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## Stauffer syndrome and prostate carcinoma, two cases in chronic haemodialysis patients

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### To the Editor:

Paraneoplastic syndromes (PS) associated with prostate cancer are very uncommon entities, they have different characteristics and are present in the context of advanced neoplasia. Stauffer syndrome (SS) has rarely been described in relation to the latter, and it is mostly described as an initial presentation of neoplasia.<sup>1</sup>

We present two clinical cases of patients with prostate cancer on haemodialysis who developed SS.

### CASE 1

A 70-year-old male with hypertension and chronic renal failure (CRF) secondary to nephroangiosclerosis on haemodialysis for three years, diagnosed of Gleason grade 4 hormone refractory prostate adenocarcinoma with bone metastases a year before starting renal replacement therapy. He was treated with goserelin and estramustine due with persistently high prostate-specific antigen (PSA) levels. During hospitalization because of catheter-related bacteriemia due to *S. agalactiae*, the patient presented with jaundice and pruritus. Laboratory tests showed a cholestatic pattern: bilirubin 29mg/dl of direct dominance, alkaline phosphatase 1713U/l, gamma-glutamyl transpeptidase (GGT) 21U/l, with normal transaminases. C-reactive protein (CRP) and ferritin, after controlling the infectious symptoms, remained elevated. Tumour markers were negative, except for PSA (1548), and viral serologies were negative (hepatitis B virus [HBV], hepatitis C virus [HCV], human immunodeficiency virus). Anti-nuclear, anti-smooth muscle and anti-mitochondrial antibodies were negative. In the computerized tomography (CT)

scan we did not find liver lesions, bile duct dilatation, abdominal lymphadenopathies or lesions consistent with metastases in bone. The symptoms due to which the patient was admitted improved, although he continuously maintained hepatic cholestasis and was discharged. A month later, he developed spontaneous subdural haematoma with secondary seizures; conservative treatment was administered and the patient died.

### CASE 2

An 84-year-old male with type 2 diabetes mellitus, monoclonal gammopathy of uncertain significance, CRF of unknown aetiology on haemodialysis for six months. He was diagnosed with prostatic adenocarcinoma with non-assessable Gleason stage (due to prior hormone treatment), with multiple blastic bone metastases two years before starting haemodialysis and was on treatment with leuprolide. He developed progressively of progressive asthenia and malaise. In the laboratory tests, we found a cholestatic pattern with bilirubin of 3.96mg/dl (direct dominance), GGT 490U/l, alkaline phosphatase 581U/l and normal transaminases. He had normal tumour markers, including negative viral serologies (HBV and HCV) and PSA. In the CT scan, we did not observe intrahepatic lesions, bile duct dilatation or abdominal or pelvic adenopathies but we did observe known blastic bone metastasis images. Due to the patient's general and progressive deterioration, we decided not to take more aggressive measures, with *exitus* also occurring while he was in hospital.

### DISCUSSION

SS is a very rare PS, described in relation to malignant tumours (renal carcinoma, lymphoma, chronic lymphocytic leukaemia, medullary thyroid cancer, leiomyosarcoma, prostate cancer, renal sarcoma and malignant schwannoma) or benign lesions (benign haemorrhagic renal cyst, pseudotumoral xanthogranulomatous pyelonephritis).<sup>2-4</sup>

It is a paraneoplastic intrahepatic cholestasis that may present as jaundice, pruritus, hepatosplenomegaly, elevated alkaline phosphatase, GGT, hyperbilirubinaemia of direct dominance, a moderate increase in liver transaminases, thrombocytosis or increased acute phase reactants (CRP, erythrocyte sedimentation rate)<sup>2,3,5</sup> with an absence of liver metastases, bile duct obstruction and other hepatocellular disorders with predominant cholestatic pattern (viral, drug-induced and alcoholic hepatitis, hypoperfusion/sepsis, primary biliary cirrhosis, infiltrative disorders).<sup>3,5</sup> This PS disappears once the tumour lesion has been controlled and in turn, in tumours, it is associated with poor prognosis.<sup>2,6,7</sup>

SS pathogenesis is not clear. It could be due to the effect of a substance secreted by neoplastic cells;<sup>2</sup> an autoimmune cross-reaction between a tumour antigen and a protein (responsible for transporting bilirubin)<sup>3</sup> or the production of cytokines (interleukin [IL]-6, granulocyte-monocyte colony-stimulating factor).<sup>5,8</sup> It has been found that there is a positive relationship between levels of IL-6 and CRP, alkaline phosphatase and GGT, and that anti-IL-6 monoclonal antibody treatment reverses most of this syndrome's biochemical abnormalities.<sup>2,9</sup>

Haemodialysis patients frequently have biochemical data showing inflammation related to various factors inherent to CRF and the dialysis technique, which in turn have been associated with increased IL-6, IL-1 and tumour necrosis factor alpha. Thus, we could hypothesize that they would have a certain susceptibility to diseases associated with micro-inflammation, such as SS. However, we found no reference to this or any case of SS in dialysis patients.

The clinical characteristics of haemodialysis patients have changed dramatically in recent years. Older,

frailer patients, with greater comorbidity and even with tumour pathologies (previously contraindicated to renal replacement therapy) have initiated chronic dialysis, which has been made possible by the improvement in haemodialysis knowledge and techniques. Thus, as nephrologists, we face new diagnostic and treatment challenges every day.

In the cases described, the occurrence of cholestasis and particularly jaundice initially led us to suspect the presence of liver metastases (rarely reported in prostate cancer).<sup>10</sup> After ruling them out, we studied the presence of infectious, tumour or autoimmune diseases; when we found no apparent causes, we associated both symptoms to SS and did not take a more aggressive approach. As described, both cases had a poor prognosis, with a survival rate of less than one month.

Knowledge, and in particular, suspicion of this syndrome could help us avoid unnecessary examinations, and recognize a terminal patient by their baseline pathology in haemodialysis.

### Conflicts of interest

The authors declare that they have no conflicts of interest related to the contents of this article.

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