We herein report a rare case of sarcoidosis presenting as bilateral vocal cord paralysis due to bilateral vagal nerve involvement. A 72-year-old woman with uveitis of the left eye complained of hoarseness and aspiration due to bilateral vocal cord paralysis. An endobronchial needle aspiration biopsy specimen of the mediastinal lymph nodes showed non-caseating epithelioid cell granuloma. Total protein and cell concentrations in the cerebrospinal fluid were increased. We diagnosed her to have sarcoidosis with bilateral vagal nerve involvement. Corticosteroid therapy improved her symptoms of hoarseness and aspiration. Sarcoidosis should therefore be taken into consideration as a potential cause of bilateral vocal cord paralysis.

Key words: sarcoidosis, vocal cord paralysis, neurosarcoidosis, vagal nerve, corticosteroid

paramedian position (Fig. 1a). Large amounts of secretions were found to be pooled in the postcricoid region and pyriform sinuses. Laboratory data on admission included a white blood cell count of 5,440 cells·mm$^3$ with 53.1% neutrophils, 36.6% lymphocytes, 7.5% monocytes, 2.8% eosinophils and C-reactive protein of 1.27 mg·dL$^{-1}$. The serum levels of angiotensin-converting enzyme (ACE) and lysozyme were elevated to 24.5 IU·L$^{-1}$ and 12.9 μg·mL$^{-1}$, respectively. The serum levels of autoantibodies and tumor markers were within their normal ranges. Serum complex fixation tests for influenza viruses A and B, adenovirus and RS virus were negative. The serum complex fixation test and (immunoglobulin) IgM and IgG for herpes simplex virus were also negative. IgG was positive for herpes zoster virus, but the IgM titer was negative, which was suggestive of a prior infection. The calcium levels in the serum and urine were also within the normal ranges. Both the tuberculin skin test and the interferon-gamma releasing assay for tuberculosis (T-spot$^\text{T}$) were negative. On admission, whole-body computed tomography scans detected bilateral hilar and mediastinal lymphadenopathy and small centrilobular and perilobular nodules in the upper lobes of both lungs, but no muscle lesions, cutaneous or subcutaneous lesions, or malignant or cardiovascular diseases (Fig. 2). A $^{67}$Ga-scintigram showed an abnormal accumulation in the hilar and mediastinal lymph nodes. Bronchoalveolar lavage revealed elevations of the fraction of lymphocytes to 30.0% and the CD4/CD8 ratio to 16.6. An endobronchial needle aspiration biopsy of the subcarinal and peritracheal lymph nodes under ultrasound guidance showed non-caseating epithelioid cell granulomas (Fig. 3). A transbronchial lung biopsy could not detect granulomatous lesions. Cultures of the lymph node specimens for mycobacteria and fungi were negative. Gadolinium-enhanced brain and spine magnetic resonance

**Figure 1.** (a) Flexible laryngoscopy on admission demonstrating bilateral vocal cord paralysis in the paramedian position. (b) One month after the corticosteroid therapy, the right vocal cord function improved, but some slight paralysis of the left vocal cord remained. (c) Four months after the corticosteroid therapy, the paralysis of both vocal cords had completely improved.

**Figure 2.** Coronal sections of neck and chest computed tomography on admission showing lymphadenopathy around the right subclavian artery (a: arrow) and the aorta (b: arrow), but the lymph nodes were not enlarged enough to compress the pair of recurrent laryngeal nerves. Nodular shadows were observed in bilateral upper lobes of the lung (c).
The causes of vocal cord paralysis include the presence of neoplasms, trauma (neck surgery, blunt injury, intubation, etc.), central nervous system disease, cardiovascular disease, autoimmune disease and infectious disease (viral, tuberculosis, mediastinal abscess, etc.) (1). These causes are classified into three patterns: ① a direct lesion of the vocal cords, ② injuries to or compression of the peripheral recurrent laryngeal nerve and ③ the inflammation of the peripheral and central nervous systems. Sarcoioidosis has the potential to cause hoarseness in all of the following ways: ① Its non-caseating granulomas could directly invade the vocal cords, ② enlarged lymph nodes around the peripheral pathway of the nerve could compress them and ③ cranial neuritis of sarcoidosis could cause vocal cord paralysis.

