Case Report

Small-cell lung cancer with Mallory-Weiss syndrome as the prominent manifestation

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Abstract: The presence of Mallory-Weiss syndrome (MWS) in patients with small-cell lung cancer (SCLC) is uncommon. MWS is characterized by longitudinal superficial mucosal laceration at the esophagogastric junction and can be caused by a variety of causes, with upper digestive tract hemorrhage as the primary manifestation. SCLC is the most invasive histological subtype of lung cancer, and approximately a quarter of all SCLC patients undergo paraneoplastic syndrome of inappropriate antidiuretic hormone secretion, such as hyponatremia. In this study, we report a case of MWS in a middle-aged patient who was diagnosed with SCLC associated with hyponatremia. Clinicians should be alerted of the presence of MWS in upper gastrointestinal bleeding, such as epigastric pain, hematemesis, or melena, and keep SCLC in mind as a potential cause for underlying disease identification.

Keywords: Mallory-Weiss syndrome, small-cell lung cancer, hyponatremia, paraneoplastic syndromes

Introduction

Mallory-Weiss syndrome (MWS) is commonly defined as a critical condition in which a sudden surge in pressure of the abdomen and stomach generates mucosal lacerations at the junction of the esophagus and the cardia, thereby causing symptoms of upper gastrointestinal bleeding [1]. Therefore, it is also known as Mallory-Weiss tear or gastro-esophageal laceration syndrome [2]. MWS tends to occur in patients in their fourth or fifth decade of life even though MWS has been observed in all age groups [2]. The incidence of MWS is higher in males than in females, with a ratio of 2:1 to 4:1 [3].

Small-cell lung cancer (SCLC) is a subtype of pulmonary neoplasms that is marked by its aggressive biological behavior and poor clinical course, which is different from that of non-small-cell lung cancer (NSCLC) [4], constituting 13%-20% of all primary lung neoplasia [5]. Originating from Kulchisky cells or argyrophilic cells in the neuroectoderm, SCLC results in paraneoplastic syndromes due to its harboring of endocrine function, and the syndrome of inappropriate antidiuretic hormone secretion (SIADH) is one of the manifestations [4]. As a critical complication of SCLC, SIADH is a consequence of the ectopic secretion of antidiuretic hormone (ADH, also known as vasopressin, VAP) and generally occurs as hyponatremia. Hyponatremia predominantly occurs in 25% of SCLC patients compared with the incidence of 2%-4% of NSCLC patients [6].

SCLC with MWS as a significant characteristic is extremely rare. In the present study, we describe a case of MWS, which was due to SCLC accompanied by hyponatremia, and possible causes based on our experience and previous studies are discussed.

Case report

A 50-year-old male (smoker) with a family history of cancer was admitted for a productive cough and right-sided chest pain of 2 months’ duration. More than a week prior to admission, he had a severe episode of the hiccups, which was associated with vomiting, occasionally coffee-ground substances (a sign of upper gastrointestinal bleeding), acid reflux, and a burning
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sensation behind the sternum. On computed tomography (CT) scans, a mass lesion of approximately 4.2 × 3.8 cm in soft tissue density was observed in the right lung hilum with enlarged mediastinal lymph nodes and nodules. In addition, patchy ground-glass opacities on bilateral lung fields were discovered (Figure 1). The fiber bronchoscope was employed to achieve a pathological diagnosis but was not successful. Subsequently, the patient experienced upper gastrointestinal hemorrhage and presented with hematochezia with one episode of hematemesis and a fever. A painless gastroscopy was employed to diagnose MWS (Figure 2) followed by biochemical investigations revealing reduced contents of serum sodium (120.3 mmol/L), serum potassium (3.19 mmol/L), serum chlorine (85.5 mmol/L), and an increased urine sodium content (459 mmol/L). The concentrations of tumor markers were as follows: carcinoembryonic antigen 5.55 ng/mL and neuron-specific enolase 21.13 ng/mL, respectively, but other markers such as alpha-fetoprotein were in the normal range. The diagnosis of limited-stage small cell lung cancer (ct4N2M0, IIIIB) was confirmed by the histopathologic findings of the lymph nodes, which were obtained by puncture via endobronchial ultrasound (EBUS) (Figure 3A and 3B). Furthermore, the immunohistochemical analysis was positive for chromogranin A, synaptophysin, thyroid transcription factor-1, PCK (focal), and Ki67 positive tumor cells, which accounted for about 80% of the total cells (Figure 3C-F).

Subsequently, the patient was referred to the Lung Cancer Center to undergo chemotherapy with cisplatin plus etoposide after receiving acid suppression, hemostasis, anti-infection, electrolyte disorder correction, and other symptomatic treatment at the Department of Digestion. At the start of chemotherapy, refractory hyponatremia was still present, and the level of serum sodium decreased to 113.8 mmol/L. Administration of fluid restriction combined with hypertonic saline infusion and supportive therapies were initiated, and the patient tolerated the regimen well. At present, he has completed the first cycle of chemotherapy and sodium levels increased and are stable.

