



Case report

Epstein-Barr virus (EBV) induced pneumonitis in an immunocompetent adult: A case report



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ABSTRACT

Epstein Barr Virus (EBV) is one of the herpes viruses that is responsible for causing infectious mononucleosis, lymphomas, and carcinomas primarily in immunocompromised individuals. We present a case of EBV-induced pneumonitis in an immunocompetent female, successfully treated with steroids. The patient is a 70 year-old female with a history of infectious mononucleosis in her teens who presented to the emergency room with worsening shortness of breath, associated with cough and fever. She underwent extensive work up and her serologic workup revealed positive anti-EBV antibodies, pointing towards the diagnosis of EBV induced pneumonitis. EBV-induced Pneumonitis is a very rare entity and is especially hardly seen among immunocompetent individuals. This interesting case shows that in this new era of viral pneumonias, EBV induced pneumonitis should be considered among differentials when dealing with lung infections. Prompt initiation of treatment with steroids or antiviral medication may result in complete recovery. The choices among treatment options can be individualized according to the severity of disease, course of disease progression, and side effect profile of medications. In our case we were able to successfully treat the patient with high dose steroids only.

1. Introduction

Epstein Barr Virus (EBV) belongs to the herpes virus family and has been widely reported to cause disseminated infection in patients of all ages. EBV is the primary agent of infection in infectious mononucleosis (IM), lymphomas, and nasopharyngeal carcinomas. One of the rare pulmonary complications of EBV infection is pneumonitis. We present one such case where an immune-competent host was found to have an EBV induced pneumonitis based on the serological evidence. After steroid treatment, our patient showed radiological and clinical improvement.

2. Case presentation

72-year-old female with a pertinent medical history of infectious mononucleosis, diagnosed forty years ago, and hypertension, well controlled on Lisinopril, presented to Emergency department (ED) for 1 week history of worsening dyspnea associated with prodromal flu-like symptoms, indigestion, and dry cough. On examination the patient

had mild crepitation up to mid-scapular level and tender cervical lymphadenopathy were noted. Patient was hypoxic with oxygen saturation of 87% on room air which improved to 92% on 3 L (L) nasal cannula (NC). Initial laboratory workup revealed normal leukocyte count, lymphopenia, low procalcitonin (0.06ng/ml) and high CRP levels (6.92 mg/dl). COVID19 PCR was reported negative. Initial chest x-ray revealed bilateral interstitial infiltrates. On day 2 of admission, the patient's oxygen requirement increased to 6L of oxygen. High Resolution Computed Tomography (HRCT) of Chest showed bilateral patchy airspace opacities involving all the lobes with mediastinal adenopathy (Figs. 1–2). During her stay, consecutive blood cultures and sputum cultures were reported negative. The Transthoracic Echocardiogram (TTE) was unremarkable. Rheumatologic panel and additional infectious workup revealed presence of lupus anticoagulant antibody, anti-beta-2-glycoprotein antibody shortness of breath as well as the oxygen requirements. This was followed by radiological improvement observed in the next couple of days. Patient was subsequently discharged on day 14 on a slow taper of steroids. Patient was followed in the outpatient pulmonary office three weeks after being discharged from hospital.

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Repeat CT chest showed resolution of the pulmonary infiltrates seen on previous imaging.

3. Discussion

Lung involvement is rare with EBV infection and is more commonly observed in immunosuppressed patients, but can also be seen in immunocompetent patients [1,2]. Pulmonary manifestations associated with EBV infections have been described in the literature more commonly as lymphadenopathy (frequently hilar and mediastinal lymphadenopathy), pleural effusions, and interstitial pneumonitis [3]. Two proposed mechanism for the interstitial edema includes accumulation of the virus secondary to rapid viral replication versus the body's own immune reaction to the infection or a combination of both [4]. In cases where early antiviral therapy is initiated, early recovery from the disease is noted with early resolution of interstitial infiltrates on chest xray [5]. In cases where the diagnosis is delayed, steroids or immunoglobulins have been successful in subsiding the immune reaction leading to rapid recovery of the symptoms [6]. Frequently acute EBV infection can be associated with antiphospholipid antibodies (aPLs) [7]. Since our patient did not fulfil any of the clinical criteria for APS, elevation of these antibodies was most likely reactive to EBV infection. According to one study, aPLs become negative when repeated in subjects once the infection resolves [8]. There are case reports of these patients developing splenic infarctions with one of the probable causes being transient activation of aPLs [8,9].

