Hyponatremia Predicts the Inferior Survival of Patients with Metastatic Renal Cell Carcinoma Treated with Molecular Targeted Therapy

Introduction and Objective: Hyponatremia is reported to be associated with poor survival in localized renal cell carcinoma (RCC) and metastatic RCC (mRCC) treated with immunotherapy. However, there are no reports on the relation between hyponatremia and prognosis of mRCC treated with molecular targeted therapy. We evaluated the prognostic significance of hyponatremia in mRCC treated with molecular targeted therapy as first line therapy and analyze other prognostic factors including neutolophilia, platelets, and C-reactive protein (CRP).
Materials and Methods: We retrospectively analyzed a database comprising 87 patients treated from April 2008 to July 2011 with sorafenib and sunitinib as first-line therapy for mRCC. Patients were divided into three groups according to sodium level: severe hyponatremia (≤134 mEq/L), mild hyponatremia (135-137 mEq/L), and normal natremia (≥138 mEq/L).
Results: Severe and mild hyponatremia was significantly associated with the presence of bone metastasis and neutrophilia (p=0.001 and p=0.006, respectively). Median cancer specific survival (CSS) time was 10.3 months. Median CSS time was 8.8 months in the patients with severe and mild hyponatremia and 32.6 months in the patients with normal natremia (*P* <0.001). Multivariate analysis showed severe and mild hyponatremia to be significantly associated with CSS (HR: 2.910; 95% CI: 1.273–6.652, *P* = 0.011). In other clinical features, neutrophilia and high CRP level (CRP ≥1.0 mg/dl) were significant prognostic factors to predict inferior CSS (*P* = 0.016 and *P* = 0.004), respectively. In Harell's C index calculation, severe and mild hyponatremia was a significant independent predictor of inferior CSS, significantly increasing the C-statistic from 0.759 to 0.820 (increase of 0.062: 95%CI: 0.007-0.116, p=0.028).
Conclusions: We found hyponatremia (<138mEq/L) to be the significant factor to predict inferior CSS together with neutrophilia and high CRP level. Moreover, hyponatremia might be significantly associated with chronic inflammation and tumor aggressiveness.