Clinics and Research in Hepatology and Gastroenterology (2021) **45**, 101515

Available online at
ScienceDirect
www.sciencedirect.com

Elsevier Masson France
EM|consulte
www.em-consulte.com/en

LETTER TO THE EDITOR

Stauffer's syndrome: A true entity?

Stauffer's syndrome is a paraneoplastic manifestation of renal cell carcinoma (RCC), consisting of non-metastatic hepatic dysfunction [1]. According to literature, manifestations of the syndrome may include hepatosplenomegaly, elevations of alkaline phosphatase (AP), γ-glutamyl transferase (γGT), erythrocyte sedimentation rate (ESR) and α-2-globulin, as well as prolongation of prothrombin time and thrombocytosis, in the absence of hepatic metastasis [2]. Also, fever, weight loss and nausea have been described. Manifestations of Stauffer's syndrome are generally reversible after nephrectomy. Therefore persistence may indicate presence of metastasis [3,4].

Although it has been estimated that Stauffer's syndrome may occur in approximately 15% of RCC patients, incidence is in fact unknown [5]. Also, there is some doubt whether Stauffer's syndrome is a real entity, since previous studies generally do not contain a disease-control group: Symptoms and signs described to the syndrome could in fact be coincidental without causal relation to RCC. We therefore identified all patients who underwent nephrectomy for RCC in a large general hospital in The Netherlands in the period: 2005—2015. A disease-control group of patients with urothelial cell carcinoma (UCC), who underwent a first-time transurethral resection of a bladder tumor (TURB) in the same time period, was established. The latter group was selected using random sampling from the total cohort of UCC patients.

We assessed the occurrence of elevated AP and γGT, since these values were available in all patients in both groups in this retrospective study. In addition other pre- and post-operative variables of interest were noted if available. The protocol was approved by the local medical-ethical committee. In the period: 2002—2015 176 patients underwent nephrectomy for RCC. The UCC disease-control group consisted of 137 patients. Patient characteristics of the UCC and TURB groups are given in Table 1. Age, sex and BMI did not differ.

In the RCC and UCC groups, 27/176 (15%) and 8/137 (6%) displayed elevated serum AP and γGT before the operation ($P < 0.01$: χ^2 test). These values normalized after the operation in 15/176 patients (8%) and 4/137 patients (3%) respectively ($P < 0.04$: χ^2 test). These 15 and 4 patients did not display comorbidities or metastases at time of nephrectomy that could potentially explain their abnormal liver values. However, in two of the RCC patients, liver tests became elevated again during the course of follow-up, and hepatic metastases were detected at three months and one year after nephrectomy, respectively. When excluding these two patients from the analysis, similar results were obtained (Table 1). Other symptoms and signs associated with Stauffer's syndrome such as weight loss, fever, elevated ESR, hyperbilirubinemia and hypoalbuminemia were predominantly found in the RCC group (Table 1). Our data support the existence of Stauffer's syndrome as real entity. Nevertheless, we acknowledge significant limitations to our work, such as the retrospective study design, without rigorous exclusion of other underlying chronic liver disease such as non-alcoholic fatty liver, viral hepatitis or hemochromatosis. In conclusion, our data support the existence of Stauffer's syndrome in patients with renal cell carcinoma. Further prospective studies are needed to unequivocally prove this contention.

Authors' contribution

C. van Roekel: study concept and design, data collection, manuscript editing and review; A.S. Bruins Slot: data analysis and interpretation, statistical analysis, manuscript preparation, editing and review; A.C. Viddeleer: study concept and design, manuscript editing and review; K.J. van Erpecum: data analysis and interpretation, manuscript preparation, editing and review; M.T.W.T. Lock: study concept and design, manuscript editing and review. All authors gave final approval of the version to be submitted.

https://doi.org/10.1016/j.clinre.2020.07.020

Table 1 Clinical and laboratory characteristics of the renal cell carcinoma (RCC) group and the urothelial cell carcinoma (UCC) group.

Characteristic	RCC	UCC	*P*-value (χ^2 test)
N	176	137	
Age (yrs: mean, range)	64 (37—89)	64 (37—86)	
Male:female ratio	1.1:1	1.3:1	
BMI (mean, range)	25 (18—33)	25 (24—27)	
Elevated AP and γGT (*n*, %): total	27/176 (15%)	8/137 (6%)	0.01
Postoperative normalization	15/176 (8%)	4/137 (3%)	0.04
After exclusion of 2 patients with subsequent metastasis, with postoperative normalization:	13/174 (7%)	4/137 (3%)	0.08
Hyperbilirubinemia	2	NM	[a]
Hypoalbuminemia	4	NM	[a]
Fever	4	0	[a]
Weight loss	6	0	[a]
Elevated ESR	7	2	[a]

NM: not measured before surgery. NA = not applicable. AP, reference range: 0—120 IU/L. YGT, reference range: 0—40 IU/L. ESR, reference rate: 0—30 mm/h in women, 0—20 mm/h in men. Bilirubin, reference range: 0—17 μmol/L. Albumin, reference range: 35—50 g/L.

[a] Differences in incidence of these findings was not tested since the subgroups were very small or no data available in one subgroup.

Funding

This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

Conflict of interest

The authors have no conflict of interest.

Références

[1] Moreira DM, Gershman B, Lohse CM, Boorjian SA, Cheville JC, Leibovich BC. Paraneoplastic syndromes are associated with adverse prognosis among patients with renal cell carcinoma undergoing nephrectomy. World J Urol 2016;34(10):1465—72.

[2] Morla D, Alazemi S, Lichtstein D. Stauffer's syndrome variant with cholestatic jaundice: a case report. J Gen Intern Med 2006;21:C11—3.

[3] Chuang YC, Lin AT, Chen KK, Chang YH, Chen MT, Chang LS. Paraneoplastic elevation of serum alkaline phosphatase in renal cell carcinoma: incidence and implication on prognosis.pdf>. J Urol 1997;158:1684—7.

[4] Palapattu GS, Kristo B, Rajfer J. Paraneoplastic syndromes in urologic malignancy: the many faces of renal cell carcinoma. Rev Urol 2002;4:163—70.

[5] nFontes-Sousa M, Magalhães H, Calais da Silva F, Maurício MJ. Stauffer's syndrome: a comprehensive review and proposed updated diagnostic criteria. Urol Oncol 2018;36:321—6.

C. van Roekel [a]
A.S. Bruins Slot [b]
A.C. Viddeleer [c]

K.J. van Erpecum [b,1,*]
M.T.W.T. Lock [a,1]

[a] *Department of Urology, University Medical Center Utrecht, Utrecht, The Netherlands*
[b] *Department of Gastroenterology and Hepatology, University Medical Center Utrecht, PO BOX 85500, 3508 GA Utrecht, The Netherlands*
[c] *Department of Urology, Ziekenhuis Gelderse Vallei, Ede, The Netherlands*

* Corresponding author.
Adresse e-mail : k.j.vanerpecum@umcutrecht.nl (K.J. van Erpecum)

[1] Both KJVE and MTWT Lock should be considered last author.

Disponible sur Internet le 29 December 2020