Original Article

Megaloblastic anemia with hypotension and transient delirium as the primary symptoms: report of a case

Qin Zhang, Xue-Ying Lv, Yun-Mei Yang

Department of Geriatrics, The First Affiliated Hospital, School of Medicine, Zhejiang University, Hangzhou, China

Received April 10, 2015; Accepted September 23, 2015; Epub October 15, 2015; Published October 30, 2015

Abstract: The present study describes a case of an elderly patient that was hospitalized secondary to hypotension and delirium. Physical examination at admission revealed bilateral positive Babinski’s sign. Laboratory examination revealed severe anemia. Bone marrow examination showed megaloblastic changes of the granulocyte and erythroid series, as well as other dyserythropoiesis. The conditions of the patient rapidly improved after vitamin B$_{12}$ treatments. Because the clinical manifestations of megaloblastic anemia are complex, this disease is often misdiagnosed in the geriatric population. Bone marrow examinations can aid in the diagnosis of anemia, but the results from these tests cannot always differentiate the type of anemia. Clinical management of the disorder is reliant upon proper classification of the type of anemia. The prognosis of megaloblastic anemia is typically good and a simple regimen of folic acid and/or vitamin B$_{12}$ is effective.

Keywords: Megaloblastic anemia, hypotension, delirium, vitamin B$_{12}$, elderly

Introduction

Megaloblastic anemia is the nutritional anemia induced by folic acid and/or vitamin B$_{12}$ deficiency [1]. This condition is frequently seen in children, but recent reports have revealed that this condition may also occur in elderly individuals. Because the clinical manifestations of megaloblastic anemia are complex, this disease is often misdiagnosed in the geriatric population. Bone marrow examinations can aid in the diagnosis of anemia, but the results from these tests cannot always differentiate the type of anemia. Clinical management of the disorder is reliant upon proper classification of the type of anemia. The prognosis of megaloblastic anemia is typically good and a simple regimen of folic acid and/or vitamin B$_{12}$ is effective [2].

Case presentation

A 75 year old male teacher was hospitalized due to “dizziness, vomiting and disturbance of consciousness for one day” on June 30, 2010. One day prior to his hospitalization, the patient reported dizziness, nausea and vomiting without an obvious cause. Subsequently he became confused, restless, and developed urinary and fecal incontinence. His admission examination revealed a body temperature of 37.1°C, pulse of 67, respiratory rate of 16 and blood pressure of 91/49 mmHg. The patient was conscious and had no yellow staining on his skin and sclera, no swelling in superficial lymph nodes and no areas of obvious bleeding. The patient had clear breath sounds without wet or dry rales. The patient had a normal sinus rhythm and his abdomen was soft. The liver and spleen were not palpable. No swelling was found in lower extremity and bilateral Babinski’s sign was positive.

The patient reported a poor vegetarian diet, which he attributed to a change in residence. In the time since his diet changed, the patient reported that he frequently experienced episodes of dizziness and bilateral weakness in both lower extremities. He had previous hospital admissions for these symptoms and had been diagnosed with cervical syndrome, for which he reported undergoing traditional Chinese medicinal treatments. The patient reported a dramatic weight loss of 10 kg in the last six months.

Routine blood examinations revealed a white blood cell count of 6.3×10^9/L, neutrophils of 85.9%, hemoglobin of 40 g/L, mean corpuscu-
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Figure 1. Changes in bone marrow on June 30: Megaloblastic changes and other dyshaematopoiesis phenomena can be found in granulocyte and erythroid series.

Figure 2. Bone marrow on July 9: No megaloblastic changes and other dyshaematopoiesis phenomena can be found.

Lar volume (MCV) of 122.9 fl, mean corpuscular hemoglobin (MCH) of 44.7 pg, mean corpuscular width of 23.1%, platelet count of 43×10^9/L. Blood clotting function was normal, blood urea nitrogen was 9.37 mmol/L, serum sodium was 132 mmol/L, lactate dehydrogenase was 1270 U/L, hydroxybutyrate dehydrogenase was 1282 U/L. Follow-up laboratory values revealed C-reactive protein of 18.0 mg/L and the parathyroid hormone levels of 89.7 pg/mL. Routine urine examination was normal and blood biochemical analysis showed a decrease in globulin and bilirubin of 26 u. Low density lipoprotein cholesterol and very low density lipoprotein cholesterol were lower than normal values. All other biochemical indexes were normal. Rheumatoid factor (RF), anti-streptolysin-o test (ASO), antinuclear antibody (ANA) and anti-neutrophil cytoplasmic antibody (ANCA) were all negative. Cranial CT scan revealed no obvious hemorrhagic focus. The cranial MRI revealed a few ischemic foci near the front and back angles of the lateral cerebral ventricles and the left centrum ovale. Cervical MRI revealed cervical degeneration of the discs at the C5/C6 and C6/C7 levels. This finding was also associated with central protrusion. Thoracic CT revealed a small amount of bilateral effusion in the thoracic cavity. A few infectious lesions were found in the left lung ligule and fibrous proliferative foci were found in both lungs. Ultrasound analysis of the heart revealed aorta atherosclerosis, left ventricular diastolic dysfunction and mild mitral and tricuspid regurgitation. No obvious abnormality was found in the thyroid. EEG analysis revealed a slow α active EEG. Bone puncure was carried out on the day of admission and revealed megaloblastic changes and other dyshaematopoiesis phenomena can be found in granulocyte and erythroid series (Figure 1).

