Neurofibromatosis type 1 with huge intrathoracic meningoceles: A case report and literature review

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Case Report

Keywords: Intrathoracic Meningocele, Neurofibromatosis 1, Thoracoscope, Spinal Deformity, Differentiated Diagnosis

Posted Date: February 22nd, 2024

DOI: https://doi.org/10.21203/rs.3.rs-3973388/v1

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Additional Declarations: No competing interests reported.
Abstract

Neurofibromatosis type 1 (NF-1) is a genetic disease that affects multiple organs and systems, leading to various clinical manifestations. In NF-1, rare intrathoracic meningoceles often occur alongside bone dysplasia. These meningoceles contain cerebrospinal fluid (CSF) and can be mistakenly diagnosed as 'pleural effusion'. In this case report, we mistakenly identified 'cerebrospinal fluid' as 'pleural effusion' and proceeded with drainage. This error posed significant risks to the patient and holds valuable implications for the future diagnosis and treatment of similar patients.

Introduction

Intrathoracic meningocele is a rare condition characterized by the bulging of the meninges through the intervertebral foramen or a defect in the vertebral body. It is most associated with neurofibromatosis type 1 (NF-1), accounting for 60 to 85% of cases[1]. Initially, patients with intrathoracic meningocele may not exhibit any signs or symptoms. However, as the disease progresses, some patients may experience chest tightness or breathlessness due to compression of the lungs. NF-1 is an uncommon chromosomal inherited disease with an incidence of approximately 1/2500-1/3000 in newborns[2]. These patients often develop scoliosis and meningocele in adulthood as a result of sclerotin dysplasia[3]. When the meningocele becomes large, patients may experience discomfort and seek medical attention. Unfortunately, due to the rarity of the condition and a lack of expertise, the meningocele may be misdiagnosed as pleural effusion. As a result, patients may undergo unnecessary drainage of a mass pleural effusion, putting them at risk of complications and even death. In this article, we present a case of a patient with huge intrathoracic meningoceles combined with NF-1.

Case report

History and Examination

A 43-year-old female patient with a history of NF-1 presented to the Hospital on 16 February 2023, complaining of chest congestion and dyspnea that had been ongoing for a month. The patient had a history of skin conditions, such as brown macule, since the age of four. At the age of 14, she underwent surgical treatment for a subcutaneous mass in her right leg, which was diagnosed as NF-1 through pathology. Although the patient had no prior family history of NF-1, her son also suffered from the condition. Over the past three years, she had experienced intermittent coughing but had not sought medical attention due to mobility problems and feelings of inferiority. One month ago, she started experiencing chest tightness and dyspnea at rest. She sought care at a local hospital, where a massive pleural effusion was discovered in the right hemithorax. In order to determine the cause, a chest drainage tube was inserted to drain the pleural fluid and provide relief from symptoms. Chemical and cytological analyses of the pleural effusion indicated that it was a transudate. The patient was then referred to the hospital to further investigate the cause of the transudate effusion.
During a routine check-up upon admission, weakened respiratory sounds were detected in the right lung. The patient presented numerous skin nodules with pedicles and café au lait spots scattered across the trunk. Additionally, a large soft mass was observed in the lower lumbar region, and several masses were found on the right lower extremity, causing difficulty in walking. No neurological signs or symptoms were observed during the examination.

A chest computed tomography (CT) scan revealed a large low-density image in the right thoracic cavity, and a defect was observed in part of the vertebral plate in the thoracic spine (Figure. 1: Chest computed tomography revealed a large low-density image in the right thoracic cavity, extending into the spinal canal, along with a defective thoracic vertebra.). In order to investigate the cause of the pleural effusion, thoracoscopy was performed. The intraoperative exploration revealed the following findings (Figure. 2: The thoracoscope confirmed the presence of a drainage tube within the thoracic cavity. The figures indicated minimal fluid accumulation and smooth pleurae, and a tissue biopsy was conducted.): (1) The pleurae showed no nodules and appeared normal, (2) only a small amount of fluid was present, and (3) the drainage tube was located in the thoracic cavity. The pleural biopsy results were normal. Routine postoperative plain chest X-rays were taken, and unexpectedly, a massive pleural effusion was evident in the right thorax, which contradicted the findings from the thoracoscopy. This raises the question of what caused the sudden accumulation of such a large amount of fluid in the pleural cavity and why it was not detected during the thoracoscopy.

