORCID: 0000-0003-2167-4509

62 years old male patient,

Complaints: Abdominal pain, weakness, fatigue, anorexia, chills (fever?), weight loss

The patient, who had no previous complaints, started to complain of abdominal pain, weakness, fatigue and anorexia in May 2019. He did not fully describe fever, but he stated that he had chills attacks. Among the examinations that performed by the doctors he visited during this period, in the abdominal computed tomography (CT), a 39mm fusiform aneurysm was detected from the renal artery level to the iliac bifurcatio without dissection, and was not advised other than follow-up. Upon the continuation of his complaints, the patient who lost 22 weight in the last 4 months and whose acute phases were found to be high in controls was admitted to the nephrology service with pre-diagnoses of mesenteric ischemia and malignancy in September 2019. There was no feature except for lumbar hernia surgery (7 years ago) in his medical and family history, and here was no other characteristics except a smoking history of 45 packs/year. In the physical examination, blood pressure and all system examinations were found to be normal.

In patient's laboratory, all parameters and protein electrophoresis were normal except c reactive protein (CRP: 20,2 mg/L), erythrocyte sedimentation rate (ESR: 59 mm/h) and creatinine (1,31 mg/dl). In addition, the autoantibodies (ANA, ENA, ANCA, anti-PR3, anti-MPO), viral and tumor markers were examined and found to be negative. It was observed that there was no significant pathology in upper gastrointestinal system endoscopy and colonoscopy that performed in other center.

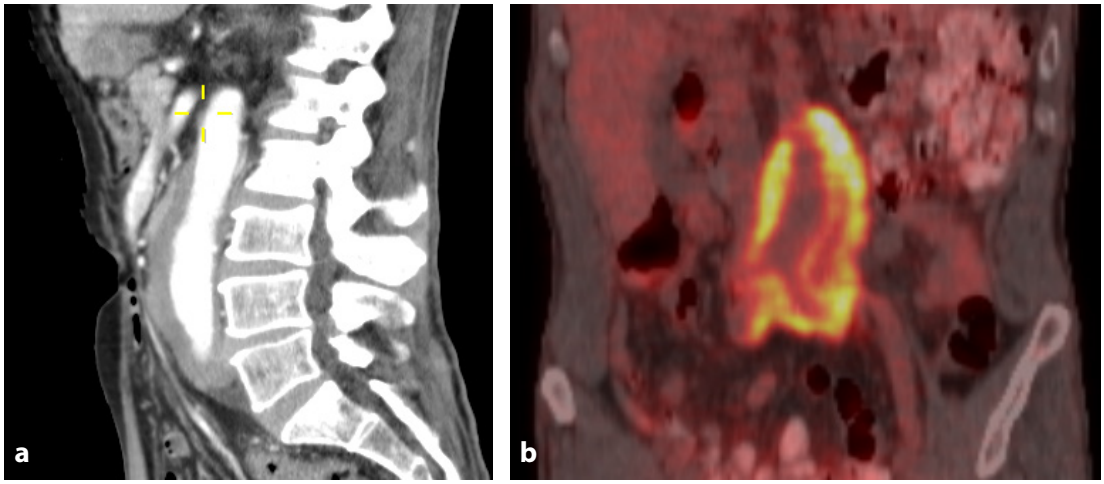

Figure 1: a) Abdominal CT-CT angiography: in the paraaortic area a soft tissue density of 2cm in the thickest part, starting from the inferior of the renal artery level to the bilateral common iliac artery, compatible with retroperitoneal fibrosis b) and c) PET BT: surrounding the aorta, a soft tissue mass showing increased metabolism in malign character (SUV max 9.7)

University of Kocaeli, School of Medicine, Department of Internal Medicine, Division of Rheumatology, Kocaeli

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No pathology was found in the thorax CT requested with a pre-diagnosis of malignancy, except for emphysematous-bronchitis changes and a few peripherally located micronodules. On Abdominal CT-CT angiography, in the paraaortic area a soft tissue density of 2cm in the thickest part, starting from the inferior of the renal artery level to the bilateral common iliac artery, compatible with retroperitoneal fibrosis and hepatomegaly (17 cm) revealed. In addition, grade 2 hydronephrosis on the left kidney due to compression of the left ureter, and multiple lymphadenopathies of approximately 1 cm in the paraaortic and aortacaval areas were detected (**Figure 1a and Figure 2a**).

