

# Neutrophilic Leukocytosis in Infectious Mononucleosis: A Case Series Report

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## Abstract

**Introduction:** Infectious mononucleosis is a relatively common childhood disease caused by the Epstein-Barr virus (EBV). Typical cases are seen in young children and are mostly clinically mild or asymptomatic. In this disease, leukocytosis with predominance of lymphocytes is found. Classical clinical symptoms associated with atypical lymphocytosis in the peripheral blood smear helps in diagnosis.

**Case Presentation:** The patients were proven cases of infectious mononucleosis disease and unlike the typical cases of this infection; they showed high ESR (erythrocyte sedimentation rate), CRP (C-reactive protein), and neutrophilic leukocytosis, instead of lymphocytosis. All of them were discharged in good general condition after receiving corticosteroids.

**Conclusions:** According to our findings, EBV infection cannot be ruled out in exudative pharyngitis, despite having neutrophilic leukocytosis, high levels of ESR and CRP. Therefore, EBV diagnostic tests should be conducted in these patients.

**Keywords:** Infectious Mononucleosis, Neutrophilic Leukocytosis, Exudative Pharyngitis

## 1. Introduction

Infectious mononucleosis is caused by the Epstein-Barr virus (EBV) and is a relatively common disease in children. Most adults have a positive serology for this disease (1, 2). Affected infants and young children show mild or no symptoms. In most cases, if pharyngitis does not improve within 3 - 4 days or does not respond to penicillin, mononucleosis pharyngitis should be suspected. Some of the symptoms that distinguish EBV pharyngitis from streptococcal pharyngitis are: splenomegaly, generalized lymphadenopathy, periorbital edema, facial puffiness, acute respiratory distress, and stridor. On the other hand, in children younger than 3 years, streptococcal pharyngitis is extremely rare (1). Lymphocytic leukocytosis is often seen in this disease (1-3). Typical clinical symptoms associated with atypical lymphocytosis in peripheral blood smear (PBS) helps the diagnosis. Serological tests involving heterophil antibodies and VCA IgM (viral capsid antigen-immune globulin M) are also used for the diagnosis (1-4). The main treatment of the disease is symptomatic therapy and resting. Some cases require short periods of corticosteroids. The most common indication for corticosteroids is the possibility of airway obstruction due to inflammation and severe enlargement of tonsils, which are largely associated with nasal speech and respiratory distress. The purpose of this study demonstrates that neutrophilic leukocy-

tosis can be seen in infectious mononucleosis and this finding cannot rule out IMN.

## 2. Case Presentation

Of the large number of children with infectious mononucleosis confirmed by clinical signs and laboratory tests admitted at Mousavi hospital in Zanjan, Iran from 2012 to 2016, there were 10 patients with neutrophilic leukocytosis instead of lymphocytosis. These patients presented fever, pharyngitis, cervical lymphadenopathy, and respiratory distress. The children were aged between 1.5 to 11 years and included 4 girls and 6 boys. All patients had less than 1 week interval between the onset of fever and their hospitalization. Patients 1 to 7 were infants between the age of 1.5 - 2 years, who were referred with severe pharyngitis, accompanied by 4 - 5 days of a fever and leukocytosis, high level of ESR and CRP. All of them were in good general condition, however, with a mild stridor. On the physical examination, severe pharyngitis with exudates were found. None of the infants were detected with another infection site rather than the throat, such as otitis media, sinusitis, cervical lymphadenitis or pneumonia. Blood cultures were negative in all cases. Two infants received oral penicillin and another one received intramuscular penicillin, however, the fever did not subside. They

