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CASE REPORT

Misdiagnosis of Bone Metastasis Cancer After Using Adefovir Dipivoxi in a Hepatitis B Patient with Fanconi Syndrome

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Abstract Adefovir dipivoxil is commonly used for treatment of chronic hepatitis B patients. We present a case of acquired Fanconi syndrome and hypophosphatemic osteomalacia in a patient with chronic hepatitis B who had been treated with ADV for 8 years. A 41-year-old man complained of severe bilateral hypochondrium pain and lower limb weakness, and he had the diagnosis of bone metastasis cancer or multiple myeloma. Laboratory results and radiologic findings suggested Fanconi syndrome with osteomalacia after hospitalized. For it is difficult to accurately diagnose in clinic and prone to misdiagnose, more attention should be paid to the kidney damage in the patients treated with long-term ADV.

Keywords Acquired Fanconi syndrome · Adefovir dipivoxil · Hypophosphatemia · Bone metastasis cancer

Introduction

China is a country of high morbidity of chronic hepatitis B. Adefovir dipivoxil (ADV) is commonly used as an antiviral agent in the treatment of chronic hepatitis B or human immunodeficiency virus (HIV) infection. Investigations revealed hypophosphatemic osteomalacia might occur in chronic hepatitis B patients with long-term use of ADV at a dosage of 10 mg daily [1]. The clinical features were acquired Fanconi syndrome, such as slowly progressive weakness, bone pain and electrolyte and mineral abnormalities. This kind of disease was prone to be misdiagnosed in clinic as bone metastasis cancer and other kidney disease, so should be brought to the forefront.

Here we report a case of acquired Fanconi syndrome and hypophosphatemic osteomalacia in a B virus (HBV) patient treated with ADV at a dose of 10 mg daily for 8 years and had been hospitalized in the hematology department.

Case Report

A 41-year-old man was admitted to our hospital with the complaint of the bilateral hypochondrium pain, lower limb weakness and spasmodic pain leading to physical inactivity. He complained of severe chest wall pain as well as lower limb weakness over the previous 6 months. The pain was initially dull and aching but worsened during physical activity, so worse that he could only walk with assistance. He had received various paregoric therapy, such as Tramadol, Ibuprofen and Oxycodone hydrochloride controlled-release tablets, but inefficacious. The ECT that he had received in other hospital showed there was multiple active bone metabolism on left eighth rib ridge joint and bilateral ribs. The syndrome was suspected as osseous metastasis from tumor. The PET–CT showed there were multiple local hypermetabolic and osteogenic bone restore focus on the left second anterior rib, the fourth, fifth, sixth and seventh rib, right fifth anterior, eighth, ninth rib, left femoral trochanter and sacrum (S1). Therefore, he came to our hospital for a hematology consultation with suspecting multiple myeloma or metastatic carcinoma.

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The patient's previous medical history included hepatitis B treated with (10 mg/d) for 8 years. Laboratory findings showed a white blood cell count of 6,000/mm^3 and blood sedimentation 3 mm/h. Analysis of his laboratory data revealed a serum sodium of 141 mmol/L and chloride of 114 mmol/L, potassium 3.3 mmol/L and creatinine 75.3 mmol/L. He had decreased level of serum phosphorus 0.39 mmol/L (0.81–1.49), uric acid (UA) 82.1 umol/L (155.0–428.0), calcium 1.98 mmol/L, elevated level of alkaline phosphatase 543.8 U/L (40–120) and creatine kinase isoenzyme 38.8 U/L (0–25). Glucosuria and proteinuria in the absence of hyperglycemia were noted. The parathyroid hormone (PTH) level was normal (30.12 pg/mL; normal range, 10–65 pg/mL). The level of calcium and phosphorus of his urine was 1.10 and 2.18 mmol/L, respectively. Therefore, it brought about the presence of a hyperchloremic nonanion gap metabolic acidosis, hypokalemia, hypophosphatemia, glucosuria, and proteinuria. The results of bone marrow picture, immunophenotyping and bone marrow biopsy were all normal. The gastrointestinal endoscopy was also normal. Dual-energy X-ray absorptiometry (DXA) showed a decreased lumbar spine bone mineral density (BMD) of 0.660 g/cm^2 (T-score, −3.5) and a total hip BMD of 0.363 g/cm^2 (T-score, −4.8). Thoracic vertebrae and chest radiography showed that the fourth, fifth, sixth and seventh rib osseous abnormality. The plain radiographs of the lumbar spine of this patient showed that lumbar vertebra was osteoporosis. The radiography of pelvic hammock was normal.

