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CASE REPORT

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Mild elevation of liver function tests associated with renal cell carcinoma in a multimorbid older patient – a case of Stauffer's syndrome

Monika Ryś[1], Karolina Piotrowicz[1], Marcin Chłosta[2], Mateusz Ostachowski[2], Barbara Gryglewska[1], Piotr Chłosta[2], Jerzy Gąsowski[1]

[1]*Department of Internal Medicine and Gerontology, Jagiellonian University Medical College, Kraków, Poland*
[2]*Department of Urology, Jagiellonian University Medical College, Kraków, Poland*

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Corresponding author
Jerzy Gąsowski
Jagiellonian University
Medical College
University Hospital
Dept. of Internal Medicine
and Geriatrics
2 Jakubowskiego Street
31-501 Kraków, Poland
jerzy.gasowski@uj.edu.pl

We describe a case of a 74-year-old patient with recurrent fever of up-to 38.5°C, nocturnal sweating, weight loss of 4 kg, non-characteristic pain, and elevation of liver function tests (LFTs), who was diagnosed with Stauffer's syndrome. The patient successfully underwent laparoscopic heminephrectomy. The histology was clear-cell carcinoma of the right kidney (cT1a). The abnormalities in laboratory tests, such as Erythrocyte Sedimentation Rate, C-reactive protein, LFTs, α2-globulin, and most clinical symptoms abated 2 weeks post-surgery. We hypothesize that elevated LFTs in renal cell carcinoma patients could help deciding in favour of surgery in cases where the initial decision would be watchful waiting.

Key Words: Stauffer's syndrome ‹› renal cell carcinoma ‹› paraneoplastic syndrome ‹› case report

INTRODUCTION

Renal cell carcinoma (RCC) is common. In Poland the incidence is 7.5 cases per 100,000 population per year, while in the USA and Canada it reaches 10–12.9/100,000 [1]. It predominates in men, peaks at the age of 60–70 years [2], and may be asymptomatic for a long time. Paraneoplastic syndromes occur in 20% of RCC cases at the time of diagnosis, and an additional 10–40% develop later [3, 4]. Patients with tumours >4 cm are candidates for prompt surgery, while smaller, localized lesions in older patients with multimorbidity may require active surveillance [5].

The paraneoplastic syndromes include non-specific symptoms, organ disorders, and metabolic disturbances that result from the release of immune and hormonal factors [4, 6]. Non-metastatic hepatic dysfunction was first described in 1961 by Herbert Maurice Stauffer [7]. He described 5 RCC cases without liver metastases, who had hypoalbuminaemia, hypergammaglobulinaemia, elevated alkaline phosphatase (AP), and prolonged prothrombin time [7] that normalized after removal of the tumour [7, 8, 9]. Later disturbances in gamma-glutamyl-transpeptidase (GGTP), alfa-2-globulin, interleukin-6, and platelets [6, 8] were added to the syndrome.

CASE REPORT

A 74-year-old patient was admitted to the Department of Internal Medicine and Geriatrics, University Hospital, Kraków, Poland, due to recurrent fever of up-to 38.5°C, nocturnal sweating, 4 kg weight loss, and non-characteristic, poorly characterizable, wandering pain in the chest, right side of neck, middle and left epigastrium, and shoulder girdle. It was not related to physical exertion, time of day, or injury. Medical history included hypertension, diabetes, hyperlipidaemia, and osteoarthritis. He denied smoking, alcohol consumption, drug abuse, and traveling to the tropics in the past year. He had been hospitalized 4 months earlier because of the pulmonary embolism for which no cause was found at that time. Admission vital signs were blood pressure (BP) 152/77 mmHg; heart rate (HR) 100/min, regular; body temperature 35.4°C; 12 breaths/minute. Physical abnormalities included aortic systolic murmur 3/6 Levine and systolic murmur over the carotid arteries. Initial laboratory tests revealed normocytic anaemia, increased erythrocyte sedimentation rate, elevated C-reactive protein (CRP), prolonged international normalized ratio (INR), increased AP, GGTP with normal alanine and aspartate aminotransferase (ALT, AST) and total bilirubin, and increased alfa-2-globulin with low normal albumin. The tumour markers and urinalysis were normal save for low-grade albuminuria (semi-quantitative assessment). The laboratory results are presented in Table 1.