did not receive antibiotics against anaerobic organisms either. Chest radiographs and abdominal ultrasounds were normal, only 1 of them had hepatosplenomegaly. Patients 8 to 10 were 6 - 11 year-old children also referred with exudative pharyngitis, mild to moderate respiratory distress, neutrophilic leukocytes, high level of ESR, and CRP, without response to treatment by penicillin. One of these children had mild splenomegaly and slight swelling of the eyelids was seen in another child. The median white blood cell, neutrophil, ESR and CRP were, 18,000 and 13,500 (75%), 48 mm/h, and 52 mg/l, respectively. Three patients had abnormal liver tests (AST, ALT). The VCA IgM, mono test and peripheral blood smear for atypical lymphocytes were performed in all patients. Atypical lymphocytes were universally observed. Most of the patients were positive for VCA IgM, Mono test was positive in only 2 cases. Airway involvement is amongst the serious complications of infectious mononucleosis and is the most common indication for initiation of corticosteroids. Therefore corticosteroids were administered to all patients with respiratory problems and complete improvement occurred in 100% of the cases. Table 1 summarizes the laboratory characteristics of all patients. Children were discharged in good general condition after receiving corticosteroids. All patients were carefully followed-up after discharge and had no complications. The important point in the second week of follow-up was a significant increase in percentage of atypical lymphocytes, reduction levels of ESR and CRP, and change of neutrophilic leukocytosis to lymphocytic leukocytosis.

### 3. Discussion

In children, infectious mononucleosis disease presents as an acute or slow disease. Its clinical symptoms are usually similar to an exudative streptococcal pharyngitis that does not respond to penicillin. However, unlike streptococcal pharyngitis, there may be findings such as respiratory problems, splenomegaly or less likely hepatomegaly. The clinically typical symptoms and presence of atypical lymphocytes in peripheral blood smear are useful to detect infectious mononucleosis. Additionally, it is possible to confirm the diagnosis by serological tests (1-4). Although it is described that young children mostly have a clinically silent infection (1), the patients in this study had clearly pharyngitis with respiratory distress depicting the severe and typical form of the disease. EBV, infections like most viral infections, is associated with lymphocytosis and a low level of ESR and CRP (4-7). Although a high level of ESR is rarely seen in EBV infections, neutrophilic leukocytosis has not been reported. Interestingly, all our patients had high levels of ESR, CRP, and neutrophilic leukocytosis, such

that the laboratory findings were similar to a bacterial infection. According to our findings, EBV infection cannot be ruled out in exudative pharyngitis, despite having neutrophilic leukocytosis, high levels of ESR, and CRP. Therefore, it is recommended that EBV diagnostic tests be conducted.

The remarkable issue in the follow-up period was the conversion of neutrophilia to lymphocytosis. Increase of the percentage of atypical lymphocytes was observed after 10 days of the onset of illness, matching with previous knowledge (2). Therefore, we can conclude that infectious mononucleosis could appear as neutrophilic leukocytosis at the onset of the disease. After the second week, with an increase in atypical lymphocytes, lymphocytosis is obvious. According to the above mentioned, in cases of exudative pharyngitis, neutrophilia, or high levels of ESR or CRP not responding to penicillin therapy, combined with organomegaly, abnormal liver functional tests, diffuse cervical lymphadenopathy, periorbital edema, and respiratory problems, infectious mononucleosis must be strongly considered and the necessary diagnostic and therapeutic measures performed. With the onset of symptoms, the virus can be detected in blood by the PCR method. At this time, VCA IgM could be still negative, thus PCR can be used for infection detection (8).

### Footnotes

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**Table 1.** Laboratory Characteristics of Patients

Case, Number	Age, Year	Sex	WBC $\times 10^3$	Nutrophil Percentile %	ESR, mm/h	CRP, mg/L	VCA IgM	Atypical Lymphocytes	Mono Test
1	1.5	Male	18	78	80	72	+	+	-
2	1.5	Female	21	70	70	93	+	+	-
3	1.5	Male	17.5	76	52	75	-	+	-
4	1.5	Male	18	70	41	36	-	+	-
5	2	Male	16.7	72	47	32	+	+	-
6	2	Female	15.3	77	46	39	-	+	-
7	2.5	Female	16	74	41	70	+	+	-
8	6	Male	28	70	30	32	+	+	-
9	8	Female	15	81	30	34	+	+	+
10	11	Male	15.4	83	44	36	+	+	+

Abbreviations: CRP, C reactive protein; ESR, erythrocyte sedimentation rate; VCA, viral capsid antigen; WBC, white blood count.

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