Discussion

Although MWS is frequently manifested in miscellaneous diseases, the underlying mechanisms of action have only been partly elucidated. Therefore, studies that focus on MWS have provided us advances in the understanding of this disease. MWS is one of the rare causes of upper gastrointestinal bleeding, accounting for...
1%-14% of all cases [7, 8]. As firstly described by Mallory and Weiss in 1929, MWS was proposed to be associated with recurrent vomiting attributed to alcoholism and eating disorders [2, 9]. During severe nausea or forceful vomiting, contractions of the diaphragm result in shearing forces and cause mucosal tears, however in less common instances, etiological factors could include hiccups, severe coughing, chest trauma, blunt abdominal trauma, epilepsy, severe acute asthma, constipation, delivery, endoscopic examination, lifting weights and many more [2, 9]. Most MWS patients mainly present with the onset of hematemesis as the initial symptom, and a large amount of bleeding needs to be differentiated from esophageal varices hemorrhage caused by liver disease [10]. However, the characteristic of MWS is the presence of vomiting inducement, and most patients lack a relevant medical history regarding liver disorders. The definitive diagnosis of MWS is dependent on endoscopy [11]. Since hemorrhage due to MWS is self-limiting, emergency gastroscopy with a higher probability of finding lesions is recommended [11, 12]. Because of excessive or prolonged bleeding in some MWS patients, and the lack of canonical physical signs for identification, if not diagnosed and treated in a timely fashion, these patients may be prone to develop shock or death. Therefore, it is critical for clinicians to be aware of MWS and administer etiological and symptomatic regimens following the identification of the pathogenesis [13].

In published studies, it has been demonstrated that MWS is an unusual sign of lung neoplasms [14]. Clinical manifestations of lung cancer are involved, which can be roughly classified into the following four categories: primary tumor, intrathoracic spread, distant metastasis, and extrapulmonary manifestations of the paraneoplastic syndrome [15]. Tumors related to MWS are rarely encountered, especially lung cancer, and most of the identified cases are related to chemotherapy. In 1977, Enck described the occurrence of MWS after chemotherapy including 5-fluorouracil (5-FU) and methyl-(2-chloroethyl)-3-cyclohexyl-1-nitrosourea (methyl-CCNU) for an obstructing adenocarcinoma of the right ascending colon [16]. After this finding, cases of chemotherapy-induced MWS in patients with recurrent cervical cancer, liver metastasis of breast cancer and lung cancer, and multiple metastatic lesions of lung cancer were observed. The antineoplastic agents involved included cisplatin, cyclophosphamide, doxorubicin, and 5-FU, which were adminis-
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tered via intravenous infusion as well as oral erlotinib, an epidermal growth factor receptor-tyrosine kinase inhibitor [14, 17, 18]. It has previously been reported that most tears only occur at the mucosal level, and despite the potential of massive bleeding, they alleviate spontaneously without surgical intervention [19]. Of the five cases mentioned above, three did not require a blood transfusion, one resolved with blood transfusion therapy, and one patient underwent operative management after failure of conservative treatment. Our patient received a diverse range of symptomatic management, and his hemorrhage mitigated without the need for a blood transfusion.

In cases like our patient’s, where one presents with MWS, while the exact reason why the patient developed MWS has not been identified, the repetitious hyperemesis arising from hyponatremia due to SIADH in an SCLC patient appears to be the most likely cause. Furthermore, the possibility of a role for the fiberoptic bronchoscopy that the patient had been subjected to before hospitalization for hematemesis could not be ruled out, because this might induce sudden nausea and vomiting, leading to cardiac mucosal tears [9]. The case described here illustrates the importance of timely identification and treatment of the underlying disease when a Mallory-Weiss tear is found, particularly in patients with SCLC. SCLC is highly malignant, but patients with hyponatremia are frequently overlooked because of inconspicuous respiratory symptoms. These patients usually present to other departments, including gastroenterology, neurology, and endocrinology, because of non-specific symptoms, such as retching, vomiting, loss of appetite, weakness, malaise, and lethargy [20]. SCLC is rendered as a diagnosis when further examinations are completed. Initially, our patient was admitted to the Department of Gastroenterology for vomiting and hemorrhage of the upper alimentary tract. Subsequently, MWS was confirmed by endoscopy, and symptomatic management was recommended. Nevertheless, hyponatremia was not corrected until chemotherapy was administered with a definite diagnosis of SCLC.

Collectively, we observed a relatively rare case of MWS in an SCLC patient that was complicated with hyponatremia due to SIADH. Thus, our findings indicate that the possibility of MWS should be considered in the differential diagnosis of epigastric pain, hematemesis, or melena. Furthermore, pulmonary neoplasia, especially SCLC, may cause paraneoplastic SIADH and hyponatremia, which may further cause MWS through nausea and vomiting. Therefore, when encountering patients with unexplained MWS, clinicians should be aware of SCLC, so as not to misdiagnose the patient.

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