An urgent abdominal CT scan with contrast revealed patchy hypodense areas in the right kidney consistent with renal infarction (fig. 1). The patient was admitted to the nephrology department, where anticoagulation with low molecular weight heparin at therapeutic doses was started. Subsequent measurements of vitamin B12, folate, antinuclear and antiphospholipid antibodies, tumor markers, and lipid metabolism were all normal. Diagnosis of mutation in the FII 20210 gene (heterozygous) and the MTHFR gene (homozygous) was confirmed, with homocysteine levels in the upper normal range. The thrombophilia study was otherwise normal. A 99m-Tc-DTPA perfusion study showed a triangular uptake defect in the upper pole of the right kidney consistent with renal infarction. A 99-Tc-DMSA renal scan confirmed diagnosis.

Patient had a favorable course, with disappearance of pain and gradual decrease in LDH. Heparin was replaced by acenocoumarol for an indefinite time, and folic acid was added due to the finding of homocysteine levels in the upper normal range.

Rapid diagnosis of renal infarction is critical if thrombolysis or surgery is to be attempted to preserve kidney function. There are several helpful tests for diagnosis, and the choice depends on test availability. CT with a contrast agent provides a fast, accurate diagnosis. Isotope flow imaging with DTPA-Tc$^{99m}$ shows an absent or decreased perfusion in the affected kidney. Doppler ultrasound has a limited value, and renal arteriography is the definitive diagnostic procedure.

Mutation in the FII 20210 gene is associated to a 30% increase in baseline prothrombin levels that predisposes to thrombotic events. Hyperhomocysteinemia may be congenital or acquired. Acquired forms are secondary to folate or vitamin B12 or B6 deficiency. Congenital forms are due to mutations in the cystathionine-b-synthetase gene or the MTHFR gene, more common, and which is associated to hyperhomocysteinemia particularly in homozygotes with folate deficiency. Hyperhomocysteinemia predisposes to thrombotic events by endothelial activation, muscle cell proliferation, and changes in NO production or sterol metabolism in endothelium.[3]

Absence of hyperhomocysteinemia in this patient with MTHFR mutation was possibly due to the fact that he was never detected vitamin B12 or B6 or folate deficiency.

Thrombophilia should be searched in patients with recurrent venous thrombotic events. However, such search does not appear to be indicated in patients with isolated arterial thrombosis, especially if they have risk factors for arterial disease.

The risk of venous thrombosis in patients with FII 20210 or MTHFR mutation is low. Its role in arterial thrombosis is unclear, with a slight risk of AMI or stroke occurrence. An increased risk exists in patients aged < 55 years and female patients, with a more significant effect if concomitant coagulation disorders and associated cardiovascular risk factors exist.[4]

As to therapeutic management, prophylaxis should be started in asymptomatic patients or patients with thrombosis associated to risk situations, and indefinite anticoagulation should be given to patients with two or more spontaneous thromboses, life-threatening thrombosis, or thrombosis linked to more than one genetic abnormality.

In our case, the patient was <55 years, and had FII 20210 and MTHFR mutations and cardiovascular risk factors (HBP, former smoker, drinker). Management would have required the previous start of indefinite anticoagulation that would have prevented the occurrence of a third thrombotic event.[5]

The interest of the reported case lies in the occurrence of renal infarction in a patient with mutation in the FII 20210 and MTHFR genes, a previously unreported clinical condition.


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## Carcinoid tumor and hypernephroma coexisting in a patient with chronic renal failure

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**To the editor:** Contraindicating the start of chronic dialysis in a patient with an advanced malignant tumor[1] may be very difficult if the patient is in a good general condition and symptom-free. An example of a situation where this may occur are patients with carcinoid tumors, an uncommon condition with a high survival rate despite its high metastatic capacity that grows slowly and has an indolent course in many cases.[2,3]

The case of a 72-year-old male patient in whom evidence of chronic renal failure for an unknown cause was detected in May 2006 during a work-up study for isomorphic macrohematuria episodes is reported. A cystoscopy and several urine cytologies showed no malignancy. The patient started hemodialysis two months later due to uremic clinical signs. An urological MRI performed a little later showed right pyelocalycial ecta-

