CASE REPORT

# Cytomegalovirus Infection in a Patient With Leukocyte Adhesion Deficiency Type 1

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**Abstract**- Leukocyte adhesion deficiency type 1 (LAD-1) is a rare autosomal recessive immunodeficiency disorder, characterized by recurrent bacterial and fungal infections without pus formation. Herein, we report a case of LAD-1 that developed into gastrointestinal cytomegalovirus (CMV) disease and manifested with persistent abdominal pain and bloody diarrhea. Although the presence of concurrent gastrointestinal CMV infection with LAD-1 is a rare condition, this case highlights the need for further research to evaluate the complex mechanisms between LAD-1 and CMV occurrence.

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## Introduction

Leukocyte adhesion deficiency type 1 (LAD-1) is a rare autosomal recessive immunodeficiency disorder, resulting from mutations in the ITGB2 gene, which encodes the common chain (CD18) of the β2 integrin family. This mutation leads to absent or severely decreased leukocyte cell surface expression of β2 integrin molecules, which are well-known for their involvement in the leukocyte adhesion to the endothelium, transendothelial migration, chemotaxis, bacterial recognition, and outside-in signaling in neutrophils (1). Failure of the aforementioned mechanisms could culminate in the defective innate host defenses against bacteria, fungi, and other microorganisms (2). This condition is usually characterized by recurrent bacterial and fungal infections without pus formation, impaired wound healing, leukocytosis during periods of infection, delayed umbilical cord separation, omphalitis, necrotizing enterocolitis, pneumonia, perirectal abscess, gingivitis, periodontitis, and sepsis, as common presenting features (3,4). Hematopoietic stem cell transplantation (HSCT) is the definitive treatment for LAD (5). Post stem cell transplantation patients may develop cytomegalovirus (CMV) infection. However, to our best of knowledge, there is no report of the gastrointestinal CMV disease in a patient with LAD-1, who has not undergone HSCT. Herein, an 11-year-old girl is presented with concomitant gastrointestinal CMV disease and LAD-1.

## Case Report

An 11-year-old girl was admitted to the Ali-Asghar Hospital, with the chief complaint of periumbilical abdominal pain, nausea, vomiting, and bloody diarrhea since three months. She was born to first cousins consanguine parents with an uneventful pregnancy. The diagnosis of LAD-1 was made at two months of age. There was a family history of LAD-1 in her sibling who died in 11$^{th}$ year of life with the diagnosis of intestinal non-Hodgkin lymphoma. The patient had a weight of 15 kilograms, which was below the 3$^{rd}$ percentile for her age. On physical examination, generalized abdominal tenderness was noted which was most marked in the periumbilical region. Initial laboratory data is presented

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in Table 1.

**Table 1. Initial laboratory data**

| Laboratory test | | Reported values | Reference values |
|---|---|---|---|
| Complete blood count | **WBC/mm$^3$** | 104200 | 4700-10300 |
| | **Neutrophils (%)** | 76 | 33-61 |
| | **Lymphocytes (%)** | 10 | 28-48 |
| | **Band cells (%)** | 14 | 0-11 |
| | **Hemoglobin (mg/dL)** | 6.6 | 10.9-13.3 |
| | **Hematocrit (%)** | 22.2 | 33.0-39.6 |
| | **Platelet count/mm$^3$** | 298000 | 183-369 |
| Liver function tests | **AST (U/L)** | 11 | 8-50 |
| | **ALT (U/L)** | 5 | 7-45 |
| | **Alkaline phosphatase (U/L)** | 409 | 115-437 |
| | **Albumin (g/dL)** | 2.5 | 3.7-5.6 |
| Stool analysis | **Ova** | Not seen | Not present |
| | **Parasites** | Not seen | Not present |
| | **WBC** | 18-20 | Not present |
| | **RBC** | 8-10 | Not present |
| | **Calprotectin** | 20 | 0.1-15 |
| | **Stool culture** | Negative | |
| Other tests | **Serum total protein (g/dL)** | 7.8 | 5.9-8 |
| | **ESR (mm/h)** | 142 | 1-8 |
| | **CRP (mg/L)** | 122 | 0-10 |
| | **Amylase (U/L)** | 25 | 23-85 |
| | **Lipase (U/L)** | 10 | 0-160 |
| | **Urinary sediment** | Inactive | |
| | **Urine culture** | Negative | |
| | **Rapid urease test** | Positive | |
| **Histopathologic examination of the gastric mucosa** | | peptic ulcer with the aggregation of lymphoid follicles | |

