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Case Report

Sunitinib Induced Life Threatening Acute Hyponatremia in a Lung Cancer Patient

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Abstract

Sunitinib has bene widely used in many different malignancies. We report here a case of a 67 year old woman with metastatic adenocarcinoma of the lungs who developed acute life threatening hyponatremia after received sunitinib 40mg a day for 20 days. Lab study is consistent with syndrome of Inappropriate antidiuretic hormone secretion(SIADH). She was admitted to medical intensive care unit and received hypertonic saline infusion, strict fluid restriction and vasopressin receptor antagonist tolvaptan. She recovered from this episode and was discharged home. Sunitinib was discontinued permanently. This is a first case report of sunitnib induced severe SIADH.

Keywords: Sunitinib; Lung Cancer; SIADH; Hyponatremia

Introduction

Case Report: A 67-year-old female with metastatic adenocarcinoma of the lungs, who has received multiple lines of chemotherapy and targeted agents since 2006. The chemo regimens included carboplatin and paclitaxel, docetaxel, Erlotinib, pemetraxate with bevacizumab, carboplatin-gemcitabine, Abraxane, vinorelbine, and topotecan. She has maintained pretty good function and quality of life. On August 6, 2014, her PET/CT showed disease progression including enlarging left cervical adenopathy, she was then tried sunitinib 50mg daily 4 weeks on and two weeks off. She tolerated the first week of sunitinib very well with shrinking left cervical adenopathy, but soon after that, she noticed increasing PleurX drainage. Her chemistry panel on August 8, 2014 showed normal serum sodium level of 135nmol/L and normal BUN, Creatinine and LFTs. Two weeks after she started on sunitinib, the cervical adenopathy is no longer palpable, but she gradually developed fluid retention with edema of the bilateral upper and lower extremities, face and both eyelids. She also complained of worsening shortness of breath and fatigue. On Day 20, sunitinib was discontinued due to worsening the above symptoms. She was found to have serum sodium of 103 nmol/L and was admitted to medical ICU. When she arrived ICU, her serum sodium was 100nMol/L, serum osmolality was 218 mOsm/kg, urine sodium was 10mMol/L, urine osmolality was 519 mOsm/kg, She was diagnosed with syndrome of Inappropriate antidiuretic hormone secretion(SIADH) and received 3% hypertonic saline and under strict water restriction for three days, her serum sodium went up to 114mMol/l. Tolvaptan was then added on day 4. Her serum sodium levels were slowly corrected to the normal ranges. Her symptoms resolved. She was then discharged to home.

Discussion

Most common adverse events associated with sunitinib therapy are fatigue, diarrhea, nausea, anorexia, hypertension, a yellow skin discoloration, hand-foot skin reaction, and stomatitis. [4]

In the placebo-controlled Phase III GIST study, adverse events which occurred more often with sunitinib than placebo included diarrhea, anorexia, skin discoloration, mucositis/stomatitis, asthenia, altered taste, and constipation [1,2].

Most of these adverse events are manageable.[2, 3] The incidence of serious adverse events are relative uncommon. Grade 3 or 4 adverse events occur in ≤10% of patients and include hypertension, fatigue, asthenia, diarrhea, and chemotherapy-induced acral erythema. Lab abnormalities associated with sunitinib therapy include elevated levels of lipase, amylase, neutrophils, lymphocytes, and platelets. Hypothyroidism and reversible erythrocytosis have also been associated with sunitinib.[1-5]. Most adverse events can be managed through supportive care, dose interruption, or dose reduction [2,3].

Dose reductions were required in 50% of the patients studied in renal cell carcinoma in order to manage the significant toxicities of this agent. A recent study done at MD Anderson Cancer Center compared the outcomes of metastatic renal cell cancer patients who received sunitinib on the standard schedule (50mg/4 weeks on 2 weeks off) with those who received sunitinib with more frequent and short drug holidays (alternative schedule).

It suggested that that the overall survival, progression free survival and drug adherence were significantly higher in the patients who received Sunitinib on the alternative schedule. Patients also had a better tolerance and lower severity of adverse events which frequently lead to discontinuation of treatment of metastatic renal cell cancer patients.[6]

Conclusion

This is the first case of sunitinib induced SIADH with life threatening hyponataemia, which improved after sunitinib discontinuation, fluid restriction, hypertonic saline solution and vasopressin receptor antagonist. Since sunitinib has been used in multiple types of malignancies, clinicians must be aware that that it could cause acute severe hyponatremia. Close monitoring during the treatment is advised. Hyponatremia is a common clinical problem and conventional treatment often is poorly tolerated and ineffective. Hypomatremia with sutinib has rarely been reported . The absence of other idedtified causes and the positive rechallenge are good argument s for an aetiological link in our case.

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