CASE REPORT

Pigmentary Retinopathy with Nephrotic Syndrome, Ménétrier's Disease, and Diabetes Mellitus


A patient with pigmentary retinopathy, nephrotic syndrome, Ménétrier's disease, and diabetes mellitus is presented. Other complications were congestive heart failure, hypothyroidism, hypertension, and hypertriglyceridemia. Hypogenitalism was also suspected. Pigmentary retinopathy is known to associate with many systemic diseases, which are classified into several syndromes. This case superficially resembles Alström's disease due to the common characteristics of pigmentary retinopathy, diabetes mellitus, renal disease, and hypogenitalism. But clinically and histologically, there are distinct differences. To our knowledge, this association has never been reported.

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Key words: Alström's disease, Laurence-Moon-Biedl syndrome, Senior's syndrome, congestive heart failure, hypothyroidism

Introduction

Pigmentary retinopathy is known to be an inherited disease, sometimes associated with systemic manifestations. Recently a middle-aged woman whose parents were consanguineous was hospitalized due to congestive heart failure. She was found to have pigmentary retinopathy, renal insufficiency, nephrotic syndrome, Ménétrier's disease, and diabetes mellitus.

Case Report

A 47-year-old Japanese woman was admitted to our hospital because of general fatigue, orthopnea, and edema. She was well the age of 45 years, when she gradually lost her sight. Her parents were cousins. The family history was unremarkable and her brother and sister were reported to be normal. She was a married woman but could not have any children. She had menopause at age 45. Two months before hospital entry, she realized that her legs were edematous. Then dyspnea and orthopnea appeared. She visited our hospital in December 1992. On physical examination, she was a poorly-nourished pale woman with thin hair. Her height was 153 cm and weight, 47.5 kg. There was marked pitting edema in the extremities. The blood pressure was 162/110 mmHg. On auscultation, systolic murmur was audible at the apex, and moist rales were heard throughout the entire lung field. Neurological examination was negative. Chest X-ray film disclosed cardiomegaly and pleural effusion (Fig. 1A). She was diagnosed as having congestive heart failure. Then she was hospitalized.

Blood examinations disclosed leukocytosis, anemia, marked hypoalbuminemia, renal insufficiency, hypertriglyceridemia, hyperglycemia, hypothyroidism, and mild hyperprolactinemia (Table 1).

Urine analysis showed 3+ for protein, 1+ for glucose, a pH of 5.5, and a specific gravity of 1.025, with 0 to 1 red blood cells and 3 to 6 white blood cells per high-power field in the sediment. The 24-hour urinary protein excretion was in the range of 3.0 to 5.5 g. Nephrotic syndrome was diagnosed.

Ultrasonographic cardiography showed pericardial effusion and poor wall motion of the left ventricle. Ultrasonography of the abdomen disclosed hepatosplenomegaly. Thoracentesis revealed that the pleural fluid was a transudate.

Furosemide and concentrated albumin were administered. Cardiomegaly, pleural effusion, and systemic edema responded to them (Fig. 1B). The body weight decreased to 34 kg, which was thought to be her dry weight.

From the Second Department of Medicine, Kobe University School of Medicine, Kobe, *the Department of Medicine, Nishiwaki Municipal Hospital, Nishiwaki and **the Second Department of Pathology, Kobe University School of Medicine, Kobe

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Reprint requests should be addressed to Dr. Jiro Masugi, the Second Department of Medicine, Kobe University School of Medicine, 7-5-2 Kusunoki-cho, Chu-o-ku, Kobe 650

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Glucose tolerance testing disclosed a serum glucose level of 154 mg/dl at baseline, 261 mg/dl at one hour, 361 mg/dl at two hours, and 335 mg/dl at three hours. Insulin levels were 21.8 μIU/ml at baseline, 36.0 μIU/ml at one hour, 47.7 μIU/ml at two hours, and 58.4 μIU/ml at three hours. A diagnosis of non-insulin dependent diabetes mellitus was made. Insulin antibody was negative. To rule out the secondary nephrotic syndrome caused by malignancies, gastroscopy was performed, which disclosed giant hypertrophic gastritis. Famotidine 40 mg per day was started. Gynecologic examination was within normal limits. Computed tomography of the abdomen was unremarkable except for hepatosplenomegaly. Ophthalmologic examination revealed pigmentary retinopathy. Chromosomal analysis showed a normal female karyotype.

