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Case Report

Small cell neuroendocrine carcinoma of the cervix complicated with mental abnormality and refractory hyponatremia: a case report

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Summary

Small cell carcinoma of the cervix (SCCC) is a rare type of cervical cancer, which has high-degree malignancy, strong invasion, and poor prognosis. It can secrete a variety of hormones because of its particularity. There is a theoretical concern that these hormones do not cause clinical symptoms. However, relatively large studies showed hyponatremia caused by hormones occur in SCCC. Here the authors discuss the clinical course of a 43-year-old woman with SCCC that presented both refractory hyponatremia and neurologic symptoms at the same time. We can attain some experience through the treatment of this patient, that treatment of the primary disease until after the correction of electrolyte disturbances is not proposed. In addition, the complications will alleviate and disappear naturally after treatment of the primary disease.

Key words: Small cell carcinoma of cervix; Neuroendocrine carcinoma; SIADH.

Introduction

Small cell carcinoma of the cervix (SCCC) is a rare type of cervical cancer that comprises 0.8-2% of invasive cervical cancer [1]. SCCC is highly aggressive and rapidly leads to lymphogenous and hematogenous metastasis. Therefore the disease progresses rapidly and has the worst prognosis in all cervical cancers. The pathological type belongs to neuroendocrine carcinoma and tumor morphology is just like small cell lung cancer. In extrapulmonary small cell carcinoma (EPSCC), the cervix is the most common site of the disease which accounts for 30% of EPSCC. It may also appear in other places such as urinary bladder, colon, and kidney [2]. In present study, HPV18 infection is most commonly associated with the pathogeny and the progression of both SCCC and the rapidly progressing cervical squamous cancer. Neuroendocrine carcinoma can lead to a variety of clinical manifestations because of its special pathological type. As a heterologous neuroendocrine tumor, the main symptom of SCCC are paraneoplastic syndromes, and of these, syndrome of inappropriate secretion of antidiuretic hormone (SIADH) is common. The characteristics of SIADH include hyponatremia, low plasma osmotic pressure, and urine sodium and urine osmotic pressure increase [3]. The authors report a case of a SCCC associated with mental disorders and hyponatremia at the same time. Here they discuss the clinical course of a 43-year-old woman with SCCC presenting both refractory hyponatremia and mental disorders at the same time.

Case Report

A 43-year-old woman, G1P0, had a spontaneous abortion 23 years ago, and then attempted assisted reproduction for two times both ending in failure. Her menstrual period is regular and she had no contact bleeding or abdominal pain. Because of consisting of vaginal discharge for two months, she went to the local hospital. The exact course of diagnosis and treatment were unknown. To rule out the chance of suspected cervical lesions, she underwent loop electrosurgical excision procedure (LEEP) which revealed poor pathological finding of SCCC with differentiation of a small number of adenocarcinoma. The result of IHC was CD31 (+), CK (+), CgA (+), Ki-67 (90%+), p16 (+), p53 (-), Syn (+), p40 (-), and p63 (-). She was also positive for HPV-18.

For further diagnosis and treatment, she came to the authors' hospital. At the initial stage of diagnosis and treatment, the patient was suffering from nausea, vomiting, dizziness. and poor sleep quality. She was given escitalopram 5 mg QD orally, and after one week, she adjusted to 10 mg QD herself. Then she began to feel tremor capitis, slowed speech, drunken state when she walked, and fell three times with no inducement. She stopped escitalopram by herself and began to take lorazepam, but the symptoms had no changed.

Her tumor was progressing rapidly during the period of improving the relevant tests and laboratory examinations. When she was admitted to hospital, the volume of vaginal bleeding was the same as menstrual period. Gynecological examination showed that vaginal fornix was partly invaded; the diameter of the cauliflower-like neoplasm in cervix was increased to 7 cm; necrotic tissue and obvious hemorrhage were visible on the surface; the size of anterior and irregular uterus was equivalent to 7 gestational weeks. Parametrial tissue on the right was thickened but bilateral side was elastic. MRI images showed that enlarged cervix and mass, had a high possibility of being a cervical malignant tumor (6.9×5.7×7.3 cm, lobulated, in the lower vagina), invasion depth

