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CARTAS

Alpha-interferon renal toxicity

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In 1982, the demonstrations of growth inhibiting properties led to the first clinical trials with IFN-α, as a biological agent used in cancer treatment. Since then, it have been applied in the treatment of several malignancies and several adverse effects were reported[1].

CASE

A 39 years old caucasian female, on the 9th january 2001, was observed for obnubilation. She had high blood pressure, anaemia, thrombocytopenia, moderate renal failure and an increase of serum LDH levels. She suffered from chronic myeloid leukaemia (CML) treated with IFN-α, hydroxyurea and cytarabine, during 48 months, with haematological response. She had no other relevant antecedents and did not take other drugs. The patient was admitted to complementary study, cancer treatment was discontinued and anti-hypertensive treatment was started.

During the first inpatient week she complained of orthopnoea, oedema and oliguria. Analysis revealed a non-immune haemolytic anaemia (Hg-7,9 g/dl, haptoglobin < 0,058 g/l, negative Combs tests, peripheral blood film showed schistocytes and spherocytes, LDH > 1.000 U/L) and renal function deterioration (ureic nitrogen-53 mg/dl and creatinine-6,8 mg/dl). The microbiological study of blood, urine and stools were negative. HBV, HCV and HIV serologies were negative. Serum values of C3 and C4 complement fractions were normal. Searches for circulating immune complexes, cryoglobulin, auto-antibodies were negative. Urinalysis showed proteinuria of 1.2 g in 24 hours. Pregnancy test was negative. Renal ultrasound was normal. The histological study of the renal biopsy specimen revealed thrombotic microangiopathy (TM) (fig. 1). The clinical evaluation and the complementary study enabled the diagnosis of hemolytic uremic syndrome (HUS).

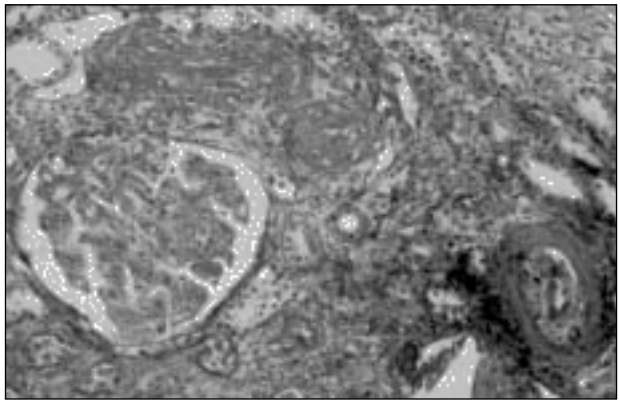

Fig. 1.—There is marked intimal edema, proliferation as well as necrosis. The vascular lumen is occluded by thrombi. The glomerular tuft is shrinked and the capilary wall is thickened showing double-contour (MT, × 200).

The patient was submitted to plasmapheresis and was treated with prednisolone 1 mg/kg, po, id. She started haemodialysis on the 14th day of internment, because of progressive worsening of renal function. The haematological abnormalities and LDH levels normalised, but there was no recovery of renal function. On the 16th february 2001 she restarted the cancer treatment with cytarabine and hydroxyurea and no recurrence of the HUS occurred. She died on the 19th september 2002 because of the CML progression.

DISCUSSION

HUS is a rare entity most frequently caused by infections, tumours, drugs, auto-immune diseases and pregnancy. There are some cases of idiopathic cause[2].

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According to the published literature, CML is not a malignancy that separately induces the HUS, unlike certain solid tumours[3]. In this case report, the haematological control of the CML prior to the manifestation of the HUS and the absence of recurrence over 19 months of survival, after its remission, are factors that turn the hypothesis of the CML to be the cause of HUS very unlikely.

The induction by chemotherapeutic agents is not described with hydroxyurea or cytarabine[3]. IFN-α has been identified as cause of TM in CML patients[4, 5]. In the presented case, the absence of HUS recurrence after reintroduction of cytarabine and hydroxyurea, strains the hypothesis of induction by IFN-α. Also in favour of these hypothesis is the known fact that the IFN-α toxicity is grater with higher doses and longer periods of administration, conditions verified in this case[1].

BIBLIOGRAPHY

1. Fischer T, Talpaz M. Biology of interferon. In: Carella AM, Daley GQ, Eaves CJ, Goldman JM, Hehlmann R (eds.): Chronic Myeloid Leukaemia, Biology and Treatment. London: Martin Dunitz Ltd; 135-49, 2001.
2. Remuzzi G, Ruggenenti P: The haemolytic uremic syndrome. *Kidney Int* 48: 2, 1995.
3. Gordon I, Kwaan H: Thrombotic microangiopathy manifesting as thrombotic thrombocytopenic purpura/haemolytic uremic syndrome in the cancer patient. *Seminars in Thrombosis and Hemostasis* 25 (2): 217-22, 1999.
4. Badid C, McGregor B, Faivre JM y cols.: Renal thrombotic microangiopathy induced by interferon α. *Nephrol Dial Transplant* 16: 846-8, 2001.
5. Ohashi N, Yonemura K, Sugiura T y cols.: Withdrawal of interferon-alpha results in prompt resolution thrombocytopenia and hemolysis but not renal failure in haemolytic uremic syndrome caused by interferon-alpha. *Am J Kidney Dis* 41(3): E10, 2003.