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Case Report

Hepatic encephalopathy and acute high fever neuroleptic malignant syndrome induced by incomplete intestinal obstruction

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Abstract: Hepatic encephalopathy and intestinal obstruction are relatively common diseases in the digestive department, but few studies evaluated the connections between them. A case of hepatic encephalopathy and high fever neuroleptic malignant syndrome (NMS) induced by intestinal obstruction are reported here. More attention should be paid to various rare diseases caused by intestinal obstruction and further understanding of these diseases, especially NMS, is important. The case also reminds non-psychiatrists and non-neurologists that when taking psychotropic or Parkinson's drugs, NMS can be considered during fever, especially those with extrapyramidal symptoms which are difficult to be explained by primary disease.

Keywords: Hepatic encephalopathy, acute high fever, neuroleptic malignant syndrome, incomplete intestinal obstruction

Introduction

With the development of society and deterioration of the environment, the influence between diseases is more and more widespread, the trend of symptoms diversification and disease complication gradually appears. This requires clinicians to have a higher overall view, a deeper understanding of the relationship between diseases, and more interdisciplinary knowledge. In this paper, a difficult case of two relatively common diseases in the Department of Gastroenterology and Neuroleptic Malignant Syndrome (NMS) is presented. The study provides greater understanding of the relationship between these three diseases, as well as NMS, so as to effectively treat related diseases.

NMS is commonly associated with increasedamount of antipsychotic, fast replacement, combined or sudden withdrawal (the use of dopaminergic drugs in patients with Parkinson disease [1]). There are also 0.07-2.2% reports of the use of conventional doses of antipsychotic drugs [2], even potassium dehydroandrograpolide-succinate injection causingthe disease [3]. The following case is mainly caused by incomplete intestinal obstruction.

Case report

A 31-year-old man was hospitalized, because of nonsense and perversion of sleep. Three days before admission, there was no obvious cause of nonsense and perversion of sleep inverted, absence of fever, headache and vomiting, unconsciousness, limb weakness, numbness, convulsions. The same day to the local hospital to consider the aggravation of schizophrenia, doctor recommend adjusting the dosage of risperidone. After returning home, the drug dose was adjusted for the first day 1 mg, 3 times/day, the second day of 2 mg, 2 times/day, the patient was slightly euphoric. The third day 2 mg, 3 times/day, the patient appeared drowsy, the speech was unclear, the directional force obstacle, in our hospital with "Disorder of Consciousness" and was thus admitted to the Department of Neurology. The patient had chronic hepatitis B for more than ten years. One

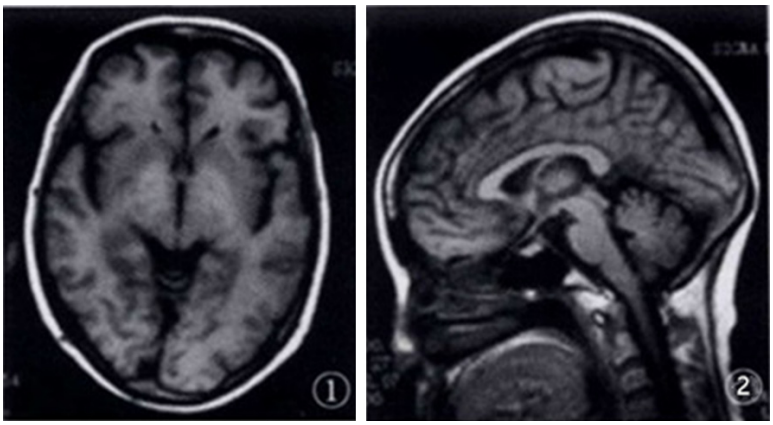

Figure 1. Bilateral globus pallidus see symmetry T1W1 signal increase shadow (1); the anterior pituitary shows increased T1W1 signal (2).

Figure 2. Extensive dilatation of small intestine, accumulation of gas, consideration of simple small bowel obstruction.

years ago, cirrhosis was found and the patient began to take Entecavir antiviral. Schizophrenia was diagnosed for two years, taking risperidone 1 mg, 2 times/day (intermittent drug from nearly three months), symptoms control was acceptable.

Physical examination: Vital signs were normal, drowsiness, speech was not clear, unable to answer, directional force obstacle, spleen under the rib was two transverse finger, bowel sound was low and weak, the rest of the physical examination was normal. The electrocardiogram, blood biochemistry, head CT and other tests were normal. Head MRI: Considering acquired hepatic degeneration (**Figure 1**), blood ammonia 145 U/L, considering hepatic encephalopathy, the patient was given symptomatic treatment, such as reducing ammonia and promoting wakefulness (risperidone 2 mg, 2 times/day). The consciousness of the patient was gradually clear.