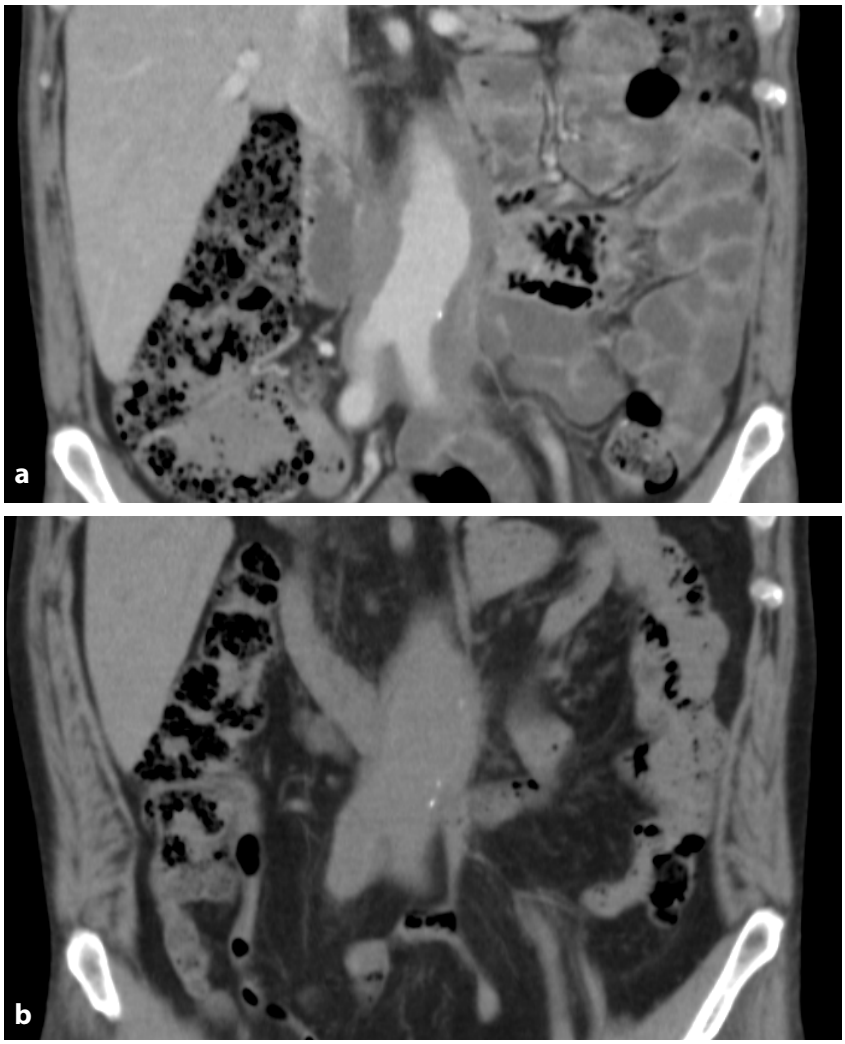
With these results, consultation was requested from both urology and rheumatology departments. While urology decided to insert pigtails due to hydronephrosis, rheumatologically IgG4 level, positron emission (PET) tomography and biopsy of the lesion were requested. IgG4 levels was 3,233g/L (0,064-0,347), and in the PET CT, a soft tissue mass showing increased metabolism in malign character (SUV max 9.7) extending from the renal level to the middle part of both common iliac arteries, surrounding the aorta was observed **(Figure 1b and 1c).** It was reported that the CT-guided biopsy of the lesion did not represent the lesion, the material was small and there were aggregates consisting of mature lymphocytes.