The initial course of treatment at the hospital included intravenous fluids and a blood transfusion. After transfusion and fluid supplementation, the patient’s urinary output increased and his heart rate remained normal, but his blood pressure remained low. The patient received a dopamine infusion over the night to maintain blood pressure at 90-140/60-85 mmHg. Further hospital course of treatment included 10 mg folic acid that was administered orally TID and 1 mg of vitamin B_{12} was injected intramuscularly QD for five days. After 5 days this regimen was changed to 5 mg folic acid administered orally TID with a 1 mg intramuscular injection of vitamin B_{12} QOD.

Routine blood analysis was reassessed on July 9 and revealed the following: white blood cell count 8.5×10^9/L, neutrophils (%) 82.8%, hemoglobin 69 g/L, platelet count 230×10^9/L, reticulocyte of 4.3%. Routine examination of bone marrow on July 9 revealed no megaloblastic changes and no other dyshaematopoiesis phenomena were found (Figure 2).

The patient’s condition gradually improved after the initial admission. Dizziness and fatigue were alleviated and the patient’s mental status and appetite improved. The patient’s pain in the neck and waist region gradually disappeared, as did the hallucinations. The patient’s blood pressure became more stable and the dopamine dose was gradually decreased until it was completely withdrawn on July 14, at which time oral administration of midodrine hydrochloride tablets was prescribed to maintain a stable blood pressure. Hemoglobin and platelets increased steadily. The patient began
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Table 1. Change in routine blood examinations

<table>
<thead>
<tr>
<th>Date</th>
<th>6/29</th>
<th>6/30</th>
<th>7/1</th>
<th>7/2</th>
<th>7/5</th>
<th>7/7</th>
<th>7/9</th>
<th>7/10</th>
<th>7/12</th>
<th>7/27</th>
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<tbody>
<tr>
<td>Hemoglobin (g/L)</td>
<td>40</td>
<td>63</td>
<td>80</td>
<td>79</td>
<td>82</td>
<td>73</td>
<td>69</td>
<td>70</td>
<td>86</td>
<td>98</td>
</tr>
<tr>
<td>MCH (pg)</td>
<td>41.7</td>
<td>38</td>
<td>34.9</td>
<td>36.1</td>
<td>35.8</td>
<td>34.4</td>
<td>32.9</td>
<td>32.6</td>
<td>32</td>
<td>30.9</td>
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<tr>
<td>MCHC (g/L)</td>
<td>339</td>
<td>364</td>
<td>365</td>
<td>376</td>
<td>364</td>
<td>336</td>
<td>345</td>
<td>338</td>
<td>328</td>
<td>325</td>
</tr>
<tr>
<td>MCV (fl)</td>
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<td>104.2</td>
<td>95.6</td>
<td>95.9</td>
<td>98.3</td>
<td>102.4</td>
<td>95.2</td>
<td>96.3</td>
<td>97.4</td>
<td>95.3</td>
</tr>
<tr>
<td>Plates (×10^9/L)</td>
<td>43</td>
<td>40</td>
<td>25</td>
<td>16</td>
<td>42</td>
<td>65</td>
<td>230</td>
<td>342</td>
<td>521</td>
<td>277</td>
</tr>
<tr>
<td>Reticulocytes (%)</td>
<td>0.7</td>
<td>0.4</td>
<td>1.1</td>
<td>1.1</td>
<td>3</td>
<td>3</td>
<td></td>
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</tr>
</tbody>
</table>

MCH: mean corpuscular hemoglobin, MCHC: mean corpuscular hemoglobin concentration, MCV: mean corpuscular volume.

Results

At a four month follow-up, the patient reported he was living in his original place of birth and he had not had any repeated episodes of the original symptoms. He reported that he had no difficulties with activities of daily living and had returned to eating a normal and healthy diet that was not restricted to vegetarian options. He reported that he was happy to be able to walk in the park every day. This patient continued a low dose folic acid and vitamin B12 regimen, and repeat blood examinations and blood pressure examinations in a local hospital were all normal at the follow-up period.