The third night the patient complained of abdominal pain, abdominal distension, and stool was not easy to solve. Three times during the period of vomiting gastric contents (the doctor on duty were given metoclopramide treatment). During the period, the patient vomited gastric contents three times (The doctor on duty gave metoclopramide respectively). Supplementary history: the patient had chronic constipation and didnot defecated a week. Physical examination: the left lower abdomen is slightly tenderness, no rebound pain and muscle tension. Immediately the abdominal plain film was taken to consider the incomplete intestinal obstruction (**Figure 2**), the patient was treated with fasting water (family refused gastrointestinal decompression), enema, rehydration, and other symptomatic treatment.

The fourth day, the patient did not have the obvious inducement to appear the fever, the highest temperature was 39 degree, the pulse was 110-120/min, breathing 30 beats/min or so, with more sweat, slight cough, runny nose, and thus the possibility of acute upper respiratory tract infection after nighttime chill was considered. Immediatelythe patient's blood was drawn and reviewed. Abnormal results are shown in **Table 1**. The patient was given oxygen inhalation, piperacillin tazobactam and levofloxacin anti-infection for three days, the effect is poor. The patient also appeared the limb rigidity, double upper limb tremor, drowsiness again. No obvious abnormalities were found in the abdomen, urinary system ultrasound, Chest+ brain CT, lumbar puncture in all indicators did not show any significant abnormalities. Blood cul-

Table 1. Results of abnormal examination of the patient

Lab test	Patient's result	Normal range
Leucocyte count	9.62 × 10^9/L	3.5-9.5 × 10^9/L
Neutrophil percentage	81.2%	40-75%
Alanine aminotransferase	85 U/L	9-50 U/L
Aspartate aminotransferase	72 U/L	5-40 U/L
Creatine kinase (CK)	620 U/L	26-140 U/L
Lactatedehydrogenase (LDH)	480 U/L	115-220 U/L
Procalcitonin (PCT)	0.7 ng/ml	<0.5 ng/ml
C-reactive protein (CRP)	10.1 mg/l	0-8 mg/l

ture, T-SPOT, 1-3-beta-D glucose level (G test) and galactomannan (GM) test, thyroid function, Widal test, Brucella agglutination test antigen, rheumatism immunization full set, bone marrow puncture and culture, a full set of virus (Epstein-Barr virus, cytomegalovirus, herpes simplex virus, rubella virus) were all negative. The results of blood biochemical abnormalities are shown in **Table 1**. There was no obvious abnormality in electrocardiogram and cardiac ultrasound.

The patient still had a high fever so,meropenem plus azithromycin was given for two days, and the patient's temperature was between 38-39.2 degrees Celsius, pulse 160 beats/minor blood pressure 90-160/60-100 mmhg. The patient was dyspneic and oxygen saturation was 88%. Review of blood gas analysis, PCT, blood routine and CRP were basic normal. The Departments of Neurology, General Surgery, Psychiatry, Respiratory Medicine, and Intensive Medicine were consulted. They considered the patient with fever caused by NMS. Antibiotics were stopped and, risperidone and metoclopramide were continued. Dopamine receptor agonist trastal was given to 100 mg/d orally, dantrolene 50 mg/d intravenous injection (25 mg after symptom improvement, oral, three times/day, gradually reduce the dosage), mask oxygen inhalation 3 L/min, ice pillow and cold pack physical cooling, rehydration, alkalize urine, maintain water electrolyte and acid-base balance; keep defecate unobstructed. A week later, the patient's temperature gradually dropped to 37.1-37.4 degrees. The blood pressure was basically stable. The muscle tone was significantly lower than before. The abdominal plain film and liver function basically returned to normal. The patient required to be discharged from the hospital and was asked to take olanzapine 5 mg qd outside the hospital, to maintain smooth stool. After three months of follow-up, the patient's temperature was completely normal and no similar condition occurred.

Discussion

There are two difficulties with this complex case diagnosis.

The first is hepatic encephalopathy, which has been misdiagnosed as an aggravating condition for schizophrenia. Many cases of clinical hepatic encephalopathy are misdiagnosed, especially for patients with frequent hepatic encephalopathy, it is easy for a doctor to form a mindset. There are many reports: cerebral hemorrhage misdiagnosed as hepatic encephalopathy; AIDS encephalopathy misdiagnosed as hepatic encephalopathy; alcohol withdrawal syndrome misdiagnosed as hepatic encephalopathy; central pontine myelinolysis misdiagnosed as hepatic encephalopathy; ketoacidosis misdiagnosed as hepatic encephalopathy and so on. In clinical practice, patients who are hospitalized for the same disease need to ask for medical history, physical examination and carry out necessary examinations so as to identify similarities and differences as early as possible.