EBV is also reported to cause Lymphocytic Interstitial Pneumonitis (LIP), a pulmonary disease characterized radiologically by bilateral lower lobe infiltrates, and histologically by a polymorphic lymphoplasmacytic cell infiltration of the pulmonary interstitium. Since EBV is recovered on the biopsy of LIP lungs, and the virus itself causes polyclonal proliferation of B lymphocytes in the interstitium we can consider EBV as one of the underlying etiologies behind LIP [10]. In one of the case reports, treatment of EBV induced LIP with high dose steroids was unsuccessful, whereas immune-modulating agents like cyclophosphamide showed remarkable recovery [11]. Few reports have mentioned use of antiviral agents like acyclovir. Although few reports have favored acyclovir in EBV associated pneumonitis [3,12] but no single antiviral agent has precedence over others. As to the best of our knowledge, one case has been reported where diffuse EBV induced pneumonitis in an infant was successfully treated with inhaled and systemic steroids [13].

Chronic active Epstein-Barr virus (CAEBV) infection is another rare and life-threatening complication associated with EBV. These patients have some symptoms that are common with acute-EBV infection in healthy patients, but their symptoms persists and progress with time. Okano et al. proposed a diagnostic criteria for the diagnosis of CAEBV [14], which includes: 1) Persistent and chronic intermittent fevers, lymphadenopathy and/or hepatosplenomegaly (other symptoms such as headache, sore throat and EBV hepatitis can also be seen); 2) EBV

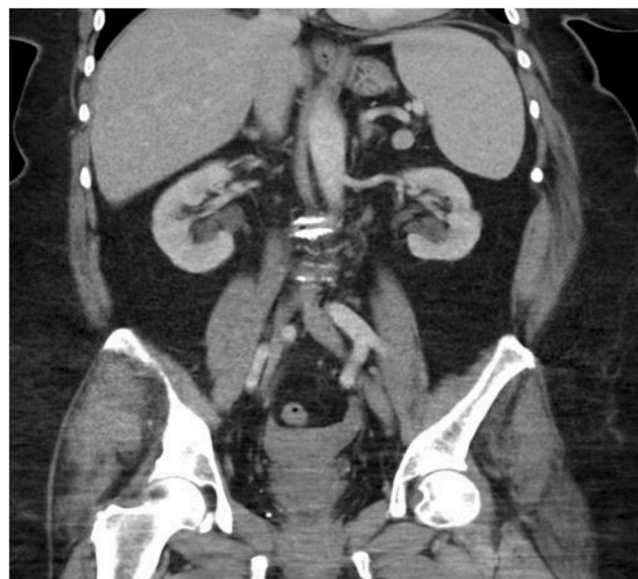


Fig. 2. Coronal section of contrast-enhanced CT demonstrating splenomegaly.

serologic tests revealing high IgG antibody titers against EBV VCA (>1:640) and EA (>1:160) and/or increase in the EBV genome (EBV DNA) in the effected tissues, including the peripheral blood; 3) Chronic illness that cannot be explained by other known disease process at the time of diagnosis. Although our patient had EBV infection in the past but it was approximately forty years ago and she did not report any constitutional symptoms or chronic disease preceding it [12,14,15]. Her serologic studies also did not qualify the criteria as well. Splenomegaly was an incidental finding on the CT scan for the chest whereas lymphadenopathy also developed only during acute phase of the disease. All her symptoms resolved with steroid therapy and this was confirmed with imaging repeated at the follow up visit. These features make a diagnosis of CAEBV unlikely in our patient.

A timely diagnosis is crucial for the effective management of EBV pneumonitis. It's important to differentiate EBV induced pneumonitis from other infectious and autoimmune etiologies. In short, patients can be treated with either steroids or anti-viral medications. Use of anti-viral medications comes with its own side effects, which calls for taking risk versus benefit profile into account. If patient is unstable antivirals can be used. Whereas in stable patients, such as the case described above, steroids can be the safer choice to begin with.

4. Conclusion

Pulmonary involvement with EBV is rare but can be fatal as it has the propensity to induce respiratory insufficiency in the immune-competent

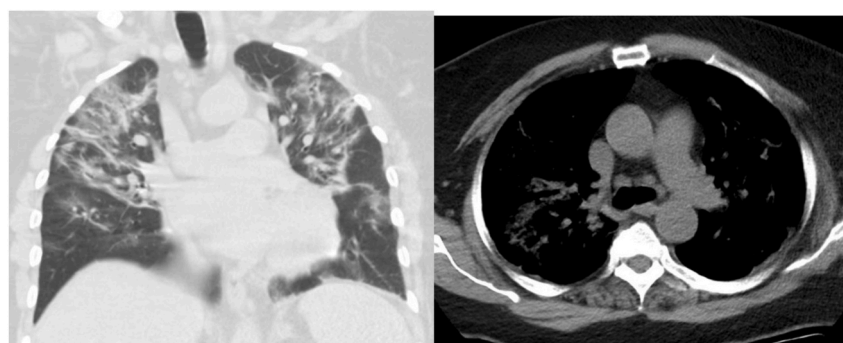


Fig. 1. (left) Coronal section of non-contrast chest CT demonstrating diffuse bilateral consolidations. (Right) Axial section of non-contrast chest CT demonstrating mediastinal adenopathy.

adults, which in most cases can be successfully treated with the use of corticosteroids alone. Given the rare nature of such cases, anecdotal evidence, such as case reports, will form a clinical basis for clinical decision making. We cannot recommend the use of only steroids for the treatment of EBV pneumonitis, but we are able present an example where a patient recovered completely without the use of antiviral therapy.