The direct invasion of the vocal cords could be the cause of bilateral vocal cord paralysis in patients with sarcoidosis (12-15). However, it is rare because the true vocal cords are considered to be spared, presumably by their lack of lymphatics (15). A flexible laryngoscopic examination can reveal a wide array of mucosal findings, which include edema, erythema, punctate nodules, a mass lesion and ulceration (13). In our case, flexible laryngoscopy revealed no abnormal macroscopic findings in the vocal cords. To rule out the possibility of direct invasion into the vocal cords categorically, a vocal cord biopsy might be needed. However, we did not perform a vocal cord biopsy because we worried that it could have the complication of worsening of the hoarseness.

Nonetheless, in approximately 75% of the patients with sarcoidosis, nodal enlargements in the right paratracheal or aortopulmonic window lesions have been identified (16), and case reports of vocal cord paralysis due to the compression of the enlarged mediastinal lymph nodes are rare (3-10, 17). Most cases of unilateral vocal cord paralysis in sarcoidosis trend to occur in the left vocal cord as a result of left recurrent laryngeal nerve palsy by the lymph nodes as they hook around the arch of the aorta (3-8). Only one case of right vocal cord paralysis due to mediastinal lymphadenopathy has been reported (17). It would therefore be quite rare for enlarged mediastinal lymph nodes to cause bilateral vocal cord paralysis by compressing the left and right laryngeal recurrent nerves around the aorta and the right subclavian artery, respectively (9, 10). In our case, the mediastinal lymph nodes were swollen, but they were not so large as to compress both of the recurrent pharyngeal nerves (Fig. 2), as shown in previous cases of bilateral vocal cord paralysis due to the compression by lymphadenopathy for sarcoidosis (9, 10).

Neurosarcoidosis, inflammation of the central and peripheral nervous systems with sarcoidosis, is estimated to constitute 5-15% of sarcoidosis cases (18). Cranial polyneuritis is the most common pattern of neurosarcoidosis and facial imaging (MRI) scans did not show any abnormal lesions, such as the swelling of the cranial nerve roots or enhanced lesions along the cranial nerve roots. The cerebrospinal fluid (CSF) protein level was elevated to 55.8 mg·mL⁻¹ and the CSF cell count was also elevated to 4 cells·mm⁻³, with 82% lymphocytes and 18% neutrophils. The cytological and culture examinations of the CSF detected neither malignant diseases nor infectious diseases. Paired CSF examinations of the CSF detected neither malignant diseases nor infectious diseases, and herpes zoster virus were all negative and did not show a significant elevation of the IgG titer in the second CSF examination (0.2 IU·L⁻¹ remained the same). We diagnosed the lymph node biopsy specimen obtained by endobronchial ultrasound-guided transbronchial needle aspiration showed non-caseating granuloma.

We started oral corticosteroid therapy at a dose of 30 mg·day⁻¹. After one month of this therapy, the serum levels of ACE and lysozyme were normalized. The CSF protein level and the cell count of the CSF were decreased to 29.7 mg·mL⁻¹ and 4 cells·mm⁻³, respectively. The CSF ACE level (0.1 IU·L⁻¹) remained the same (CSF lysozyme was not measured). The patient’s breathy voice gradually improved and flexible laryngoscopy showed an improvement of the right vocal cord function, but some slight paralysis of the left vocal cord remained (Fig. 1b). She was able to swallow successfully and a drinking water test showed no aspiration. We tapered the oral prednisone to 25 mg·day⁻¹ and then reduced the dose by 5 mg every four weeks. Four months after the corticosteroid therapy, she was treated with 15 mg·day⁻¹ of oral prednisone; no recurrence of her symptoms had occurred, and her left vocal cord function had also improved (Fig. 1c).

