Spontaneous intracranial hypotension complicated by malignancy-induced disseminated intravascular coagulation: A case report

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Abstract-

Purpose: Spontaneous intracranial hypotension (SIH) is a rare type of headache. The association of SIH with malignancy and disseminated intravascular coagulation (DIC) has not previously been reported.

Case Report: A 60-year-old woman had orthostatic headache for more than one month before admission. MRI of brain showed diffuse pachymeningeal enhancement with bilateral subdural hematoma. MR myelography revealed epidural fluid collection and possible CSF leakage at the level of C5 to C6. DIC due to carcinoma of unknown origin was found based on evidence of malignant pleural effusion and multiple bone metastases. After correction of coagulopathy, the patient received an epidural blood patch. Unfortunately, follow-up brain MRI showed disease progression. The patient died of acute respiratory failure four weeks after admission.

Conclusion: This is the first case report of an association between SIH and DIC due to malignancy. Further case studies are needed to provide further support of this association.

Key Words: spontaneous intracranial hypotension, disseminated intravascular coagulation

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INTRODUCTION

Spontaneous intracranial hypotension (SIH) has an estimated annual incidence of about 5 per 100,000[(1)]. SIH results from spontaneous leakage of cerebrospinal fluid (CSF) and subsequent low CSF pressure. The typical clinical feature is orthostatic headache. Other features include nausea, spinal pain, diplopia and tinnitus [(2)]. Diagnostic confirmation of SIH requires evidence of low CSF pressure (less than 60 mm CSF) by lumbar puncture or evidence of CSF leakage on imaging studies. Conservative treatments involve adequate hydration and strict bed-rest. If these approaches fail, an epidural blood patch (EBP) is often successful [(2)]. Most patients with SIH have a favorable outcome; however, mortality has been reported due to serious complications, such as subdural hematoma (SDH) or multiple strokes [(3, 4)].

Disseminated intravascular coagulation (DIC) is

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a hemostatic abnormality characterized by excessive coagulation and fibrinolysis, causing bleeding and thrombosis. Common causes of DIC include sepsis, malignancy and trauma [5]. DIC is not only an indicator of poor prognosis from underlying diseases, but also a contraindication for invasive procedures, such as EBP.

Possible risk factors for SIH include connective tissue diseases and bariatric surgery [6,7]. To the best of our knowledge, no publications have reported an association among SIH, malignancy and DIC. In this report, we present a case study of a 60-year-old female with SIH and concurrent DIC due to malignancy.

CASE PRESENTATION

This 60-year-old female was a retired cosmetologist who was relatively healthy prior to this incident. She experienced a bilateral headache, described as a swollen and heavy sensation, in the occipital and nuchal areas for about one month before admission. The uncomfortable sensation was precipitated by a postural change from reclining to standing, and it subsided soon after reclining again. However, acute onset of dizziness, nausea and vomiting developed three days before admission. In the meantime, her headache changed from moderate to severe intensity over her whole head, and postural changes no longer exacerbated her headache. Due to this symptom progression, she visited our emergency department.

In the emergency department, her systolic blood pressure was 176 mmHg, and diastolic blood pressure 103 mmHg. Her consciousness level was intact, and no focal neurologic signs were observed. Laboratory data showed anemia (hemoglobin level: 9.6 g/dL), thrombocytopenia (platelet count: 49000 cells/mm3) and prolonged INR (1.24). Further surveys found decreased fibrinogen levels (95 mg/dL) and increased D-Dimer levels (14.62 μg/ml), and DIC was diagnosed accordingly. Brain CT showed a subacute subdural hematoma of about 8-12 mm in thickness in the left frontotemporoparietal region, about 8 mm in thickness in the right anterior frontal region and very thin-layered subdural hematoma along the falx and right part of the tentorium. Brain MRI revealed not only bilateral SDH, but also diffuse pachymeningeal enhancement, deformity of the midbrain and diencephalon and slight distention of the transverse sinus (Figure 1). MR myelography showed evidence of CSF accumulation along right intervertebral foramen to right paraspinal region at the level of C5-6, and CSF leakage from C5-6 level was suspected (Figure 2). Furthermore, MR myelography revealed right-sided pleural effusion.

EBP treatment was not done immediately because of a concern of coagulopathy. After fresh frozen plasma and plateletpheresis transfusion for several days, prolonged INR and low platelet count were corrected to INR: 1.09, platelet count: 177000 cells/mm^3. Immediately after correction of coagulopathy, EBP was conducted at the level of T6-7 using 18 ml of autologous blood. We chose

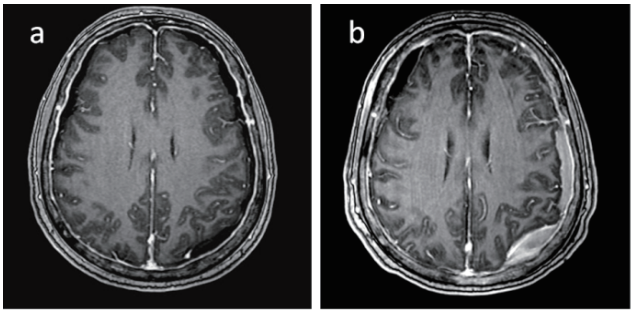

Figure 1. Comparison of T1-weighted brain MRI during admission (a) and one week after EBP treatment (b) showed disease progression. Both images show characteristics of SIH, including diffuse pachymeningeal enhancement and bilateral SDH.

