Sarcoidosis presenting as bilateral optic neuritis after ChAdOx1 nCoV-19 vaccination

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Abstract

Sarcoidosis is an idiopathic granulomatous disease and can virtually affect any organ system. Multiple factors, including tubercular antigens organic and environmental exposures, have been implicated in its pathogenesis. In addition to drugs, sarcoid-like reactions have been reported following varicella and influenza vaccination. Few reports of erythema nodosum and Lofgren syndrome have been reported after the COVID-19 vaccination, though no histologic diagnosis was pursued in these cases. We herein report a case of sarcoidosis presenting with bilateral acute onset vision loss with a temporal association with COVID-19 vaccination (ChadOx-1 n-COV, COVISHIELD™). Symptoms started within two weeks of receiving the vaccine. Alternate causes for optic neuritis were excluded. Transbronchial lung biopsy showed the presence of non-caseating epithelioid cell granulomas. The patient received high-dose corticosteroids immediately after diagnosis, albeit with incomplete clinical improvement in vision on a three-month follow-up. In conclusion, we report a novel case of sarcoidosis-related optic neuritis following COVID-19 vaccination.

Introduction

Sarcoidosis, an idiopathic inflammatory disease, is characterized by the formation of noncaseating epitheloid-cell granulomas. Although the condition can affect virtually any organ, lungs, lymph nodes, skin and eyes are most frequently affected [1,2]. The granulomatous inflammation associated with this disease can affect any part of the eye and its adnexa. It can cause progressive visual impairment and blindness, which can be the initial manifestation of the disease [3-6]. Here we present the case of a patient who presented with bilateral vision loss following COVID-19 vaccination, which was diagnosed as secondary to sarcoidosis. Patient was managed with high dose steroids, with marginal short term clinical improvement in vision.

Case Report

A 56-year-old lady, a homemaker, presented with acute onset progressive painless loss of vision of the left eye for 20 days, followed by sudden, painless vision loss of the right eye ten days

later. The patient also had occasional complaints of ill-defined, diffuse chest pain over the anterior chest bilaterally for ten days. She gave history of receiving her first dose of COVID-19 vaccination (ChadOx-1 n-COV, COVISHIELD^{TM}) twelve days prior to onset of symptoms; other past medical history was unremarkable. On ophthalmologic examination, there was no light perception on both eyes, with bilateral pupils reacting sluggishly. Fundus examination revealed a pale disc with distinct margins. Vitals were stable and systemic review was unremarkable. Chest X-ray revealed hilar prominence with lower zone predominant interstitial infiltrates bilaterally (Figure 1A). Routine blood investigations were within normal limits. Electrocardiogram was normal; echocardiography was unremarkable. Ultrasound of the abdomen did not show any organomegaly or lymphadenopathy. CT chest (Figure 1 B,C) showed mediastinal lymphadenopathy with bilateral lung infiltrates with tiny nodularity involving bilateral lower lobes. The patient was subjected to MRI brain and orbit (Figure 1 E,G) in which bilateral optic nerve showed an increase in T2 signal intensity suggesting signs of optic neuritis. There was no evidence of any significant abnormality involving eye lobes, extraocular muscles, pituitary gland, and cavernous sinuses. Serum calcium, 24-hour urinary calcium, and serum angiotensin-converting enzyme (ACE) levels were ordered. Mantoux test was done; interferon gamma release test (IGRA) was also sent. She was also worked up to rule out autoimmune causes was sent including antinuclear antibodies (ANA), antineutrophilic cytoplasmic antibodies (ANCA), and aquaporin-4 antibodies. Viral markers i.e., human immunodeficiency virus (HIV) serology, hepatitis B surface antigen (HbsAg), and hepatitis C virus antibodies (HCV Ab) were also sent. In view of high clinicoradiologic possibility of sarcoidosis and organ threatening disease, patient was initiated on high dose steroids. Pre-bronchoscopy nasopharyngeal swab for COVID-19 real-time reverse transcription polymerase chain reaction test (SARS-CoV-2 rRT-PCR) was negative. On the same day, flexible bronchoscopy was performed to obtain a histologic diagnosis. There was no endobronchial abnormality. Bronchoalveolar lavage (BAL) was taken from right lower lobe. Conventional transbronchial needle aspiration (c-TBNA) was performed from subcarinal (station 7) and right lower paratracheal (station 4) lymph nodes. Endobronchial and transbronchial lung biopsies (TBLB) were taken from the right lower lobe lateral basal segment. On rapid onsite evaluation of TBLB touch smear, granulomas without necrosis were identified. BAL and c-TBNA sample smears were negative for acid fast bacilli (AFB); cartridge based nucleic acid amplification test (CBNAAT) for TB was negative; cytology was negative for malignant cells. C-TBNA and TBLB specimens showed the presence of noncaseating granulomatous inflammation (Figure 1D). Other causes of isolated optic neuritis were ruled out. Serum calcium, 24-hour urinary calcium and serum angiotensin-converting enzyme (ACE) levels were normal. Mantoux test and IGRA was negative. Viral markers, ANA and ANCA were negative; aquaporin-4 antibodies were negative. MRI did not support a diagnosis of neuromyelitis optica spectrum disorder [7]. After three days of pulse steroids, she was initiated on 1/g/kg prednisolone alongwith supportive treatment. At one month follow up, she had marginally improved visual acuity to finger counting at three meters. On three month follow up, her visual acuity had improved to 6/60 bilaterally.