Discussion

We herein report a rare case of bilateral vocal cord paralysis due to the bilateral vagal nerve involvement of sarcoidosis. An endobronchial needle aspiration biopsy specimen of the mediastinal lymph nodes showed non-caseating epithelioid cell granuloma. Total protein and cell concentrations in the CSF were increased. The corticosteroid therapy led to an improvement of the vocal cord paralysis.
nerve paralysis occurs most frequently (11, 19). One case of bilateral vocal cord paralysis was accompanied by facial paralysis, which was also indicative of cranial polyneuropathy, including the bilateral vagal nerves and facial nerve (9). However, a definite diagnosis of cranial polyneuropathy is difficult because it is usually impossible to obtain pathological findings during a patient’s lifetime. For the diagnosis of neurosarcoïdosis, clinicians need to rule out the other causes of cranial polyneuropathies carefully, such as an infection or a malignant disease (malignant lymphoma and neurolymphoma). Brain or spinal MRI scans and CSF examinations could be helpful for the diagnosis. In our case, brain or spine gadolinium-enhanced MRI could not detect any lesion from the cortex to the nucleus ambiguus in the medulla. Although gadolinium MRI is superior to normal MRI in detecting central nervous system (CNS) manifestations of sarcoïdosis, it does not rule out the diagnosis of neurosarcoïdosis, especially in patients with only cranial neuropathies or in those treated with a corticosteroid (20). Furthermore, none of the unenhanced or gadolinium-enhanced MRI manifestations of sarcoïdosis is specific to the disease. Elevated protein levels, pleocytosis and an increased spinal pressure have been reported in about half of the patients with cranial nerve paralysis, peripheral neuropathy and meningitis (20). Although the elevation of CSF ACE may be reasonably specific (94-95%) for CNS neurosarcoïdosis, it is insensitive (24-25%) (21). Elevations of CSF lysozyme and β2-microglobulin revealed disease activity in CNS neurosarcoïdosis (22). Although we could not find elevated levels of CSF ACE or lysozyme in our case, the elevations of total protein and cell count would support the existence of bilateral vagal neuritis associated with granulomatous inflammatory lesions of sarcoïdosis. Moreover, these findings were normalized with the improvement of the vocal cord paralysis. These results suggest that our case had bilateral vagal nerve involvement that led to the bilateral vocal cord paralysis. We were able to rule out the possibility of Guillain-Barré-like neuropathy of sarcoïdosis in our case because the patient did not have the symptoms of an antecedent infection, a weakness of the extremities, a sensory disturbance or an albuminocytologic dissociation (23).

Corticosteroid therapy is performed in most cases of vocal cord paralysis with sarcoïdosis (3, 5-10, 17). One case was caused by both compressive lymphadenopathy and cranial polyneuropitis (10). All of the other cases were caused only by compressive lymphadenopathy (3, 5-10, 17). Except for one case (4), oral prednisone therapy at a dose of 0.5-1 mg·kg⁻¹·day¹ could resolve almost all of the vocal cord paralyses within one to two weeks in the unilateral cases (3, 5-10, 17). High-dose intravenous methylprednisone therapy was administered in the bilateral cases (8, 9) (Table). In our case, oral prednisone therapy could improve the bilateral vocal cord paralysis.

In summary, we herein reported a rare case of bilateral vocal cord paralysis due to the bilateral vagal nerve involvement of sarcoïdosis. Clinicians should be aware of the bilateral vagal nerve involvement of sarcoïdosis as a potential cause of bilateral vocal cord paralysis. Corticosteroid therapy would be effective for the sarcoïdosis patients with bilateral vocal cord paralysis due to bilateral vagal nerve involvement.

The authors state that they have no Conflict of Interest (COI).

Acknowledgement

We thank Dr. Takashi Hirano for the assessment of the vocal cord function.

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