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Mixed Cryoglobulinaemia in a Patient after Kidney Transplant

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Dear Editor,

Hepatitis C virus infection (HCV) is associated with cryoglobulinaemia[1], mainly mixed type II, associated or not with membrane-proliferative glomerulonephritis. The prevalence of cases with clinical symptoms is 1:1,000,000, but 40-60% of the patients with HCV have elevated cryoglobulins. In transplant patients, who were previously HCV positive,[2-4] this is an important cause of *de novo* glomerulonephritis. In these patients the prevalence of cryoglobulinaemia after transplant is 2.7-45%.

We present a case of a 63 year old patient with renal failure due to postpartum cortical necrosis, on haemodialysis since 1980. She was HCV positive. In a liver biopsy performed in 1986 slight chronic portal and lobular inflammation without any signs of activity were seen, since then there has been ALT elevation 2-3fold.

The patient underwent her first transplant in 1992, and lost graft function due to glomerulopathy of the transplant in 1996. The second transplant was performed in 2001. The patient received immunosuppression with mofetil mycophenolate, tacrolimus and steroids. The patient had a maximum panel reactive antibody (PRA) prior to transplant of 52%, which decreased to 0% during the months prior to transplant surgery. Plasma creatinine was stable (1.5-1.7 mg/dl), proteinuria positive and less than 500 mg/24 hours. In January 2007 prednisone was discontinued, with a subsequent increase of proteinuria that reached nephrotic proportions in January 2009. The HCV viral load was persistently positive.

The patient is admitted in February 2009 to Pneumology due to non-condensing respiratory infection and stable renal function. Clinical symptoms improve on antibiotic therapy. One week later the patient presents arthromyalgia, fever, oedemas and petechial lesions in lower limbs (Figure 1). The patient presents progressive deterioration with dyspnoea, leukocytosis, anaemia and creatinine rise (4 mg/dl), requiring therefore haemodialysis due to oligoanuria.

We ruled out haemolytic-uremic syndrome (peripheral blood smear with no schistocytes, normal platelet count, and absence of severe hypertension). ANCA and anti-GBM were negative, ruling out these causes of secondary rapidly progressive renal failure. The patient was positive to plasma cryoglobulins (30%), complements (C4 <2; C3 111) and rheumatoid factor (positive; 408 U/l). The HCV viral load was 31,263,906 copies/ml, genotype 1. Renal biopsy showed changes compatible with cryoglobulinaemic membrane-proliferative glomerulonephritis, glomeruli with a proliferative membrane pattern, cell proliferation and hyaline thrombi. With a diagnosis of membrane proliferative glomerulonephritis associated with HCV, treatment with plasmapheresis was begun, causing reversion of skin and lung lesions, but the patient remained dialysis-dependent. Given the advanced renal failure, treatment with pegylated interferon and ribavarin was begun, and haemoglobin was closely monitored. Four months later the viral load was undetectable.

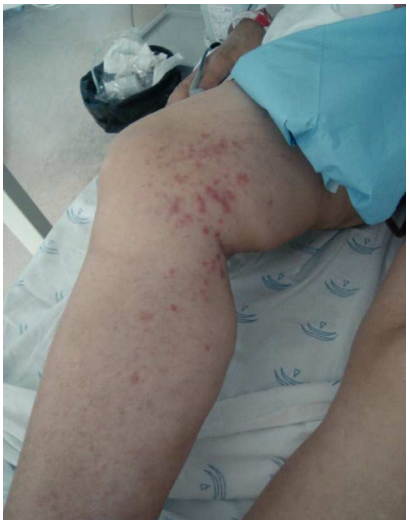

Figure 1. Vasculitis Skin lesions

HCV treatment was chosen, with pegylated interferon and ribavarin,[1,3,5] but in patients with renal failure, creatinine clearance must be monitored. According to the levels of creatinine clearance, ribavarin and/or pegylated interferon may not be advisable or it may be necessary to monitor haemoglobin levels. In cases in which this occurs plasmapheresis may be used or drugs such as rituximab[3] used for (renal, neurological or skin) exacerbations. Once overcome, antiviral drugs will be administered. Furthermore, pegylated interferon is contraindicated in patients that have undergone transplant,[5] but in our case the patient had already returned to dialysis.