Discussion

The key characteristics of this case included: 1) Elderly male patient; 2) Primary symptoms of hypotension and delirium; 3) Severe anemia; and 4) Megaloblastic anemia as evidence through bone marrow examination. The patient’s condition improved after treatment with folic acid and vitamin B12.

Megaloblastic anemia is a nutritional anemia induced by deficiencies of folic acid and/or vitamin B12. Vitamin B12 deficiency is frequently seen in the clinic and the incidence of this disorder increases with age. Dietary vitamin B12 deficiency, rare in childhood, although is common in the elderly. More than 9% of the anemia cases in elderly people are induced by vitamin B12 deficiency, while 3-12% of the geriatric population has low vitamin B12 levels [3-5]. The patient in this case study ate poorly and had a primarily vegetarian diet due to changes in his residence. Intestinal absorption decreases with age, so this factor along with a poor diet may have contributed to the vitamin B12 deficiency. The significant 10 kg weight loss during the previous year was disconcerting, but systemic physical examination revealed that the weight loss was not likely attributable to cancer, hyperthyroidism, diabetes or other common diseases. Routine blood examination for this patient showed severe anemia and his MCV, MCH and mean corpuscular width were also significantly higher than normal levels. In addition, lactate dehydrogenase was significantly increased and mild jaundice was detected, indicating that ineffective hematopoiesis in bone marrow or hemolysis of red blood cells. These results supported the diagnosis of megaloblastic anemia, which was verified by characteristic changes in the bone marrow examination on the day of admission. The bone marrow morphology was significantly improved after treatment. After the patient was treated with folic acid and vitamin B12 for 12 days, reticulocytes increased by 4.3%, hemoglobin and platelets both gradually increased, and other clinical symptoms also improved. We concluded the diagnostic treatment was effective, which strongly supported the diagnosis of megaloblastic anemia. Sustained improvements were seen at follow-up examination.

The first documented case of postural hypotension induced by vitamin B12 deficiency was reported by Kalbfleish and Woods in 1962 [6], and this condition was considered to be related to autonomic neuropathy. The symptoms asso-
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Vitamin B<sub>12</sub> is an important element for monoamine metabolism. Both vitamin B<sub>12</sub> and folic acid are involved in homocysteic acid methylation to synthesize methionine and ademetionine. Vitamin B<sub>12</sub> and folic acid deficiency can lead to disorders within the methylation process and result in the accumulation of homocysteic acid, which may subsequently lead to mental illness [10]. The neurologic manifestations of folate deficiency overlap with those of vitamin B<sub>12</sub> deficiency and include cognitive impairment, dementia, depression, and, less commonly, peripheral neuropathy and subacute combined degeneration of the spinal cord [11]. Vitamin B<sub>12</sub> deficiency has diverse cutaneous and ophthalmic manifestations [12, 13]. Vitamin B<sub>12</sub> deficiency has no or mild symptoms in the early stages, but can lead to substantial neurological impairments if left untreated. This progression can include segmental demyelination and axonal degeneration, which are characterized by weakness of lower extremities, numbness, unsteady gait, and/or psychiatric symptoms, including cognitive dysfunction, memory loss, schizophrenia, etc. Psychiatric disorders induced by vitamin B<sub>12</sub> deficiency may also occur before the appearance of the anemia [14]. It has been reported that vitamin B<sub>12</sub> and folic acid deficiency can lead to conscious disturbances and delirium, which are frequently seen in elderly individuals [15, 16]. The patient in this case suffered from delirium and the possibility of parenchymal diseases was ruled out after cranial MRI and other examinations. Although the vitamin B<sub>12</sub> level was not measured, the mental status of the patient improved after he was administered vitamin B<sub>12</sub> and folic acid tablets. Differential diagnosis including vitamin B<sub>12</sub> deficiencies should be considered in older patients with psychological disturbances.

Conclusion

Bone marrow examinations can aid in the diagnosis of anemia, but the results from these tests cannot always differentiate the type of anemia. Clinical management of the disorder is reliant upon proper classification of the type of anemia. The prognosis of megaloblastic anemia is typically good and a simple regimen of folic acid and/or vitamin B<sub>12</sub> is effective.

Disclosure of conflict of interest

None.

Address correspondence to: Dr. Xue-Ying Lv, Department of Geriatrics, The First Affiliated Hospital, School of Medicine, Zhejiang University, 79 Qingchun Road, Hangzhou 310003, China. Tel:+86-13758264260; Fax: +86 571-87236806; E-mail: XueyingLvdoc@yeah.net

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