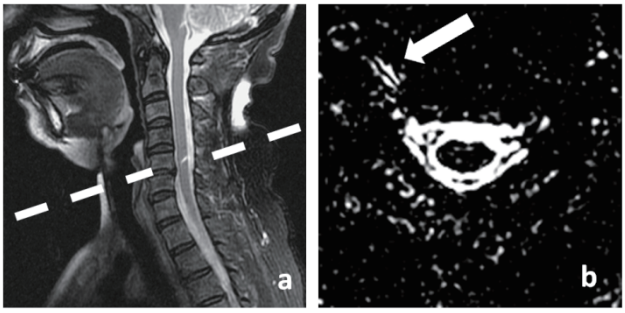

Figure 2. Sagittal view of T2-weighted spine MRI (a) and transverse view of heavily T2-weighted MR myelography at level C5-6 (b). Dashed line in (a) indicates the level of (b), and arrow in (b) indicates CSF accumulation along the right intervertebral foramen to the right paraspinal region, showing the site of CSF leakage.

to conduct EBP at T6-7 rather than C5-6 due to technique and safety concerns. However, symptoms such as headache, nausea and vomiting did not resolve in the days following the first EBP.

Meanwhile, we investigated the possibility of malignancy due to presence of DIC. Serial surveys, including chest and abdomen CT, whole body bone scan and whole body PET scan revealed right-sided pleural effusion and multiple suspected bone metastases in whole spine, sternum and pelvic bone, but no definite tumor mass was found. Subsequent thoracentesis and pleural effusion cytology indicated adenocarcinoma. Carcinoma of unknown primary origin was suspected.

Symptoms of nausea and headache progressed within one week after the first EBP treatment. Follow-up brain MRI showed persistence of pachymeningeal enhancement and greater SDH compared with the previous MRI (Figure 1), indicating disease progression over the three week inter-scan interval.

Delirium, hemoptysis, hematuria and dyspnea developed one week after EBP treatment. The family decided not to perform a blood transfusion or other invasive procedures due to the poor prognosis of carcinoma of unknown primary origin. Dyspnea worsened rapidly, and the patient passed away due to respiratory failure three days after the onset of dyspnea.

DISCUSSION

This case report presents a challenging case with SIH and DIC due to malignancy. The diagnoses of SIH, DIC and malignancy were confirmed by brain MRI, MR myelography, coagulation profile and pleural effusion cytology. To the best our knowledge, this is the first case report demonstrating an association between SIH and DIC due to malignancy.

Malignancy and DIC may have been risk factors for SIH in this patient. Possible mechanisms include: (1) direct tumor invasion through dura and arachnoid mater, and (2) failure to repair CSF leakage due to coagulopathy. To the best of our knowledge, this is the first report of an association between SIH and coagulopathy due to malignancy. Further case reports are needed to support this association.

In the present case, DIC complicated the management of SIH. EBP is considered the first line management for SIH refractory to conservative treatment. However, DIC is a contraindication to EBP. Furthermore, coagulopathy may cause EBP failure. Although the therapeutic mechanism of EBP remains unknown, blood clot formation likely plays a role. In our case, we tried to correct coagulopathy by intensive transfusion of fresh frozen plasma and plateletpheresis. Unfortunately, this patient was unresponsive to EBP.

Although carcinoma of unknown origin has a poor prognosis [8], EBP or alternative treatments could be palliative treatments to reduce patient discomfort. A second EBP, epidural fibrin glue injection or surgical repair could be considered as second line management after failure of the first EBP. Previous studies have shown success rates of the first EBP to be around 30-60%, and subsequent EBPs had cumulatively higher success rates [9,10]. Furthermore, targeted EBP aimed at CSF leakage segments was more effective than blind EBP [11]. A second targeted EBP using a larger blood volume could have been an option for the current patient if coagulopathy was controlled. Second, previous case studies reported that epidural fibrin glue injection may be an alternative to EBP [12]. Fibrin glue injection might have been beneficial in this case because patients with coagulopathy have been shown to have impaired fibrin formation. However, the efficacy of epidural fibrin glue injection remains to be validated by large-scale randomized controlled trials. Third, surgical repair of the CSF leak could have been considered in this case if all non-surgical managements failed. The advantage of surgical repair would be that the SDH drainage could be done concurrently.

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