



## Eyelid edema as a rare manifestation of infectious mononucleosis

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### ABSTRACT

We report the case of a 44-year-old woman presenting with edema of the upper eyelids and enlarged salivary glands. Slit lamp examination found features of bilateral dacryoadenitis with no abnormalities in the anterior and posterior segments. Based on

the clinical manifestations and additional test results, the diagnosis of infectious mononucleosis was confirmed.

**KEY WORDS:** infectious mononucleosis, eyelid edema, dacryoadenitis.

### INTRODUCTION

Edema of the eyelids is a condition commonly encountered in daily ophthalmic practice. However, the multifactorial etiology of this symptom makes it diagnostically challenging. Edema may be a manifestation of conditions involving the eyelids or orbital structures, or an indication of an underlying systemic disease.

The basis for appropriate diagnosis includes carefully taken medical history and meticulous palpation of the eyelids and the orbital region, followed by indirect ophthalmoscopy. However, in many cases, diagnostic imaging examinations together with laboratory tests are also necessary.

In this report, we present the case of chronic bilateral eyelid edema occurring as a rare manifestation of infectious mononucleosis.

### CASE REPORT

A 44-year-old female patient was admitted to the ophthalmology department with upper eyelid edema present for 1.5 months, with accompanying parotid gland enlargement persisting for 10 days. The patient was otherwise healthy and did not take any medications. Physical examination revealed bilateral upper eyelid edema with a slight reddening of the skin (Figure 1). On palpation, bilateral lacrimal gland enlargement accompanied by enlargement and tenderness of both parotid glands were found. Anterior and posterior ocular structures visualized by indirect ophthalmoscopy revealed no abnormalities. Bilateral Schirmer's test performed without anesthesia showed 5 mm of moisture on the filter paper. Contrast-enhanced orbital MRI found symmetrical enlargement of both lacrimal glands. MRI of the head with

contrast showed mild enlargement of both parotid glands and thickening of the paranasal sinus mucosa. An additional ultrasound examination of the salivary glands confirmed bilateral parotid swelling without features of cervical adenopathy. Abdominal CT scan revealed mild liver enlargement. Laboratory tests showed elevated levels of alanine aminotransferase (ALT) – 34 U/l (normal value < 33 U/l), total bilirubin – 1.9 mg/dl (normal value < 1.1 mg/dl) and antibody titers: anti-EBV IgM – 1.07 S/CO (positive > 1.00) and IgG – 38.77 S/CO (positive > 1.00). In blood counts, deviations from normal values were detected for monocytes – 15.7% (normal range 2.0-12.0), eosinophils – 7.9% (normal range 0-5.0), and PDW – 9.0 fl (normal range 12.0-20.0). No leukocytosis was present on laboratory testing.

Based on the overall clinical picture and the results of additional tests, infectious mononucleosis and Sjögren's syndrome were considered in the differential diagnosis. Following hospital discharge, the patient was referred to the outpatient clinics for rheumatology and infectious diseases for further follow-up, diagnostic work-up, and possibly treatment.

A month after hospital discharge, during a follow-up ophthalmic examination in an ophthalmology outpatient clinic, the patient reported that all her previous symptoms had resolved. Slit lamp examination revealed no abnormalities of the adnexa or the anterior and posterior ocular segments. Following an outpatient consultation with a specialist in infectious diseases, it was determined that the patient had an episode of infectious mononucleosis manifesting as lacrimal gland involvement with a self-limiting course not requiring pharmacotherapy. The patient is currently waiting for

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**Figure 1.** Bilateral edema of the upper eyelids, more pronounced in the outer sections, with a slight reddening of the skin in the affected area



**Figure 2.** Clinical features after a 3-month follow-up

a rheumatology consultation. During the patient's 3-month follow-up, no recurrence of ocular symptoms was observed (Figure 2).

## DISCUSSION

Acute dacryoadenitis presents as swelling of the outer portion of the upper eyelids which gives rise to characteristic S-shaped ptosis. Other possible manifestations include edema and irritation of the palpebral conjunctiva, which contribute to pain in the upper temporal part of the orbit [1, 2]. The etiology of the disease is multifactorial, with postulated causes including viruses (mumps virus, Epstein-Barr virus, cytomegalovirus) and bacteria (*Staphylococcus aureus*, *Neisseria gonorrhoeae*) as well as chronic conditions such as sarcoidosis or Sjögren's syndrome [1, 2].