Initially, the differential included: infection, rheumatic disease, and cancer including haematological malignancy. Computed tomography (CT) showed a 17 mm renal mass at the upper pole of the right kidney and hypodense (45 Hounsfield units) liver. Chest CT showed a nodule of 12 x 6 mm in the sixth segment of the left lung, and basal fibrosis. No chest or abdominal lymphadenopathy was noted. Positron emission tomography (PET) with fluorodeoxyglucose (FDG) did not show metabolic activity that could be associated with lung cancer. Initial urologic advice – based on the tumour size, radiographic morphology, patient's multimorbidity, and the fact that the patient's initial attitude towards surgery was negative – was active surveillance with follow-up CT after 6 months. During hospitalization fever of up to 39°C, progressive weakness, and pain recurred. Empirical ceftriaxone was started. The diagnostics of infection was expanded. Blood and urine cultures were negative, as were the tests for SARS-CoV-2, hepatitis B virus, hepatitis C virus, Epstein-Barr virus, Borrelia, human immunodeficiency virus, cytomegalovirus, and syphilis. Trans-thoracic echocardiography revealed no valvular vegetations. The decision was made against lumbar cerebrospinal fluid puncture. Dental examination was unrevealing. With persistent fever, ceftriaxone was replaced by meropenem. The autoantibody screening was negative, as were monoclonal proteins in serum. The complement system was normal. The radiograms of the shoulder girdle, and cervical and lumbosacral spine showed advanced osteoarthritis. Patient was consulted by a rheumatologist, after which polymyalgia rheumatica was excluded as a cause of fever and pain. At this point the diagnosis of Stauffer's syndrome was proposed. The decision was made to perform laparoscopic partial resection of the left kidney. An exophytic, bipartite tumour of about 20 mm in diameter was removed, with no evidence of vascular invasion or extracapsular extension. The histopathological examination confirmed the diagnosis of clear-cell carcinoma (cT1a). The follow-up laboratory tests after 2 weeks showed a decrease of GGTP and AP, and normal prothrombin time. There was no recurrence of fever, pain, or sweating during the first month after the procedure. PET CT with 18F-cholin ruled out metastases. The patient was referred for standard follow-up, and he has been reported to be free from symptoms one year after surgery.

Table 1. *Selected baseline and follow-up laboratory values*

Parameter	Normal range	Hospitalization	Follow-up
Leukocytes	4.00–10.00 (10^3/uL)	9.47	8.13
Haemoglobin	14.00–18.00 (g/dL)	11.9	11.0
Haematocrit	40.00–54.00 (%)	34.1	34.3
Platelets	140.00–440.00 (10^3/uL)	337.0	352.0
ESR	<15.00 (mm/h)	88.0	–
CRP	<5.00 (mg/l)	88.7	8.19
Total bilirubin	0.00–21.00 (umol/l)	8.277	7.71
AST	10.00–50.00 (U/L)	35.0	15.0
ALT	10.00–50.00 (U/L)	30.0	11.0
Alkaline phosphatase	40.00–129.00 (U/L)	155.0	68.0
GGTP	8.00–61.00 (U/L)	126.0	51.0
Albumin	36.00–52.0 (g/L)	35.7	–
Alfa2-globulin	5.00–7.90 (g/L)	11.42	–
Prothrombin time	12.0–16.0 (s)	14.4	11.3
INR	0.90–1.20	1.31	1.00
Creatinine	62.00–106.00 (umol/l)	130.0	89.8

ESR – erythrocyte sedimentation rate; CRP – C-reactive protein, AST – aspartate aminotransferase; ALT – alanine aminotransferase; GGTP – gamma-glutamyl-transpeptidase; INR – international normalized ratio