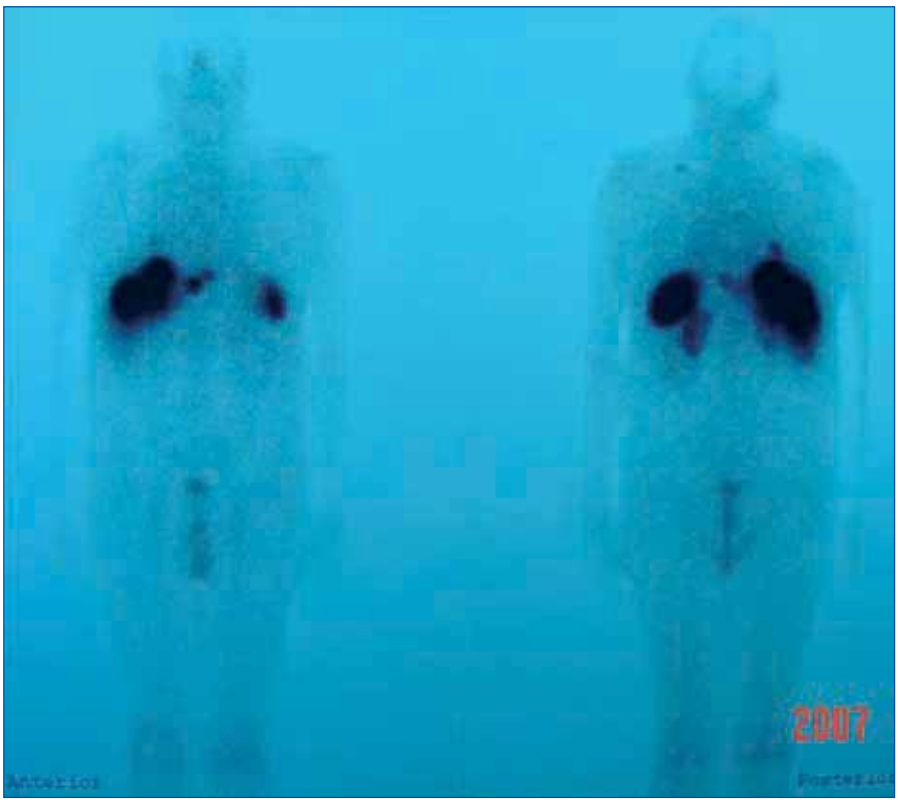


**Figura 1.**

sis with a pelvic filling defect approximately 2.5 cm in diameter suggesting a urinary tract tumor, as well as multiple hepatic lesions. FNA of the liver showed carcinoma consistent with metastasis from a neuroendocrine tumor. An oncological octreotide scan, performed in August 2006, revealed scintigraphic uptake suggesting lesions with a high density of somatostatin receptors in the liver. The presence of foci with a high uptake in the thoracic study suggested the diagnostic possibility that the primary tumor was of pulmonary or bronchial origin (fig. 1), but a subsequently performed CT scan of the chest and abdomen showed no obvious lesions in mediastinum or lungs. However, the patient was still asymptomatic, with a good general condition and tolerating well hemodialysis sessions. The only remarkable findings were resistance to erythropoietin and a consequent trend to anemia. Under the control of the oncology department, patient was treated with intramuscular somatostatin analogs, but never had a carcinoid syndrome (episodes of flushing, dyspnea, diarrhea, or right valve disease). Because of occasional recurrence of hematuria with discomfort in the right lumbar area and based on the suspicion of a non-endocrine tumor because of the absence of scintigraphic uptake in the octreotide scan, a control urological MRI was performed half a year later. MRI showed persistent hepatic lesions mainly in the right lobe, and an infiltrative lesion in the right pyeloureteral junction causing significant dilation of the collecting system. There was an additional mass that lobulated the cortical contour of the same kidney, appeared to communicate with the renal pelvis lesion, and had a greater axis of 4.2 cm. Based on these findings, the case was re-evaluated by the oncology and urology departments, and a right nephrectomy was performed. The postoperative course was very torpid. Transfusion of several red cell packs and debridement of an intraabdominal abscess were performed, despite which the patient died a few days later. A renal pathological study revealed a grade 3-4 renal cell carcinoma with wide necrotic areas and a predominance of eosinophilic cells. Lymph nodes isolated from renal fat and hilum had no neoplastic infiltration.

Carcinoid tumors are neoplasms originating from cells of the neuroendocrine system. Two thirds of these tumors are located in the gastrointestinal tract (41.8% in the small bowel, 27.4% in rectum, and 8.7% in stomach).[3] Pulmonary and bronchial carcinoid tumors have also occurred. Typical tumors have well differentiated cells and usually involve the hilum, but less common, atypical tumors also occur in more peripheral locations and in older patients.[2] Tumors may secrete hormones, causing the classical carcinoid syndrome, but there are also non-secreting tumors. Severity depends on tumor size and the extent of metastases, particularly if they occur in the liver. In addition to conventional imaging tests, scintigraphy is essential to study the extent of this neoplasm.[3]