The available scientific reports on infections of the lacrimal glands highlight the role of the Epstein-Barr virus [1]. Infectious mononucleosis caused by the Epstein-Barr virus is an acute illness accompanied by fever [3]. The incubation period is 30-50 days, and prodromal symptoms developing gradually over a period of 1-2 weeks include malaise and

headaches [4]. The condition presents clinically as pharyngitis, generalized lymphadenopathy, hepatosplenomegaly, and skin rash [3-6]. Infectious mononucleosis was first linked to ophthalmic manifestations including upper eyelid edema and dacryoadenitis in 1950 [1, 3]. Based on the scientific reports, the Epstein-Barr virus may be a possible, though rare, cause of unilateral or bilateral inflammation of the lacrimal gland in young patients [1, 4]. Other ocular manifestations associated with the acute form of this disease have also been reported in the literature [3]. The most prevalent include conjunctivitis, photophobia, and blurred vision [3], while episcleritis, uveitis, optic neuritis, optic disc edema, retinal edema, retinal hemorrhages, extraocular muscle paralysis, ptosis or nystagmus occur at a lower frequency [3, 7]. Ocular manifestations are typically noted in patients with long-term disease [3].

The diagnosis of infectious mononucleosis is based on the presenting signs and symptoms, and laboratory blood test results [4]. The blood count very commonly shows leukocytosis with a highly differentiated lymphocyte count along with the presence of atypical enlarged lymphocytes, which represents a characteristic feature of the disease [8]. Immunological findings include the detection of non-specific heterophilic antibodies in the Paul-Bunnell-Davidsohn reaction or specific antibodies against the Epstein-Barr (EBV) virus using more advanced assay techniques [4]. Rhem *et al.* propose a comprehensive assessment of patients with acute dacryoadenitis [1]. Individuals presenting with acute symptoms of inflammation of the lacrimal gland with coexisting exophthalmos and restricted ocular motility or other alarming symptoms suggestive of orbital involvement require an imaging examination or biopsy of the lacrimal gland in order to exclude an infiltrative or neoplastic process [1]. Associated regional lymphadenopathy may be indicative of a viral syndrome, and patients should be evaluated by laboratory tests of specific antibody levels [1]. Serological evaluation of Epstein-Barr virus infection is based on an immunoglobulin panel [1]. Antibodies against the viral capsid antigen are detected with the onset of clinical manifestations of the disease, approximately six weeks after exposure [1]. While IgM class antibodies decline to low levels within a few weeks, IgG class antibodies persist indefinitely [1]. Antibodies to the nuclear antigens of the virus increase in titer several weeks after the onset of symptoms of infection and remain detectable for years [1]. The presence of antibodies to the capsid antigen with either the absence or increase of antibodies to the nuclear antigens of the virus is diagnostic for a recent viral infection [1]. However, without isolating the virus or detecting an antigen or nucleic acid in the lacrimal gland or conjunctival secretions, positive serological tests indicative of Epstein-Barr virus infection may prove insufficient [1]. Tests based on molecular diagnostic techniques are needed to determine whether Epstein-Barr virus infection has any causal relationship with dacryoadenitis [1].

As a rule, dacryoadenitis persists for 4 to 6 weeks, and the effects of topical or systemic anti-inflammatory or anti-infective therapies are difficult to determine, as the disease is typically self-limiting [1, 3]. Consequently, the issue of wheth-

er therapy contributes to shortening the duration of the disease or reducing complications is still to be determined [1].

Interestingly, there have also been reports discussing the role of the Epstein-Barr virus in the pathogenesis of Sjögren's syndrome [4, 9, 10]. The association has been suggested based on the detection of the Epstein-Barr virus antigen in the lacrimal [11] and salivary gland [10] tissue in patients with Sjögren's syndrome, in amounts exceeding that detected in the tissues of healthy individuals who also developed symptoms of Sjögren's syndrome, such as patients shortly after Epstein-Barr virus infection [4, 9, 12]. It has been hypothesized that the development of Sjögren's syndrome after Epstein-Barr virus infection in these patients may be due to an abnormal immune response to the virus [4, 10-12]. It is as yet unclear whether the presence of clinically manifest acute parotitis and/or dacryoadenitis has any significance in these patients [4].

In the presented case, the differential diagnosis involved a range of other disease entities including idiopathic orbital inflammation, idiopathic dacryoadenitis, Sjögren's syndrome, sarcoidosis, lymphoma or primary lacrimal gland tumor [13, 14].

Our patient presented with edema of the upper eyelids and bilaterally enlarged lacrimal glands, mild enlargement

of the liver along with elevated laboratory parameters indicative of liver inflammation and positive IgM and IgG anti-EBV antibody titers, i.e. findings characteristic of infectious mononucleosis, but with no typical leukocytosis. However, a case of mononucleosis infection in a pediatric patient with conjunctival involvement but without accompanying leukocytosis has already been reported in the literature [8]. Another diagnostic difficulty is the age of the patient. Based on the available scientific reports, Epstein-Barr virus infections are especially prevalent among adolescents and children [15, 16]. Taking into consideration the patient's overall clinical picture and positive anti-EBV antibody titers, a diagnosis of eyelid edema secondary to infectious mononucleosis was made.

In summary, dacryoadenitis is a rare complication of infectious mononucleosis [4]. The risk of this infection should be considered in the differential diagnosis of acute dacryoadenitis, since lacrimal gland involvement may obscure other signs and symptoms of infectious mononucleosis, leading to delayed treatment [3, 4].

## DISCLOSURE

The authors declare no conflict of interest.

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