Gastrointestinal Involvement at the Junction of Wolman Disease and COVID-19

A 47-day-old baby girl was referred to our center with a prediagnosis of Wolman’s Disease, after adrenal calcification was detected in her ultrasonography taken as a result of abdominal bloating and vomiting. The patient was born after 38 weeks of gestation, 4780 g, by cesarean section due to macrosomia. There was first degree consanguineous marriage in his family history. Physical examination revealed abdominal distension, hepatosplenomegaly, and hypotonia. Peripheral smear showed lymphocytes with xanthomatous nuclei. LAL was measured as 0.9 nmol/spot/hour. A possible pathogenic homozygous mutation in the LIPA gene, c.652C>T, was detected. Sebilella alfa treatment was started when she was 82 days old at a dose of 1 mg/kg/week. After weight gain and abdominal acidity, the enzyme dose was increased to 1.5 mg/kg/week and 3 mg/kg/week, respectively. The patient was discharged to receive weekly ERT treatment. The patient was admitted to the hospital for the second time when he was 6 months and 21 days old when he applied with the complaint of bloody stool. Laboratory tests revealed thrombocytopenia, mild transaminase elevation and leukocytosis. SARS-CoV-2 Real Time polymerase chain reaction (PCR) was positive in oropharyngeal and nasopharyngeal swab samples. No treatment was given for SARS-CoV-2 because of cough, respiratory distress, low saturation and lack of uptake on chest X-ray. The dose of sebilella alfa was increased to 4 mg/kg/week. SARS-CoV-2 Real Time PCR result was negative on day 21 and he was discharged. A 5.5-month-old patient who was admitted for the first time was also administered the same treatment dose of the alfa. While the patient was given the dose of 3 mg/kg/week, the occasional bloody stools in the follow-up was referred with the preliminary diagnosis of intestinal ischemia and perforation. The patient underwent laparotomy because of the suspicious presence of subdiaphragmatic free air on abdominal computed tomography (CT). Intraoperative intestinal macroscopic appearance was consistent with necrotizing enterocolitis. (Figure 2) All meconium and part of the intestines were covered with yellow-white hard caseous lesions, the largest of which was 4-5 cm. It was observed that the content was also caseous when excised. No perforation was detected. Pathological examination of lymph nodes revealed diffuse xanthomatous histiocytic infiltration and histochimically submucosal staining with oil-red-O. The lymph node sample was found to be positive for COVID-19 PCR. The dose of sebilella alfa was increased to 5 mg/kg/week for the patient who developed postoperative sepsis. The patient was discharged, whose symptoms regressed. He is currently 18 months old and his outpatient follow-up continues.

DISCUSSION

Wolman disease, which is a clinical disease emerging as a result of LAL deficiency in the infantile period, is seen in the clinic malabsorption, diarrhea, abdominal distention, growth retardation due to gastrointestinal involvement; hepatomegaly, high transaminases, impairment in bleeding parameters due to hepatic involvement; adrenal calcification, adrenal insufficiency due to adrenal accumulation. The average life expectancy in Infantile Wolman Disease was 3.7 months, before ERT. Life expectancy with sebilella alfa reached 24 months. It was observed that there was improvement in appetite aminotransferase and alanine aminotransferase values, hepatomegaly and growth with sebilella alfa (3 mg/kg/week) that we followed up. The dose of sebilella alfa was increased to 5 mg/kg/week due to the persistent and severe course of gastrointestinal symptoms and insufficient weight gain. The most demonstrative form of lymph node involvement in Wolman’s disease, enlarged lymph nodes in the mesentry in mice with lysosomal acid lipase deficiency, was found to be due to lipid deposition in macrophages rather than lymphocyte proliferation. In autopsy series, viral nucleocapsid protein was found to be positive in lymph nodes by immunohistochemical methods. However, after SARS-CoV-2 infection, no data was recorded regarding involvement of lymph nodes while SARS-CoV-2 antibodies (IgG and IgM) and COVID-19 PCR were negative. SARS-CoV-2 can bind more to the gastrointestinal tract compared to the lungs. Studies have reported that bloody stools, one of the gastrointestinal symptoms, is seen in 4% of COVID-19 infection. The patient we followed up did not have a history of bloody stool until SARS-CoV-2 infection. We think that COVID-19 infection is associated with SARS-CoV-2 infection. The case was also investigated in terms of food allergies and infectious causes, and these diseases were also excluded. Cases presenting with acute abdomen in SARS-CoV-2 infection have been reported. These patients were given antimicrobial therapy and intensive care support. At SARS-CoV-2 cases in children, whose is the symptoms of acute appendicitis, has been reported multiple mesenteric lymphadenitis in imaging. Surgical treatment was not required in these patients, but SARS-CoV-2 treatment was given due to lung involvement. Viral spread may continue up to 1 month after COVID-19 infection with gastrointestinal symptoms. There is no clear information about whether viral replication continues in organs after COVID-19 infection, and if so, for how long it will continue in which organs. Our patient is important because she is the first case to show severe mesenteric lymph node involvement despite treatment and COVID-19 PCR positivity in the lymph node.

REFERENCES


Figure 1. Vacuolated lymphocyte seen on peripheral blood smear.
Figure 2. Multiple lymphadenopathies in the mesentery and dilated bowel loops are seen intraoperatively macroscopically.