Reversible hyponatremic encephalopathy mimicking pseudoprogression in a glioblastoma patient

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Abstract

Aim: Pseudoprogression of high-grade glioma is defined as an increase in enhancement and/or edema on radiologic exam but without increased tumor activity.
Methods: We present a rare case of a hyponatremic encephalopathy in a 56 year-old Albanian woman, previously diagnosed for a malignant glioma. This case was attended in early 2017 at the Department of Neurosurgery, University Hospital Center "Mother Teresa" in Tirana, Albania.
Results: The patient presented worsening headaches, lethargy and confusion. Brain CT-scan revealed diffuse cerebral swelling. Laboratory exams revealed a severe hyponatremia. Rapid intravenous hypertonic sodium chloride and close cardio-respiratory monitoring led to the regression of clinical and radiological abnormalities.
Conclusion: Our experience indicates that hyponatremic encephalopathy should be included in the working hypotheses of pseudoprogression of high-grade glioma.

Keywords: high-grade glioma, hyponatremia, pseudoprogression.

Introduction

Hyponatremia can be succinctly defined as an abnormally low plasma sodium concentration. Clinical descriptions have been plentiful. Symptoms frequently attributed to hyponatremia were apathy, weakness, nausea, vomiting, headache as well as seizures or coma (1). Among cancer patients, the largest body of evidence comes from small cell lung cancer (2). When hyponatremia is associated with primary brain tumors, the serious neurological symptoms and hyponatremic-induced brain edema may lead to major sequelae that are often unrelated to hyponatremia (3).

On the other hand, high-grade glioma is the most common malignant cerebral tumor of the adult with a high propensity to recur (4). The most difficult task in the management of these patients remains the distinction between true progression and pseudoprogression. The latter is defined as a subacute reaction with inflammation, edema and increased abnormal vessel permeability, recently prescribed as treatment-related effect (5). Concomitant radiochemotherapy with temozolomide and epileptic seizures are well-known etiologic factors that could induce pseudoprogression (5).

Herein, we report the case of an Albanian adult patient treated and followed on for a high-grade glioma of corpus callosum in whom a severe hyponatremia induced a reversible pseudoprogression. Our aim is to increase the awareness of the medical community about the potential role of hyponatremic encephalopathy on inducing radiological abnormalities mimicking the progression of cerebral gliomas.

Case report

An otherwise healthy 56 year-old woman was diagnosed in early 2017 for a malignant glioma extending across corpus callosum. The glioma was biopsied and found to be an anaplastic astrocytoma. In attendance of radiation therapy, she was proposed temozolomide based chemotherapy. When she received the first cycle of Temozolomide, she also discontinued the corticosteroids. At her 16th day of temozolomide uptake, she showed up at the emergency department for progressively worsening anorexia, headaches, lethargy and confusion later associated with impaired response to verbal and painful stimuli, hallucinations and urinary incontinence. Brain CT-scan revealed effacement of cortical sulci and areas of parenchymal low-attenuation compatible with diffuse cerebral swelling (Figure 1, panel A). Laboratory exams revealed a severe hyponatremia, 116 mmol/l. Rapid intravenous hypertonic sodium chloride, high doses of corticosteroids and close cardio-respiratory monitoring were initiated. The clinical symptoms regressed within two weeks and CT-scan of control confirmed the lessening of cytotoxic brain edema (Figure 1, panel B).

One month later, she underwent the radiation therapy which was well-tolerated.