Treatment with prednisolone 40 mg per day started for nephrotic syndrome. After two weeks of the therapy, the 24-hour urinary protein excretion decreased in the range of 1.1 to 1.5 g. However the control of blood glucose worsened and inflammatory reaction appeared. Hyperglycemia was controlled by insulin, antibiotics were administered, and steroids were slowly withdrawn. However pneumonia developed rapidly and it did not respond to antibiotics. Culture of the sputum disclosed methicillin-resistant staphylococcus aureus. She died of acute respiratory failure in March 1993.

Autopsy revealed that kidneys were slightly small. No gross cysts were seen on the surface. Light microscopy disclosed proliferation of mesangial and endothelial cells (Fig. 2A). Electron microscopy disclosed the thickening of basement membrane and deposits in mesangial matrix (Fig. 2B). Glomerulosclerosis was not present. A diagnosis of membranoproliferative glomerulonephritis (MPGN) was made.
The stomach had increased folds in height and thickness, forming a convoluted surface (Fig. 3A). On microscopic examination, hyperplasia of the mucus-producing cells and elongation of the fundic glands were present (Fig. 3B). Ménétrier’s disease was diagnosed.

The lungs were heavy and whitish, and microscopically diagnosed as bronchopneumonia. The pancreas had amyloid infiltration. The uterus was atrophic and microscopically a decrease in endometrial glands was recognized. There were no remarkable findings in the thyroid gland, heart, adrenal glands, and ovaries.

Discussion

The present patient, born of consanguineous marriage, had
pigmentary retinopathy, nephrotic syndrome, Ménétrier’s disease, and diabetes mellitus. Clinically, congestive heart failure and hypothyroidism were also present, but at autopsy no organic diseases were found in the heart and the thyroid. Hypogonitalism was also suspected because of sterility, early menopause, and uterine atrophy at autopsy. The main reason of edema, pleural effusion, and pericardial effusion was thought to be severe hypoalbuminemia due to nephrotic syndrome and Ménétrier’s disease.

Pigmentary retinopathy is known to be associated with systemic diseases. These are classified into several syndromes (Table 2). Among these syndromes, Alström’s disease (1) is superficially most similar to the present case based on the common characteristics of pigmentary retinopathy, renal insufficiency, diabetes mellitus, and hypogenitalism. But the clinical picture of Alström’s disease is an obese child who suffers from blindness and deafness, and in adulthood develops slowly progressive chronic nephropathy. Microscopically, the renal disease is characterized by glomerular hyalinization with tubular basement membrane thickening, tubular atrophy, and interstitial fibrosis (2).

Bardet-Biedl syndrome and Laurence-Moon syndrome usually are associated with obesity, mental retardation, and dwarfism (3). Severe progressive renal disease has been noted to occur in only 15% of these syndromes (4).

The most common of the renal diseases associated with pigmentary retinopathy is Senior’s syndrome (renal retinal dysplasia). This disease is also called medullary cystic disease or juvenile nephronophthisis (5). Microscopic or occasionally macroscopic cysts in the corticomedullary lesions are present. Other renal histologic findings of this disorder are similar to those of Alström’s disease (1).

Alport’s syndrome is a familial disorder characterized by progressive nephritis, sensorineural deafness, and ocular defects. Renal disease manifests itself at an early age. Afflicted females usually have little renal dysfunction while most males develop renal insufficiency. Deafness occurs in approximately two-thirds of affected persons. Cataracts are most common eye lesions and pigmentary retinopathy is uncommon. No distinguishing histologic features of the kidney by light microscopy are noted (6).

Patients with cystinosis develop damage to various organs including kidney, thyroid, eyes, central nervous system, pancreas, and muscle. Cystine crystals are seen by light microscopy in those organs (7). In oxalosis, calcium oxalate deposits are widespread in various tissues (8).

To our knowledge, the association of pigmentary retinopathy with Ménétrier’s disease, nephrotic syndrome, and diabetes mellitus has never been reported. Pigmentary retinopathy is known to be associated with systemic diseases, but the clinical picture does not fit into any of the previously described entities.

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**References**

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