Case Report

Autopsy Case of Dubin-Johnson Syndrome with Pneumonia and Abetalipoproteinemia-like Lipid Profile

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We report the autopsy of a 79-year-old Japanese woman with Dubin-Johnson syndrome accompanied by pneumonia, an abetalipoproteinemia-like lipid profile and acanthocytosis. On admission, physical examination of the patient revealed malnutrition. Blood tests revealed marked inflammatory changes and mild liver dysfunction. Chest X-ray indicated bilateral pneumonia. Total cholesterol, low-density lipoprotein (LDL) cholesterol and triglyceride levels were 89 mg/dL, 5 mg/dL and 6 mg/dL, respectively. Peripheral blood smears revealed numerous acanthocytes. Despite the administration of antibiotics and nutritional support, the patient died. Autopsy revealed a black liver, atrophy of fat tissue on the mesentery, and pneumonia with bilateral pleural effusion. We believe that the abetalipoproteinemia-like lipid profiles in this case were caused by malnutrition and the inflammatory changes rather than the direct effects of Dubin-Johnson syndrome. We base this conclusion on the following three findings: 1) the patient’s lipid profile before hospitalization was in the normal range, 2) her serum LDL cholesterol and triglyceride levels gradually increased after nutritional support began, and 3) blood tests revealed marked inflammatory changes (C-reactive protein 9.0 mg/dL; interleukin-6 16.4 pg/mL). This case provides important information that enhances our understanding of lipid metabolism under conditions of malnutrition and inflammation.


Key words; Malnutrition, Inflammatory cytokines, Lipid metabolism, Acute phase response

Introduction

Low serum cholesterol levels are common in critically ill patients with infectious diseases, acute myocardial infarction, or malignant diseases¹-⁴. Changes in serum lipid levels are common in the acute phase response⁵,⁶, and malnutrition is also known to be a cause of hypocholesterolemia⁷. However, it is unusual for a patient to present with depleted lipoproteins, such as occurs with abetalipoproteinemia, even if the patient is critically ill or malnourished. Abetalipoproteinemia is a congenital disorder characterized by (a) a marked decrease in or the absence of apoprotein B-containing lipoproteins and (b) the appearance of acanthocytes in the peripheral blood. The molecular cause of abetalipoproteinemia is a deficiency of a microsomal transfer protein that plays an important role in lipoprotein particle assembly⁸. Here, we report the unprecedented case of a patient with Dubin-Johnson syndrome accompanied by pneumonia, with an abetalipoproteinemia-like lipid profile and acanthocytosis.

Case Presentation

A 79-year-old woman was admitted in October 2004 because of dyspnea and pyrexia. She had an elevated serum bilirubin level in the past and had suffered from jaundice during childhood, but she had not undergone any special examinations such as liver biopsy or laparoscopy. She had been treated with trihexyple-
nidyl hydrochloride and levodopa for the past 5 years for restricted movement in her upper and lower extremities due to multiple system atrophy. She had been confined to a wheelchair for 1 year, and her appetite was reduced. Pyrexia and dyspnea appeared approximately 2 weeks before she was admitted to hospital. On presentation, she was diagnosed with pneumonia and hospitalized for urgent treatment.

On admission, the patient’s body weight and body mass index were 38 kg and 16.6 kg/m², respectively. Her arm circumference, triceps skinfold thickness and calf circumference were 17.2 cm, 0.4 cm and 24 cm, respectively. These physical examination findings indicated malnutrition. The patient’s body temperature was 37.8°C, and the appearance of her bulbar conjunctiva was consistent with jaundice. Fine crackling sounds over both lower lung fields were heard on auscultation. Neither the liver nor spleen was enlarged. Pitting edema was present in the lower extremities. Neurologically, the presence of tremor and the cogwheel phenomenon were compatible with the previous diagnosis of multiple system atrophy.

Blood tests revealed marked inflammatory changes: C-reactive protein 9.0 mg/dL; interleukin-6 (IL-6) 16.4 pg/mL; white blood cell count 9,600/μL (indicative of mild liver dysfunction); total bilirubin 4.1 mg/dL; direct bilirubin 2.7 mg/dL; aspartate aminotransferase 81 IU/L; and alanine aminotransferase 164 IU/L. Serum levels of total protein and albumin were 5.0 g/dL and 2.2 g/dL, respectively. A shadow indicative of pneumonia was seen bilaterally in the lower lung fields on a chest X-ray (Fig. 1).