Discussion

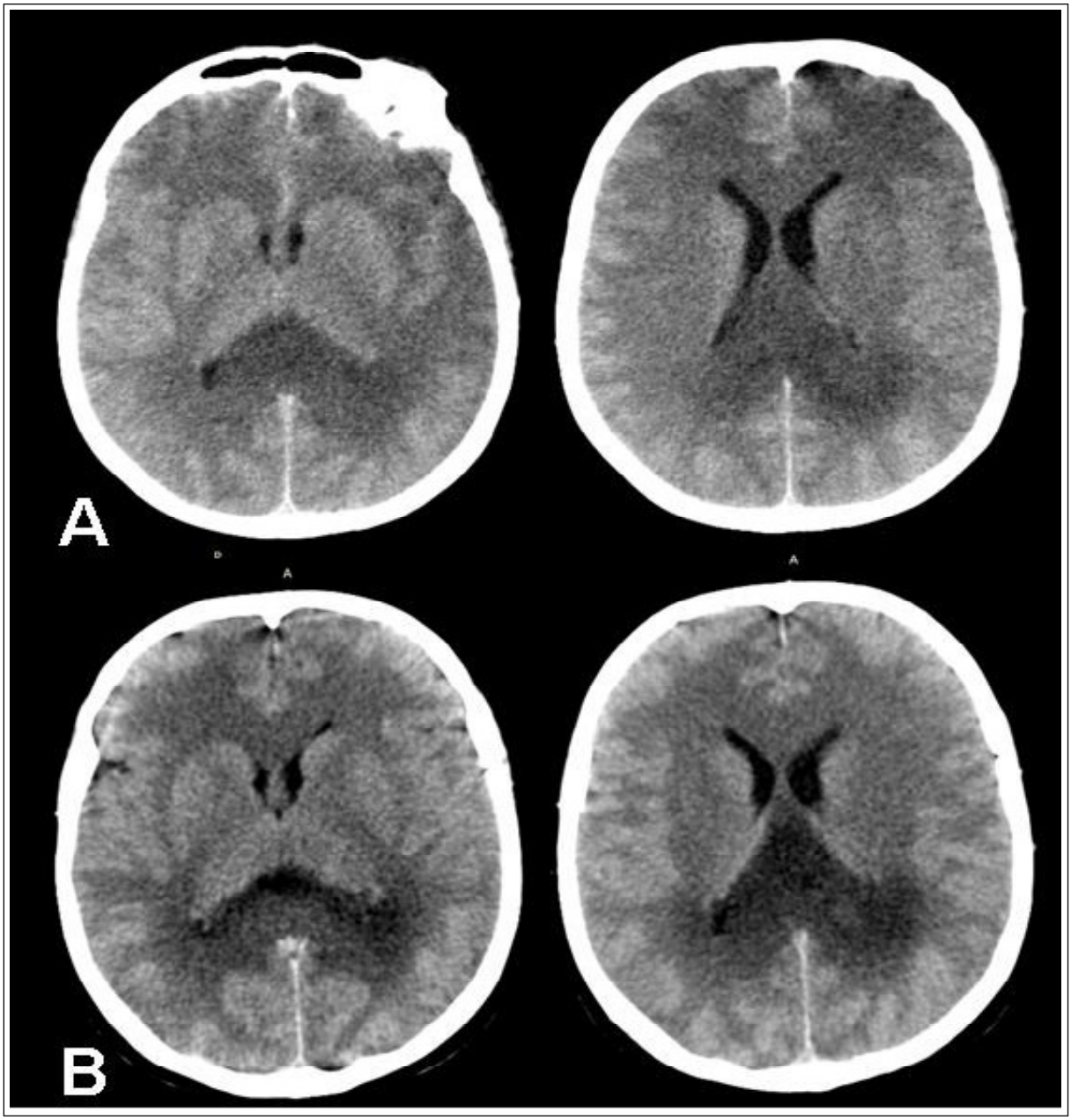
Pseudoprogression is defined as an increase in enhancement and/or edema on MRI but without increased tumor activity. It is seen in 14-32.3% of GBM patients treated with standard regimen (5). In almost 60% of cases, pseudoprogression occurs within the first three months after completing treatment, but may occur after more than six months (5). Our patient had had one cycle of temozolomide. Although temozolomide may induce pseudoprogression, the early occurrence of the radiological progression makes pseudoprogression unlikely.

A review of the published work surprisingly did not yield any previous cases of pseudoprogression resulting from acute hyponatraemia in high-grade glioma patients.

Additionally, there were no cases of clinical deterioration attributed to acute hyponatremia. If these happened, the clinicians may have assumed that such manifestations were due to the primary pathology, the high-grade glioma.

About one-third of the patients with pseudo-

Figure 1. CT-scan showing the effacement of cortical sulci and areas of parenchymal low-attenuation compatible with diffuse cerebral swelling *(panel A)*; CT-scan of control confirming the lessening of cytotoxic brain edema *(panel B)*



progression have new clinical symptoms (6). Symptomatic pseudoprogression may show signs of raised intracranial pressure, seizures, or rarely focal neurological deficits (7).

Early symptoms of encephalopathy due to acute hyponatremia include nausea, vomiting, headache, lethargy (1). Late signs include bizarre behaviour, seizures, coma and respiratory arrest (1). In our report, the patient experienced nausea, vomiting, lethargy and confusion, highly suggestive for a tumor progression. Hyponatremia and diffuse brain edema (even in distance from the primary site of

tumor) led us to the diagnostic of a pseudo-progression. The appropriate treatment (NaCl) should be given with the aim of increasing serum sodium by 1mmol/l/h (8,9). The endpoint/target should be a symptomless patient or serum sodium of at least 130mmol/l. Our patient's serum sodium increased from 118 to 133 in two days. The encephalopathy improved strikingly, the patient did not develop the osmotic demyelination syndrome and brain edema successfully regressed.

In conclusion, hyponatremia-induced edema or pseudo-progression is a rare etiology in patients with high-grade glioma. However, it should be included in the differential diagnosis of glioma pseudoprogression as in our case.

Conflicts of interest: None declared.

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