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reached the deep muscularis, the serosa, and posterior fornix of vagina were possibly invaded; multiple uterine fibroids, double appendix cyst, and pelvic and inguinal small lymph nodes (maximum short diameter was 0.8 cm) were found. The head MRI showed bilateral cerebral multiple punctate abnormal signal, considering the focal demyelination. The results of electrolure showed Na^+ 114 mmol/L, CL^- 83mmol/L, and the other examinations were normal. After hospitalization, considering that the severe hyponatremia should not exclude the side effects of antidepressant treatment and sudden discontinuation of the drug, the authors gave her daily intravenous sodium 8-10 g, but after one week, the concentration of Na+ was still 116-120 mmol/L. After the relevant tests and laboratory examinations improved, adrenal diseases which may cause abnormal secretion of antidiuretic hormone were excluded, and SIADH was most commonly associated with the disease. Because of the local advanced cervical tumor, surgery could not be performed directly. So the authors gave her one course of neoadjuvant chemotherapy with cisplatin (100 mg) and paclitaxel (90 mg) through arterial IV. The sodium was still given after one course of neoadjuvant therapy. After chemotherapym her Na+ level increased to 120-126 mmol/L, and her mental symptoms improved. Nausea, vomiting, dizziness, and head tremor disappeared. Two weeks later, the diameter of the cervical tumor was reduced to 4 cm. Then the patient underwent radical hysterectomy and bilateral tuboovariectomy. Two days after the operation, serum Na^+ level had risen to 136 mmol/L, mental symptoms disappeared, and speech rate returned to normal. The pathologic result was cervical neuroendocrine tumors (SCCC), visible necrosis, tumor invasion, and deep muscle layer (more than 1/2 cervical wall thickness, several local total layer) involving endocervical shallow muscle layer, visible vascular tumor thrombus, and double uterine with no tumor tissue. IHC showed Ki-67 (about 98%+), p53 (part+), C-erB-2 (-), p16 (+), EMA (+), Syn (+), CgA (part+), and cancer metastasis was seen around the iliac vessels lymph nodes. The patient is currently under sequential chemotherapy and radiotherapy.

Discussion

Cervical neuroendocrine carcinoma (NECC) includes small cell carcinoma, large cell carcinoma, typical and atypical carcinoid, and of those, small cell carcinoma is the most common one. IHC plays an important role in the diagnosis [4]. There are many reports about small cell lung cancer accompanied with refractory hyponatremia [5], but few psychiatric symptoms have been reported, and only one case was found in the literature [6]. SCCC combined with intractable hyponatremia are rarely reported, and even fewer with concomitant psychiatric symptoms. Kuriakose *et al.* reported one case of SCCC with low sodium epilepsy presenting as the first symptom. After one-year therapy by chemotherapy and radiotherapy, the patient died of liver and intracranial metastasis [7]. Chronic hyponatremia is defined as reduced serum sodium levels, which fall to 120 mmol/L in 48 hours or even more. Brain cells can be influenced by the solute discharge, and promote water migration to improve brain edema caused by compensatory hyponatremia. However the risk of osmotic demyelination lesions increases. Studies have showed that long-term adverse effects caused by chronic hyponatremia mainly include gait instability, prone to falls, osteoporosis, fractures, and involvement of the central nervous system with orientation and cognitive impairment [8-11]. For the present patient, who suffered from cervical cancer and accompanied by psychiatric symptoms, was still mainly related to intractable hyponatremia. It was important to control the tumor on the basis of eliminating the organic lesions which caused the hyponatremia. In this patient, blood sodium levels rose and symptoms improved after local arterial interventional chemotherapy, and blood sodium was completely restored after tumor resection. Although previous studies have shown that small cell carcinoma can secrete many hormones, such as ACTH, 5-HT, etc., there are no hormone-induced symptoms. However, this patient presented with visible SIADH symptoms. Whether or not they were in relation to the antidepressivedrugs she took on her own, may need to be further established.

Through the treatment of this patient, we should be vigilant of SCCC and the symptoms resulting from hormonal changes. Treatment only electrolyte disorders, while neglecting the primary disease should be avoided. Before the tumor is controlled, even if the electrolyte is corrected, sodium supplementation can only be maintained at a low level. So the treatment of neuroendocrine tumor with hyponatremia, first of all, the primary disease should be treated. For these patients, preoperative evaluation, intraoperative detection, and postoperative supplementation are very important. Intraoperative stimulation and complications caused by excessive intraoperative and postoperative perfusion, such as cerebral edema, should also be avoided. Since antidiuretic hormone secretion is associated with small cell carcinoma, it has been suggested that the presence of hyponatremia can be seen as a sign of tumor recurrence, or whether hyponatremia is a prognostic factor in patients with cancer. Hermes *et al.* [12] believed that hyponatremia is the independent risk factors influencing the prognosis of small cell lung cancer. Whether SCCC has the same prognosis still requires further research.

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