In conclusion, other causes were excluded, such as multiple myeloma, metastatic carcinoma and other tumors. Meanwhile, a diagnosis of Fanconi syndrome and hypophosphatemic osteomalacia was made and thought to be caused by the antiviral medication. Thus, he switched over from ADV to entecavir, and took neutral phosphate orally (disodium hydrogen phosphate 73.1 g +monopotassium phosphate 6.4 g +water 1,000 ml).One month later, several laboratory parameters returned to normal, and his pain was considerably relieved. Correspondingly, the patient no longer needed a cane for walking. Follow-up six months, Hepatitis B virus DNA concentration maintain normal by detecting the blood once a month.

Discussion

Here we reported a case of Fanconi syndrome and hypophosphatemic osteomalacia in a chronic hepatitis B patient. This patient had taken adefovir at a dose of 10 mg per day for 8 years. The patient demonstrated several features of acquired Fanconi syndrome, including bone pain, electrolyte and mineral abnormalities, and evidence of renal tubular dysfunction.

Fanconi syndrome is a generalized dysfunction of the proximal renal tubules without primary glomerular involvement [2, 3].

It is typically characterized by variable degrees of phosphate, amino acids or glucose wasting by the proximal tubules. In addition, hypokalemia, hypouricemia, metabolic acidosis and low-molecular-weight proteinuria can be part of the clinical spectrum. The resulting electrolyte imbalance and osteomalacia cause symptoms of muscle weakness, fatigue, bone pain, and fractures. Acquired forms of Fanconi syndrome are caused by paraproteinemia, Sjögren syndrome, primary biliary cirrhosis (PBC) and drugs such as cisplatin [4–6]. Osteomalacia is a metabolic bone disease that leads to softening of the bones and can be caused by hypophosphatemia [7]. The clinical features of hypophosphatemic osteomalacia were slowly progressive distal muscle weakness, bone pain or even fracture. For its difficulty to accurately diagnose in clinic, more attention should be paid to.

Acquired Fanconi Syndrome is not rare. There was some important pathogenesis of Fanconi syndrome. First, drug: included aminoglycosides, valproate, methyl-3-chromone, paraquat [8],L-lysine [9], tetracycline, ifosfamide and adefovir. Second, tumor such as multiple myeloma and amyloidosis and so on [10]. Third, heavy metal poisoning, such as chromium and lead. Fourth, immune factors, such as primary Sjgren's syndrome and drug allergy and so on.

ADV [11], the prodrug of adefovir and a structurally similar acyclic nucleoside analogue, is known to cause adverse events when used in the treatment of HIV infection at dosages of 60–120 mg/day and has been shown to exhibit nephrotoxicity, typically taking the form of a gradual increase in serum creatinine with a concomitant decrease in serum hosphorus.

In our literature review, we found six reports of China and eleven reports of other countries of severe hypophosphatemia from 2002 to 2012. The time range of occurring adverse reaction oral ADV was 2–4 years. The case we report had taken ADV orally for eight years, so diagnostic-suspicious bias to multiple myeloma and metastatic carcinoma at the beginning.

We suggest that chronic hepatitis B patients who take ADV over a long period of time should be checked with regular laboratory monitoring, including tests of serum phosphorus, creatinine, potassium and calcium. If laboratory tests indicate that Fanconi syndrome is possible, ADV should be replaced by other antiviral agent in order to prevent complications.

Conflict of Interest The authors declare no conflict of interest.

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