It is known that carcinoid tumors are sometimes associated to other tumors. Approximately 15% of carcinoid tumors arising in the small bowel are associated to non-carcinoid neoplasms, most of them adenocarcinomas of the gastrointestinal tract.[4]

It is noteworthy how, in the case reported, the study of a symptom such as hematuria led us to diagnose a very advanced chronic renal impairment, a carcinoid tumor, and finally, a hypernephroma. It should also be noted that a metastatizing tumor, a carcinoid tumor in our case, may follow an indolent course. The patient was in a good general condition, and his death was eventually caused by other reason. The need for a scintigraphic test such as an oncological octreotide scan is stressed, as the absence of uptake showed us that the renal tumor was not a carcinoid. Moreover, primary renal carcinoid tumor is extremely infrequent.[5]

We think that coexistence of a carcinoid tumor and hypernephroma is casual, because only another case in which a carcinoid tumor in the cecal appendix and a renal cell carcinoma coexisted in the same patient was found in the literature.[6]

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# IgA nephropathy and lupus anticoagulant: an incidental association?

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**To the editor:** IgA nephropathy is the most common chronic primary glomerulonephritis, leading to progressive renal failure in at least one third of patients.[1] No association of this disease with the lupus anticoagulant (LA) has been found in the literature. The occurrence of IgA nephropathy in two sisters, one of whom had LA, is reported.

## CASE 1

A 26-year-old female patient with a history of acne and recurrent urinary tract infection. She was studied for gross hematuria after upper respiratory tract infections. Physical examination was normal. Laboratory test results included: creatinine 1.4 mg/dL, hematocrit 25%, prothrombin activity 87%, APTT 44.7 seconds , fibrinogen 434 mg/dL. Immunological test results included: IgG 1260 mg/dL (N: 751-1560), IgA 667 mg/dL (N:82-453), IgM 190 mg/dL (N: 46-304), C3 88 mg/dl (N: 79-152), C4 27.8 mg/dl (N: 16-38), negative ANA. Urine sediment showed 6-10 RBCs/field. Proteinuria in a 24-hour sample was 3 g/day. A renal pathology study confirmed the existence of IgA nephropathy. As the patient had a prolonged cephalin time, a hypercoagulability study was performed, showing a positive result for IgM anticardiolipin antibodies, 50.7 MPL/mL (N < 11).

## CASE 2

A 29-year-old female patient with personal and clinical history similar to her sister (case 1). Physical examination was normal. Results of laboratory blood tests included: Creatinine 1 mg/dL. Normal complete blood count. Coagulation: Prothrombin activity 84%, APTT 39.5 sec. Negative LA and anticardiolipin antibodies. Immunological tests showed the following values: IgG 1470 mg/dL, IgA 388 mg/dL, IgM 417 mg/dL, C3 100 mg/dL, C4 28.6 mg/dL. ASLO, ANA, and anti-DNA antibodies were negative. Urine sediment showed more than 40 RBCs/field. No protein was found in a 24-hour urine sample. Renal biopsy confirmed the existence of nephropathy with IgA mesangial deposits.

## DISCUSSION

IgA nephropathy is characterized by IgA mesangial deposits associated to a proliferative mesangial glomerulonephritis. Its pathogenesis is not fully known, but there is increasing evidence of the formation of immune complexes containing IgA that would be deposited in mesangium and would induce glomerular damage.[2]

The primary antiphospholipid syndrome (PAPS) is characterized by recurrent thrombosis, multiorgan damage, and abortion, as well as the presence of LA and/or anticardiolipin antibodies.

LAs are antibodies directed against plasma proteins such as b2-glycoprotein I, prothrombin, or annexin V.[3,4] In case 1, a basic coagulation study detected a prolonged cephalin time, and a subsequent hypercoagulability study was positive for LA anticardiolipin antibodies, but there were no associated clinical signs consistent with PAPS.

Association of LA and anticardiolipin antibodies with various autoimmune and rheumatic diseases (SLE, scleroderma, psoriatic arthritis…) has been reported in the literature,[5] but there are no reports of an association with IgA nephropathy, except in cases having, in addition to LA, the clinical signs of PAPS.[6] It is also possible that this patient initially had or may have subsequently developed a Schönlein-Henoch glomerulonephritis or a lupus nephropathy. These are both conditions with mesangial IgA deposits that pathologists are sometimes unable to differentiate from pure mesangial glomerulonephritis.

In the reported cases, the finding of LA alone, without other signs of PAPS, in only one of the sisters (with the same nephropathy and the same clinical sign of hematuria following upper respiratory tract infections) raises the question whether this association was incidental or its occurrence was related to a common immune pathogenetic mechanism.

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