Sunitinib induced life threatening acute hyponatremia in a lung cancer patient

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Abstract: Sunitinib has been 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 sunitinib induced severe SIADH.

Keywords: sunitinib; lung cancer; SIADH; hyponatremia

Introduction: Sunitinib is a potent multi-targeted tyrosine kinase inhibitor, which inhibits vascular endothelial growth factor (VEGFR), platelet derived growth factor (PDGER), stem cell factor receptor (Kit) and others [1, 2]. It has been approved to treat metastatic renal cell carcinoma, advanced gastrointestinal stromal tumor (GIST) and well-differentiated pancreatic neuroendocrine tumor [3-5] and has also been showed to be active for many malignancies such as non-small cell lung cancer and thyroid cancer [6,7]. Sunitinib can cause many adverse reactions such as hand-foot skin reaction, hypertension, proteinuria, diarrhea, hypothyroidism, arterial thrombosis, bleeding and cardiac toxicities [3]. Here we report the first case of sunitinib induced life threatening hyponatremia.

Case Report

A 67-year-old female with metastatic adenocarcinoma of the lung, who had received multiple lines of chemotherapy and targeted agents since 2006. The chemotherapy regimens included carboplatin and paclitaxel, docetaxel, Erlotinib, pemetrexate with bevacizumab, carboplatin-gemcitabine, Abraxane, vinorelbine, and topotecan. She had 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 treatment very well with shrinking 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 liver function test. Two weeks after she started on sunitinib, the cervical adenopathy was 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 of the above symptoms. She was found to have serum sodium of 103 mmol/L and was admitted to medical ICU. When she arrived ICU, her serum sodium was 100mMol/L, serum osmolality was 218 mOsm/kg, urine sodium was 218 mOsm/kg, 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 levels were slowly corrected to the normal ranges on day 10. Her symptoms resolved. She was discharged home.

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Discussion: In the published clinical trials, the most common reported adverse reactions associated with sunitinib therapy are fatigue, asthenia, fever, diarrhea, nausea, vomiting, mucositis/stomatitis, skin discoloration, asthenia, altered taste, constipation, hypertension, rash, hand-foot skin reaction, and myalgia. These adverse events are usually manageable. The most common grade 3/4 laboratory abnormalities included lipase, amylase and neutrophils, and platelets. The incidence of serious adverse events is relative uncommon, these include hepatotoxicity, cardiovascular events such as myocardial ischemia, myocardial infarction, left ventricular dysfunction, cardiac failure, prolonged QT-intervals and Torsade de pointes, as well as hypothyroidism, hypoglycemia, osteonecrosis of jaws, severe hemorrhagic events and impaired wound healing. Most adverse events can be managed through supportive care, dose interruption, or dose reduction.

This is the first case of sunitinib induced SIADH with life threatening hyponatremia, which improved after sunitinib discontinuation, fluid restriction, hypertonic saline infusion and vasopressin receptor antagonist. The mechanism of the sunitinib induced hyponatremia remains unclear.

Conclusion

Since sunitinib has been shown to provide clinical benefit for multiple different types of malignancies, clinicians must be aware that it could cause acute severe hyponatremia. Close monitoring and prompt intervention during the treatment are critical and should be advised.

References