In our patient we blamed the persistent proteinuria on possible chronic changes, although it may have been related to cryoglobulinaemia. We would like to highlight the importance of keeping this possibility in mind, since this condition is quite frequent with a subclinical presentation and can lead to kidney transplant failure.[2]

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Hyponatraemia, Hypopotassaemia and Pre-renal Acute Renal Failure as a Presentation of Cystic Fibrosis

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Dear Editor,

Cystic fibrosis is a hereditary disease with a recessive autosomic pattern. It is characterised by ecrine and exocrine gland abnormal function that causes chronic lung conditions, abnormally concentrated sweat and pancreatic failure. The usual symptoms are seen in infancy and are respiratory, such as cough and recurrent respiratory and digestive complications such as meconium ileus.[1] A reduced percentage of cases reaches adulthood without being diagnosed due to partial mutations.[2] It is rarely associated with volume decrease and metabolic alkalosis and it is seen during the summer season due to lack of fluid loss replenishment.

We present the case of an adult man who entered the nephrology department with a diagnosis of volume decrease, alkalosis, hypopotassaemia and acute renal failure.

Case report

The case is a 29 year old man who had been referred 6 years before to nephrology outpatient services by the emergency room because he was suffering from intense diaphoresis, muscular weakness and arthralgia. In the emergency room the following laboratory values had been found: Na 128, K 2.8, urea 71 and glucose 139.

Among his personal medical history were multiple fractures due to a traffic accident, appendectomy and frequent respiratory infections. On physical examination he presented a blood pressure of 110/74 mmHg, a heart rate of 100 bpm and skin and mucose membrane dehydration. Nothing else of note was seen in the course of the physical examination. The most relevant values seen in the laboratory were: (emergency room analysis) Hb 17.8, Na 128, K 2.9, urea 71, pH 7.56, HCO_3 25, PCO_2 28.9, base excess 3.30; (consultation analysis: 2 days later, when the emergency room had already rehydrated the patient) Hb 13.6, VSG 6, Cr 0.87, lipase 1,287, osmolarity in serum 2.94, Ca 8.87, phosphatase 2.6, pH 7.35, PCO_2 57, HCO_3 31.2, Na(O) 18 mEq/24 h, Cl (O) 8 mEq/24 h, proteinuria 0.21 g/24 hours. The condition was interpreted as heat stroke.

The following year, coinciding with the summer season, the patient once more had intense diaphoresis, renal failure, hypopotassaemia and hyponatraemia that were resolved with hydration. The patient was advised to ingest fluids and electrolytes during the summer.

The following year the patient suffered from the same condition and in view of the history of profuse sweating as a consequence of the hydroelectrolyte disorder, a sweat test was requested and they found positive the following: chlorine (sweat) 83 (normal 28). A genetic test for cystic fibrosis using the INNO-LIPA CFTR 12 and CTFR 17 technique was normal.

The next year the patient had a recurrence of the same clinical condition, and suspecting cystic fibrosis, a spermogram was performed and showed complete azoospermia. On abdominal CT a pancreas with thickened body and head was seen. There were no other findings. The genetic study using the OLA-PCR technique was repeated and the results were normal, although CFTR (IVS8) 5T polymorphism was found. Since further abnormalities were suspected the molecular study of the CFTR gene was continued. For this reason, a genetic-molecular study was requested and the following genotype obtained: 1811+1,6kba>G/A1006E, 5T,V562I. The patient was sent to the cystic fibrosis unit.

Discussion

The relation between salty skin and early death has been known for a long time, cystic fibrosis was described in 1930 and was called cystic fibrosis of the pancreas because this organ was the most affected, even though later it was known that the condition affected all exocrine glands.[3] The disease is due to the mutation of the cystic fibrosis gene that codes for a membrane protein that can be a ion canal, this causes an alteration of chloride secretion and modifies all exocrine secretions.

The case is a young patient who comes to consultation due to dehydration in summer. Once the patient recovered, no further studies were performed, but when the patient had a recurrence of symptoms during the same time of year further attention was given to the sweating as it was considered related to the reason for the condition. The sweat test is the most important diagnostic method for the detection of cystic fibrosis.[4] And in this case it was positive. Subsequently a genetic test was requested, this was negative and once the patient recovered, there was no further insistence on