DISCUSSION

The key feature of Stauffer's syndrome is the elevation of liver function tests (LFTs) in the absence

of hepatic metastases, which subsides after removal of the tumour [8]. Other laboratory features described in the literature include the following: hyperbilirubinaemia, hypoalbuminaemia, and elevation of alfa-2-globulin, IL-6, platelets, prolonged prothrombin time, and erythrocyte sedimentation rate [6, 7, 8, 10]. The most common abnormality in the laboratory tests is elevation of AP, which occurs in 90% of cases [6, 7]. The pathophysiology is poorly understood [3, 6, 7, 10]. The lysosomal enzymes and hepatotoxins may be released from a tumour and generate hepato-cellular injury [6]. This may involve periportal inflammation and generation of autoantibodies against hepatic proteins. This also stimulates release of alkaline phosphatase [3, 6]. Furthermore, the link between RCC-induced elevation of IL-6 and hepatic injury has been postulated [6]. This has been supported by the results of liver biopsies, which revel hepatitis with lymphocytic infiltration and hepatocellular degeneration [6]. The significance of alpha-fetoprotein for diagnosis, prognosis, and assessment of possible recurrence of RCC is of paramount importance. Persistent or recurrent elevation of AP after nephrectomy or heminephrectomy indicates the existence of residual tumour or tumour recurrence. However, the decrease of serum alkaline phosphatase levels does not guarantee that the disease has been completely cured. It has been demonstrated that the lack of decrease of LFT level after tumour resection is associated with a poor prognosis [8].

The awareness of paraneoplastic syndromes may help in decision-making concerning the appropriate therapeutic approaches. The presented case underscores the multi-specialty nature of the diagnostic process initially required to solve the possible differential. It also points to the possibility that many cases of Stauffer's syndrome may be overlooked. Although our finding is casuistic, we hypothesize that inclusion of elements of mildly expressed Stauffer's syndrome in the decision process may help in the decision about which radiographically detected renal masses should be promptly removed.

CONFLICTS OF INTEREST

The authors declare no conflicts of interest.

References

1. Fiebig J, Kraywinkel K. Epidemiology of renal cell carcinoma in Germany. Onkologe. 2019; 11: 79-87.
2. Capitanio U, Montorsi F. Renal cancer. Lancet. 2016; 387: 894-906.
3. Palapattu GS, Kristo B, Rajfer J. Paraneoplastic syndromes in urologic malignancy: the many faces of renal cell carcinoma. Rev Urol. 2002; 4: 163.
4. Kim HL, Belldegrun AS, Freitas DG, et al. Paraneoplastic signs and symptoms of renal cell carcinoma: implications for prognosis. J Urol. 2003; 170: 1742-1746.
5. Campbell SC, Novick AC, Belldegrun A, et al. Guideline for Management of the Clinical T1 Renal Mass. J Urol. 2009; 182: 1271-1279.
6. Tanous B, Alsaud A, Mahmoud KE, Yassin MA. A Rare Presentation of Stauffer's Syndrome Associated with Renal Cell Carcinoma. Case Rep Oncol. 2020; 13: 742-746.
7. Sharma N, Darr U, Darr A, Sood G. Stauffer syndrome: a comprehensive review of the icteric variant of the syndrome. Cureus. 2019; 11: e6032.
8. Fontes-Sousa M, Magalhães H, da Silva FC, Maurício MJ. Stauffer's syndrome: a comprehensive review and proposed updated diagnostic criteria. Urol Oncol. 2018; 36: 321-326.
9. Chavarriaga J, Fakih N, Cataño J, Villaquiran C, Rodriguez S, Patino G. Stauffer syndrome, clinical implications and knowledge gaps, does size matter? Case report. BMC Urol. 2020; 20: 1-5.
10. Morla D, Alazemi S, Lichtstein D. Stauffer's syndrome variant with cholestatic jaundice. J Gen Intern Med. 2006; 21: C11-C13. ■