Declaration of competing interest

The authors report that there is no conflict of interest associated with this article.

References

- [1] O.A. Odumade, K.A. Hogquist, H.H. Balfour Jr., Progress and problems in understanding and managing primary Epstein-Barr virus infections, *Clin. Microbiol. Rev.* 24 (1) (2011) 193–209, <https://doi.org/10.1128/CMR.00044-10>.
- [2] Carl Nieweld, Robert Hilton, Ross Summer, Pneumonitis secondary to EBV-specific cytotoxic T-lymphocytes, *Chest* 154 (2018) 423A, <https://doi.org/10.1016/j.chest.2018.08.386>.
- [3] R.T. Schooley, R.W. Carey, G. Miller, et al., Chronic Epstein-Barr virus infection associated with fever and interstitial pneumonitis: clinical and serologic features and response to antiviral chemotherapy, *Ann. Intern. Med.* 104 (1986) 636–643. PMID : 3008616.
- [4] A. Krumbholz, T. Sandhaus, A. Göhlert, et al., Epstein-Barr virus-associated pneumonia and bronchiolitis obliterans syndrome in a lung transplant recipient, *Med. Microbiol. Immunol.* 199 (4) (2010) 317–322, <https://doi.org/10.1007/s00430-010-0165-y>.
- [5] T.E. McManus, P.V. Coyle, J. Lawson, J.S. Elborn, J.C. Kidney, Epstein - barr virus pneumonitis, *Ulster Med. J.* 78 (2) (2009) 137–138.
- [6] Q. Yin, M. Chen, L. Liu, Y. Wu, F. Liu, L. Chen, Immunocompetent adult infected with epstein-barr virus presenting as severe respiratory insufficiency: a case report, *Int. J. Clin. Exp. Med.* 10 (2017) 4011–4013.
- [7] E. Ben-Chetrit, Y. Wiener-Well, A. Fadeela, D.G. Wolf, Antiphospholipid antibodies during infectious mononucleosis and their long term clinical significance, *J. Clin. Virol.* 56 (4) (2013) 312–315, <https://doi.org/10.1016/j.jcv.2012.12.011>.
- [8] S. Khan, S. Saud, I. Khan, S. Prabhu, Epstein barr virus-induced antiphospholipid antibodies resulting in splenic infarct: a case report, *Cureus* 11 (2) (2019), e4119, <https://doi.org/10.7759/cureus.4119>. Published 2019 Feb 22.
- [9] S. van Hal, S. Senanayake, R. Hardiman, Splenic infarction due to transient antiphospholipid antibodies induced by acute Epstein-Barr virus infection, *J. Clin. Virol.* 32 (3) (2005) 245–247, <https://doi.org/10.1016/j.jcv.2004.07.013>.
- [10] A.K. Saemundsen, D.T. Purtilo, K. Sakamoto, et al., Documentation of Epstein-Barr virus infection in immunodeficient patients with life-threatening lymphoproliferative diseases by Epstein-Barr virus complementary RNA/DNA and viral DNA/DNA hybridization, *Canc. Res.* 41 (11 Pt 1) (1981) 4237–4242.
- [11] H.K. Yum, E.S. Kim, K.S. Ok, H.K. Lee, S.J. Choi, Lymphocytic interstitial pneumonitis associated with Epstein-Barr virus in Systemic Lupus Erythematosus and Sjögren's Syndrome. Complete remission with corticosteroid and cyclophosphamide, *Korean J. Intern. Med.* 17 (3) (2002) 198–203, <https://doi.org/10.3904/kjim.2002.17.3.198>.
- [12] H. Kimura, Pathogenesis of chronic active Epstein-Barr virus infection: is this an infectious disease, lymphoproliferative disorder, or immunodeficiency? *Rev. Med. Virol.* 16 (4) (2006) 251–261, <https://doi.org/10.1002/rmv.505>.
- [13] T. Ankermann, A. Claviez, H.J. Wagner, M. Krams, F. Riedel, Chronic interstitial lung disease with lung fibrosis in a girl: uncommon sequelae of Epstein-Barr virus infection, *Pediatr. Pulmonol.* 35 (2003) 234–238. PMID : 12567394.
- [14] M. Okano, K. Kawa, H. Kimura, et al., Proposed guidelines for diagnosing chronic active Epstein-Barr virus infection, *Am. J. Hematol.* 80 (2005) 64–69. PMID : 16138335.
- [15] J.I. Cohen, E.S. Jaffe, J.K. Dale, et al., Characterization and treatment of chronic active Epstein-Barr virus disease: a 28-year experience in the United States, *Blood* 117 (22) (2011) 5835–5849, <https://doi.org/10.1182/blood-2010-11-316745>.