Abbreviations used: WBC, white blood cells; AST, aspartate aminotransferase; ALT, alanine aminotransferase; RBC, red blood cells; ESR, erythrocyte sedimentation rate; h, hour; CRP, C-reactive protein

Abdominal X-ray showed minor dilatation of small intestine loops and horizontal colon. Abdominopelvic ultrasonography demonstrated increase thickness of right intestinal loops. On the suspicion of inflammatory bowel disease, mesalazine (Pentasa), albumin infusions, as well as the intravenous (IV) antibiotic in the form of amikacin were initiated. She received blood transfusion as well. Subsequently, laboratory data showed WBC of 96600/mm$^3$, hemoglobin of 8.4 mg/dL, hematocrit of 27.6%, RBC count of $3.66\times10^6$/mm$^3$ (normal range: 4.0-$4.9\times10^6$/mm$^3$), mean corpuscular volume (MCV) of 75.4 fL (normal range: 72.7-86.5 fL), and platelet count of 203000/mm$^3$. The patient's symptoms continued. Her antibiotic regimen was substituted by the combination of metronidazole, vancomycin, and amikacin on the 7$^{th}$ day. Five days later, the patient developed fever, and intravenous immunoglobulin (IVIG) replacement was commenced, consequently. In addition, IV antibiotics in the form of ciprofloxacin, vancomycin and meropenem were started. On investigation, the hemoglobin level of 7.4 mg/dL, platelet count of 395000/mm$^3$, and total leukocyte count of 8600/mm$^3$ were reported. Her ESR was 142 mm/h and the CRP level was 111 mg/L. The endoscopic examination of the gastrointestinal tract was performed, through which, mild to moderate esophagitis, moderate gastritis, moderate duodenitis, together with erosive colitis were reported. CMV IgG as well as the herpes simplex virus 1 (HSV-1) IgG were found to be

positive (their levels were 100 U/ml, normal range <14, and 36.9 U/ml, normal range <1.1, respectively), while the CMV IgM was shown to be negative. CMV polymerase chain reaction (PCR) was also positive in the colonic biopsy specimens. Subsequently, a diagnosis of CMV infection with LAD-1 was made. IV ganciclovir was added in view of the aforementioned results. The child recovered in a 4-week period and the condition was established by the negative CMV PCR in the colonic biopsy specimens and was asymptomatic for six months.

## Discussion

LAD-1 is a rare inherited immunodeficiency disease, which usually presents during infancy or early childhood, presenting multiple manifestations, the severity of which have been attributed to the degree of surface expression of CD18 and CD11. This condition has been classified to moderate and severe phenotypes, according to the degree of CD18 expression (1-30% expression of CD18, and <1% expression of CD18, respectively) (6). This disease was first described more than two decades ago. Since then, more than 300 cases have been reported, with few reports on the concomitant congenital CMV infection and LAD-1. However, to the best of our knowledge, gastrointestinal CMV disease has not been reported in LAD-1, thus far.

The (CMV, classified as a herpes virus, can produce various clinical manifestations, based on host's immune condition and age (7). Gastrointestinal CMV infection, which typically presents injuries similar to ulcers, mostly affects the colon, the esophagus, and the stomach; while, distal small intestine involvement is a rare condition. This type of infection, which is a rare phenomenon, mostly affecting immunodeficient patients, could either be part of a widespread CMV infection or remain isolated in the gastrointestinal tract (7).

To date, the coincidence of congenital CMV infection and LAD-1 has been reported in two patients worldwide. Rai *et al.,* have recently reported a patient with congenital CMV, who presented severe CMV pneumonitis, recurrent skin infections, bronchopneumonia and otitis media, and was subsequently diagnosed as LAD-1 with natural killer cell deficiency (8). The other case of an infant with LAD-1 with developmental delay associated with a congenital CMV infection has been presented by Strickler *et al.,* (9).

Herein, we represented a case of LAD-1 that developed into gastrointestinal CMV disease and manifested with persistent abdominal pain and bloody diarrhea. Our case underscores the importance of exploring the possibility of gastrointestinal CMV infection as a possible complication in LAD-1 patients with obvious gastrointestinal manifestations. Development of CMV infection in LAD patients could provide insight into the probable role of β2 integrins in the host immunity against viral infections.

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