

Leukocyte Adhesion Deficiency

Clinical Background

Leukocyte adhesion disorders (LAD) are a primary immune deficiency affecting phagocytic blood cells.

Epidemiology

- Incidence – <1/1,000,000
- Age – usually identified in infancy or early childhood

Inheritance

- Heterogeneous mutations in the CD18 leukocyte integrin gene
- At least 3 defects known (LAD-I, LAD-II, LAD-III)
 - LAD I – integrin expression defect
 - LAD II – selectin defect
 - LAD III – defect in integrin activation
- Autosomal recessive inheritance

Pathophysiology

- Blood neutrophils are the first line of defense against bacterial and fungal infection
- Initial neutrophil adherence is weak but becomes strong with the aid of beta integrin interactions
- LAD involve defects in integrin expression leading to defective adhesion of neutrophils, leading to increased susceptibility to bacterial and fungal infections

Clinical Presentation

- LAD I – characterized by delayed separation of the umbilical cord, recurrent soft tissue infections, chronic periodontitis, marked leukocytosis and lack of neutrophils in tissue infections
- LAD II – same features as LAD I, but also growth and mental retardation abnormalities but with no delay in separation of umbilical cord
- LAD III – same features as LAD I and severe bleeding tendency

Treatment

- Early intervention for periodontal disease
- Preventive antibiotics for infection
- Allogeneic bone marrow transplant for severe disease

Diagnosis

- Indications for testing – child with recurrent infections and in whom more common immunodeficiencies have been ruled out; tissue infections with absence of inflammatory cells
- Laboratory testing
 - CBC reveals leukocytosis with neutrophilia (even in the absence of infection but exaggerated during infection)
 - Flow cytometric analysis
 - CD11b and CD18 expression on leukocytes
 - No expression – 75% die in infancy
 - 1-10% – 33% survive to age 40 years
 - >10% – mild deficiency which may not be recognized until late teen years

Differential Diagnosis

- Neutropenic disorders
- Agranulocytosis
- IRAK-4 deficiency
- Job syndrome
- Chronic granulomatous disease
- Myeloperoxidase deficiency

Lab Tests

Indications for Laboratory Testing

Tests generally appear in the order most useful for common clinical situations. For test-specific information, refer to the test number in the ARUP Laboratory Test Directory on the ARUP Web site at www.aruplab.com.

Test Name and Number	Recommended Use	Limitations	Follow Up
CBC with Platelet Count & Automated Differential 0040003 Method: Automated Cell Count with Flow Cell Differential	Recommended testing to reveal leukocytosis with neutrophilia		
Neutrophil Receptor Profile 0095921 Method: Flow Cytometry	Diagnose LAD		

General References

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Webber EC, Church J, Rand TH, Shah AJ. Leukocyte adhesion deficiency in a female patient without delayed umbilical cord separation. *J Paediatr Child Health.* 2007; 43 (5) :406-408.

Reviewed by

Hill, Harry R., MD. Group Medical Director, Laboratory of Immunology, ARUP Laboratories, and Executive Director of the ARUP Institute for Clinical and Experimental Pathology; Professor and Division Head, Pathology (Clinical), University of Utah

Wittwer, Carl T., MD, PhD. Medical Director, General Flow Cytometry Laboratory and Advanced Technology Group at ARUP Laboratories; Professor of Pathology, and Adjunct Professor of Biomedical Engineering, University of Utah

Diagnostic Algorithm(s)

PDF algorithm(s) available at www.arupconsult.com.

Immunodeficiency Evaluation for Chronic Infections in Adults and Older Children Testing Algorithm

Immunodeficiency Evaluation for Chronic Infections in Infants and Children Testing Algorithm

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