Sorafenib induced tumor lysis syndrome in an advanced hepatocellular carcinoma patient

Wu-Shiung Huang, Chang-Hsu Yang

INTRODUCTION

Molecular targeted therapy is currently the new treatment modality for advanced cancer. Sorafenib is an oral multi-kinase inhibitor that blocks tumor growth and cell proliferation by targeting Raf kinase, VEGFR-2, VEGFR-3, and PDGFR-β[1]. Sorafenib was approved by the FDA in 2007 to treat hepatocellular carcinoma (HCC)[2]. An uncontrolled sorafenib phase II study in 137 patients with advanced HCCs confirmed that the higher pERK patients had a longer time to progression compared to the lower pERK patients[3,4]. Therefore, sorafenib is a specific target drug for the Raf/MEK/ERK pathway and pERK could be a useful biomarker. Sorafenib showed efficacy in prolonging patients’ survival in a previous SHARP trial[5]. The study obtained an overall 44.9% improvement and the sorafenib group had a partial response rate of 2.3% (n = 7) vs placebo of 0.7% (n = 2). Sorafenib opens a new era for advanced HCC treatment. However, that sorafenib might induce tumor lysis syndrome (TLS) had never been reported in previous studies. Here, we report sorafenib induced TLS in an advanced HCC male patient. This reported case developed multiple organ failure (liver failure, renal failure and respiratory failure) and metabolic acidosis. Despite intensive hemodialysis and other supportive therapy, he succumbed to the complication of tumor lysis syndrome.

CASE REPORT

A 55-year-old male patient with hepatitis B-related liver cirrhosis was found to have advanced hepatocellular carcinoma. His AFP was initially 9828 µg/L and rapidly dropped to 5597 µg/L in ten days after oral sorafenib treatment. However, he developed acute renal failure, hyperkalemia, and hyperuricemia 30 d after receiving the sorafenib treatment. Tumor lysis syndrome was suspected and intensive hemodialysis was performed. Despite intensive hemodialysis and other supportive therapy, he developed multiple organ failure (liver, renal, and respiratory failure) and metabolic acidosis. The patient expired 13 d after admission.

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Key words: Sorafenib; Tumor lysis syndrome; Hepatocellular carcinoma; Hemodialysis; Hyperkalemia

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Australia) was shown to be 48.800 IU/ml (273.288-288.000 IU/ml). The patient failed to respond to the medication. His general condition deteriorated after TLS developed. Llovet et al reported that sorafenib could significantly extend median survival and prolong the time of radiologically detected progression by approximately three months compared with a placebo in individuals with advanced HCC in a background of liver cirrhosis 

They evidenced progression by approximately three months compared with a placebo in individuals with advanced HCC in a background of liver cirrhosis. The degree of abnormalities in his uric acid and phosphorus fulfill the criteria of TLS as defined by Cairo-Bishop [8]; however, our case had no initial calcium data due to hyperkalemia treated with calcium gluconate. The initial serum calcium was 2.32 (2.2-2.6) mmol/L and dropped to 1.65 mmol/L ten days later. The decrease of calcium level over 25% also matched the Cairo-Bishop definition of TLS [8]. Hyphosphatemia did happen in the sorafenib treatment group (11/297) vs control group (2/302) (P < 0.001) in Llovet et al’s SHARP study [3]. Phosphorus in our case was 5.4 (2.7-4.5) mmol/L and did not go over 6.5 mmol/L as Cairo-Bishop definition of TLS, which might be the result of sorafenib effect. The diagnosis of TLS is poor with a high mortality rate in solid tumor. Prevention of TLS by hydration, alkalization, or therapy to correct metabolic disturbance can be effective for some hematological malignancies [9-11]. Based on previous reports, hemodialysis can be helpful in improving the clinical course and can even cure TLS in some patients [6-10]. This case had a satisfactory initial course following the sorafenib therapy; however, his condition deteriorated after TLS developed. Llovet et al reported that sorafenib could significantly extend median survival and prolong the time of radiologically evidenced progression by approximately three months compared with a placebo in individuals with advanced hepatocellular carcinoma (HCC) with well-preserved hepatic function was within normal limits before, and 10 d after, treatment. The occurrence of TLS in this patient could be the combination of effective therapy due to sorafenib chemosensitivity of the HCC, the use of diuretics with secondary dehydration, and advanced HCC with large tumor burden. Diuretics induced secondary dehydration could result in acute renal failure, but after effective hydration and supportive therapy, hyperkalemia and hyperuricemia persisted. Therefore, sorafenib induced TLS was the more likely cause of the symptoms described.

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liver function, naive to systemic therapy. In comparison with the control group given the placebo, they reported that sorafenib was significantly associated with more diarrhea of any grade, weight loss, hand-foot skin reaction, alopecia, anorexia, and voice changes[5]. However, in their report, TLS was not mentioned. We believed that TLS is a rare side effect of sorafenib treatment. Once it occurred, however, TLS can induce multiple organ failure with a catastrophic outcome.

In conclusion, in the therapy of HCC with sorafenib, especially in patients with high tumor burden and showing a good initial response, the possible occurrence of TLS should be kept in mind and appropriate laboratory data should be monitored. Once TLS developed, the prognosis was poor even when intensive hemodialysis was given.

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