The cause of hepatic encephalopathy in this patient is relatively rare chronic constipation, and even constipation eventually forms an incomplete intestinal obstruction. In clinical practice, it must be emphasized the importance of regular defecation, especially for all patients with liver and liver disease-related diseases. There is evidence that chronic constipation is a potential risk factor for many diseases, such as cardio-cerebrovascular disease, mental and psychological diseases (including NMS), and anxiety. Especially for the elderly chronic refractory functional constipation, the treatment time is long, the curative effect is poor. In clinical treatment of constipation and even incomplete intestinal obstruction, it is necessary to be vigilant for the aggravation of intestinal obstruction caused by enemato pay attention to the sudden cardiac arrest caused by gastrointestinal decompression, and the effect of the depth of gastric tube insertion on the decompression effect. If necessary, the insertion depth of gastric tube should be moderately adjusted.

The second diagnostic difficulty is rare fever. Fever has been the most difficult problem in clinic because of its many etiology, miscellaneous and lack of specific detection methods. Although laboratory testing technology and medical level have been improved continuously, but 15% to 50% of unexplained fever is still unable to clear the pathogenicity [4], curative effect is poor.

There are many risk factors for NMS. Relatively rare: stress, menstrual cramps, frequent fluctuations in PD, constipation, intestinal obstruction, surgery and seasonal change, the combination of lithium salt [5], metoclopramide, promethazine and tricyclic antidepressant application, intermittent infection, a few patients with motor function fluctuations, hyper metabolism disease, non-intestinal drug administration, previous occurrence of NMS, especially young men and postpartum women; irondeficiency, malnutrition, heavy drinking, certainencephalopathy (dementia, delirium, encephalitisor tumor*etc*.) [6], levodopa holiday therapy. The inducement in this case is that the rapid change of the drug dosage, the application of metoclopramide and the combination of intestinal obstruction.

The NMS diagnosis is based on Levenson criteria. The recent literature is summed up as: high fever (no initial infection basis, before other symptoms appear, antipyretic analgesics is generally ineffective. Later, it may be complicated with lung, urinary tract infections, *etc*. When fever has severe extrapyramidal symptoms, with other symptoms of plant neurological dysfunction, low heat can be); myotonia (slow movement, muscle stiffness) or extrapyramidal symptoms (akinesia, stupor, dysarthria, dysphagia or silence *etc*.); serum CK increased (slightly elevated, more than four times higher is more meaningful). Secondary symptoms: recurrent tachycardia (normal value is more than 25%); changes in blood pressure (systolic or diastolic blood pressure greater than or equal to 25%; diastolic blood pressure change is greater than 20 mmHg in 24 hours and systolic pressure change is greater than 25 mmHg); dyspnea (normal value is more than 50%) [7]; change of consciousness is the day light and night heavy; hyperhidrosis (sweating); white blood cell elevation. At the same time with the three main symptoms or have two main symptoms and four secondary symptoms, excluding malignant hyperthermia, lethal catatonia, 5-hydroxytryptamine syndrome, serotonin syndrome, heat stroke, anticholinergic drug poisoning, lithium intoxication, the general central nervous system infection, infectious diseases, toxic diseases, metabolic diseases, NMS can be diagnosed. Addonizizio reports that urinary incontinence is also useful in the diagnosis of this disease. Patients with PD should be considered NMS if there is a sudden exacerbation of symptoms or high fever within a short period, although there is no drug change (including dosage) [8], this kind of patients if the drug side effects such as hallucinations and other psychiatric symptoms do not suddenly reduction or even stop immediately. Anti-Parkinson drugs combined with anti-psychotic drugs should be extra careful, the patients' reaction was closely observed in the use and the level of creatine kinase was monitored regularly.

After considering NMS, it is necessary to discontinue the pathogenic drug as early as possible. Patients with PD also need to give the pre-dose of dopamine replacement therapy before NMS. Sixty-three percent of the patients improved in one week after disabling the drug. There is also residual disease symptoms of Parkinson's disease and catatonia for weeks reported after the relief of acute symptoms [9]. At the same time, it is suggested that early combined application of muscle relaxant dantrolene sodium and small dose of dopamine receptor agonist bromocriptine. Pay attention to prevention and treatment of complications. The patients who are refractory to symptoms can be considered electroconvulsive therapy. There was a report on the effective treatment of large doses of vitamin B6 and vitamin E [10].

In conclusion, the case reminds us that malignant syndrome may be considered when fever is difficult to diagnose. Special attention should be paid to rare causes of hepatic encephalopathy and the rare conditions caused by intestinal obstruction as an inducement.

Disclosure of conflict of interest

None.

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