Total cholesterol, low-density lipoprotein (LDL) cholesterol, triglyceride and high-density lipoprotein (HDL) cholesterol levels were 89 mg/dL, 5 mg/dL, 6 mg/dL, and 50 mg/dL, respectively. The serum level of apoprotein B was 7 mg/dL and the activity of lecithin-cholesterol acyltransferase (L-CAT) was less than 50 U/mL (Table 1). Peripheral blood smears revealed

Table 1. Lipid profile of the patient on admission.

<table>
<thead>
<tr>
<th>Serum lipids</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Total cholesterol</td>
<td>89</td>
</tr>
<tr>
<td>LDL cholesterol</td>
<td>5</td>
</tr>
<tr>
<td>Triglycerides</td>
<td>6</td>
</tr>
<tr>
<td>HDL cholesterol</td>
<td>50</td>
</tr>
<tr>
<td>Free fatty acids</td>
<td>0.04</td>
</tr>
<tr>
<td>Lipoprotein (a)</td>
<td>3</td>
</tr>
<tr>
<td>PLP cholesterol</td>
<td>3.4</td>
</tr>
</tbody>
</table>

Apoproteins

| A-1                        | 107 |
| A-II                       | 8.4 |
| B                          | 7   |
| C-II                       | 1.8 |
| C-III                      | 4.7 |
| E                          | 4.2 |
| L-CAT                      | < 50|

RLP: remnant-like particle

Fig. 1. Chest X-ray taken on admission. Shadows indicating pneumonia were observed bilaterally in the lower lung fields.

Fig. 2. A peripheral blood smear revealed the presence of numerous acanthocytes.
numerous acanthocytes (Fig. 2).

Antibiotic therapy began on the first day of admission. Total parenteral nutrition (TPN), with 17% glucose and essential amino acids, was administered from the fourth day of admission; however, the patient died on the 21st day of admission. Autopsy revealed a black liver, atrophy of fat tissue on the mesentery (Fig. 3, 4) and pneumonia with bilateral pleural effusion.

Changes in serum lipids before and after hospitalization are summarized in Fig. 5. Serum levels of total cholesterol and triglycerides before hospitalization were within the normal ranges (total cholesterol 167 mg/dL; triglycerides 81 mg/dL), and after TPN began, serum levels of LDL cholesterol and triglycerides increased gradually, but HDL cholesterol levels decreased.

Results and Discussion

Here we report an unprecedented case of a patient with Dubin-Johnson syndrome, accompanied by pneumonia, and with an abetalipoproteinemia-like lipid profile and acanthocytosis. The mechanism underlying the development of the abetalipoproteinemia-like lipid profile was complicated in this case, but is nevertheless interesting to consider. As the patient’s total cholesterol and triglyceride levels before hospitalization were in the normal ranges, we do not consider that the cause of the abetalipoproteinemia-like lipid profile in this case was abetalipoproteinemia due to a congenital disorder or the direct effects of Dubin-Johnson syndrome. This supposition is supported by the fact that the lipid profile was improved by nutritional support after hospitalization. Dubin-Johnson syndrome is an autosomal recessive disorder characterized by chronic conjugated hyperbilirubinemia, a dark and greenish liver, and the characteristic lysosomal accumulation of a black melanin-like pigment in the he-
inflammation, also reduce serum cholesterol levels. These studies are needed to evaluate the influence of malnutrition and inflammation on lipid metabolism. However, further understanding of lipid metabolism under conditions of malnutrition and inflammation may provide important information that will enhance our knowledge of the pathogenesis of hypercholesterolemia in sepsis and critically ill or injured patients. Crit Care, 2003; 7:413-414.


9) Dubin IN and Johnson FB: Chronic idiopathic jaundice with unidentifed pigment in liver cells; a new clinicopathologic entity with report of 12 cases. Medicine (Baltimore), 1954; 33:155-179.