At this stage, please make the patient's IgG4-Related Disease Response Index Scoring and state the total activity score with the number of damaged organs.

Results of IgG4-Related Disease Response Index Score

Before Treatment	**Activity**			**Damage**	
Organ/site	Organ/Site Score (0-3)	Symptomatic (Yes/No)	Emergency (Yes/No)	Yes/No	Symptomatic (Yes/No)
Lymph Nods (Site- abdominal)	2	No	No	No	No
Retroperitoneal Fibrosis	2	Yes	Yes	Yes	Yes
Constitutional symptoms that cannot be attributed to any organ involvement (weight loss, fever, fatigue due to active IgG4 related disease)	2	Yes	No	No	No
Total activity score Organ/Site (x2 if it is urgent) 8	Total urgent organ : 1 Total symptomatic (active) organ : 2 Total number of urgent organ : 1 Total symptomatic (damaged) organ : 1 Physician global disease activity score : 70/100				

Continuation of the case: 48 mg methylprednisolone was started in the patient who was diagnosed with IgG4-related disease with these results, and pigtail was inserted by the urology. After 4 days from the procedure, the patient had a fever up to 38.4°C, and his CRP increased to 149.9 mg/L. There was seen +2 nitrite and +3 leukocytes in his urine, and ESBL (+) E coli was grown in the urine and blood cultures. Meropenem 1gr 3x1 was started parenterally, and treatment was continued with only corticosteroids and antibiotics between October 2019 and January 2020 due to recurrent urinary tract infections. In January 2020 CRP, ESR and platelet value were detected 54.6mg /L, 86 mm/h and 450000/mm3, respectively, and 7.5mg oral methotrexate was added to the patient's treatment when cultures were clean (creatinine: 0.93 mg/dl, GFR: 73,5 ml/dk). The steroid was tapered gradually, but the methotrexate dose of the patient whose creatinine values varied between 0.9-1.4mg/L could not be increased. Under this treatment, the patient's acute phases regressed (CRP: 4,8mg/L, ESR: 24mm/h), but renal functions were deteriorated (creatinine: 1,7 mg/L, GFR: 44,5 ml/dk) in the 6th month of the treatment and in the left kidney parenchyma echoes, grade 1-2 an increase in favor of parenchymal disease was detected in renal ultrasonography. Upon this, methotrexate was discontinued and azathioprine 100mg was started. In September 2020, the control abdominal CT performed, and reduction in the mass (12 mm), grade 3 on the right and grade 2 hydronephrosis on the left **(Figure 2b)**. The pigtail was removed in October 2020.



Şekil 2: Abdominal CT a) Before treatment (September 2019): a soft tissue density of 2cm in the thickest part, b) After treatment (September 2020): reduction in the mass (12 mm)

In the last visit (November 2020), the patient had no complaints, and it was observed that the acute phases were normal (CRP: 2.46 mg /L, ESR: 12 mm/hour). The creatine value of the patient was 1.5 mg /dl and the treatment continued with azathioprine 100 mg and methylprednisolone 4mg.

For after treatment stage, please make the patient's IgG4-Related Disease Response Index Scoring and state the total activity score with the number of damaged organs.

Results of IgG4-Related Disease Response Index Score after treatment

After Treatment		**Activity**		**Damage**	
Organ/Site	Organ/Site Score (0-3)	Symptomatic (Yes/No)	Urgent (Yes/No)	Yes/No	Symptomatic (Yes/No)
Retroperitoneal Fibrosis	1	No	No	Yes	No
Total activity score Organ/Site (x2 if it is urgent) 1		Total urgent organ : 0 Total symptomatic (active) organ : 0 Total number of urgent organ : 1 Total symptomatic (damaged) organ : Physician global disease activity score : 10/100			