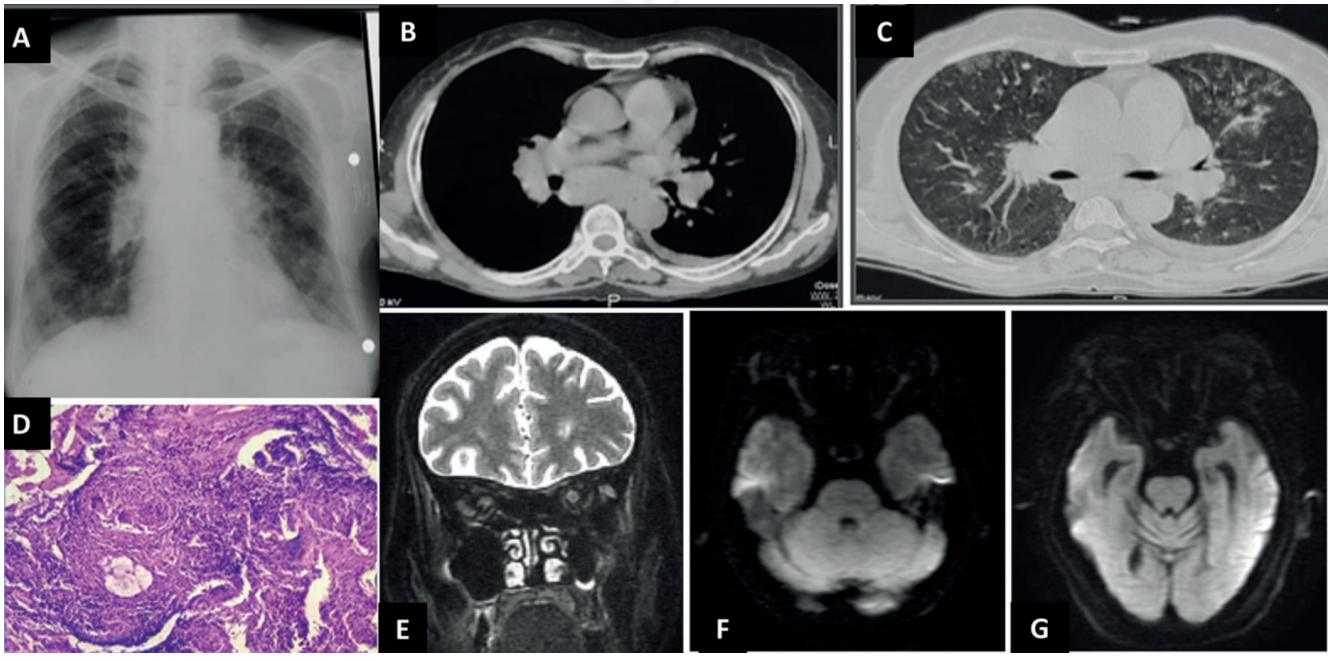

Figure 1. A) Chest X-ray posterior-anterior view showing hilar prominence and lower zone predominant interstitial infiltrates bilaterally. B) Mediastinal window of high-resolution computed tomography (HRCT) chest showing mediastinal lymphadenopathy. C) Lung window of HRCT chest showing lung infiltrates with nodularity. D) Histopathology picture of transbronchial lung biopsies specimen showing non caseating granuloma. E) T2 weighted fat saturated coronal image shows T2 hyperintensity involving retrobulbar portion of bilateral optic nerves. F) Axial diffusion weighted image shows mild diffusion restriction involving bilateral optic nerves, with mildly high signal in trace image. G) This shows a normal control axial diffusion weighted image for comparison whereby optic nerves do not show high signal on trace image.

Discussion

Involvement of the optic nerve occurs in about 1-5% of sarcoidosis, even though uveitis is the most common ocular inflammatory response in this condition [3-6,8]. There are different mechanisms by which optic nerve involvement, such as inflammation of the nerve itself, infiltration or compression by an inflammatory mass, ischemic complications of choroidal inflammation, glaucoma leading to secondary optic nerve involvement, disc granulomas, optic perineuritis or hydrocephalus. Treatment consists of systemic corticosteroids alongwith other immunosuppressants. However, optic nerve involvement has been associated with poor visual outcome [8].

Patients with sarcoidosis appear to be at greater risk of severe COVID-19 and adverse outcomes, owing to disease per se, respiratory functional abnormalities as well as ongoing immunosuppression [9,10]. Moreover, COVID-19 per se has been associated with new onset of autoimmune diseases including sarcoidosis [11,12]. Therefore, vaccination against SARS-CoV-2 is recommended for patients of sarcoidosis [13]. COVID-19 vaccination, albeit, has been associated with limited cases of ophthalmologic adverse events, including autoimmune optic neuropathies [14]. Also, COVID-19 vaccination associated erythema nodosum has been reported in few cases. The vaccines implicated include protein subunit vaccines (MVC-COV1901, Medigen) [15], replication deficient viral vector vaccines (ChadOx-1, Astra Zeneca), mRNA vaccines (BNT162b2, Pfizer; mRNA-1273, Moderna) [16,17] as well as with combinations (first vaccination with ChadOX-1, Astra Zeneca; second vaccination with CX-024414, Spikevax, Moderna) [18]. Also, one patient had recurrence of erythema nodosum three days after the second dose of mRNA vaccine (Pfizer-BioNTech BNT162b2) [19]. Most cases with vaccine associated sarcoidal reactions have had cutaneous or limited disease, with excellent short-term outcomes. Some cases of COVID vaccination associated autoimmune optic neuritis also showed remarkable response to high dose corticosteroids [20]. However, in our case, the patient had sarcoidosis with bilateral optic neuritis, and a suboptimal outcome.

Conclusions

COVID-19 vaccination has been associated with various autoimmune phenomenon including erythema nodosum and myelopathies. Optic neuritis is a known complication of various other vaccinations including influenza, BCG and COVID-19. Erythema nodosum has been described post COVID-19 vaccination, however, sarcoidosis presenting with optic neuritis, has not been reported. Whether this is a chance phenomenon, or an adverse effect of the vaccine, needs to be evaluated. Prospective follow-up of sarcoidosis patients for relapses after COVID-19 vaccination is necessary to answer this question.

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