**Diagnostic Analysis**

To investigate the cause of the significant pleural effusion, a chest tube was once again inserted in the hospital. Approximately 1000 ml of clear and colorless liquid was gradually drained, resulting in an improvement in her chest tightness. However, she experienced a headache the following day and found relief by lying flat on her back. Subsequently, an analysis of the hydrothorax revealed a white blood cell count of $11 \times 10^6$/L, lactate dehydrogenase level of 36U/L, total protein level of 3.7 g/L, and glucose level of 3.21 mmol/L. Cytology examination confirmed the absence of malignant tumor cells in the pleural effusion. Furthermore, thorough examination and data analysis ruled out heart failure, hepatic and renal dysfunction, hypothyroidism, and hypoproteinemia.

The pleural fluid appeared clear and transparent, and the patient experienced a postural headache after the pleural effusion was drawn. Upon analyzing the pleural effusion, we discovered that it was actually CSF. CSF hydrothorax is typically a result of traumatic injury or spinal column surgery. However, this patient did not have a history of trauma or surgery in the spinal column or chest. We reviewed the chest CT and identified a low-density image connected to the canalis vertebralis (Figure. 1). Subsequently, a thoracic magnetic resonance imaging (MRI) was performed (Figure. 3A: (A1-A2) Both the sagittal and horizontal axial views of the thoracic vertebrae demonstrate a discontinuity between the T4-T8 vertebrae. (B1-B2) The MRI reveals that the thoracic vertebrae are protruding towards the right. (C1-C2) A right thoracic meningocele has developed, there is a connection between the 'pleural effusion' and the spinal canal.), which revealed thoracic scoliosis (Figure. 3A), discontinuity at the right T4-T8 vertebral appendix
Importantly, the MRI showed that the 'pleural fluid' had the same intensity as CSF. Therefore, it can be inferred that a thoracic spinal meningocele had formed, leading to the drainage of CSF and causing the patient's postural headache. However, we observed a drainage tube in the chest during the thoracoscopy. This may have been caused by the tube shifting into the chest cavity. Consequently, upon admission, we were unable to drain fluid from the tube that had been inserted at a local hospital.

Discussion

NF-1 is a rare genetic disease that impacts various systems including the skin, bones and joints, respiratory system, and nervous system[4]. Intrathoracic meningocele, although relatively uncommon, is often associated with NF-1. It has been observed that 60–85% of thoracic meningoceles occur in individuals with NF-1 due to dural hypoplasia and intervertebral foramen enlargement, which are the primary contributing factors to the development of intrathoracic meningocele. Intrathoracic meningocele can be asymptomatic, but when the bulging area compresses the lungs, it can cause symptoms such as chest tightness and dyspnea. Asymptomatic patients can be treated conservatively, while patients with obvious symptoms may require surgical treatment[5]. The main goal of treatment is to reduce lung compression and relieve symptoms. Some studies have explored the use of fixed-pressure valves for vesicoperitoneal shunting to treat giant intrathoracic meningoceles[6]. For patients who cannot tolerate general anesthesia, shunting under local anesthesia may be a preferable option. However, a case report by Cho et al. in 2015 described a patient with bilateral giant meningocele in the thoracic cavity who did not experience significant symptom relief or changes in cystic mass and fluid volume after peritoneal bladder shunt surgery. As a result, the patient had to undergo thoracotomy, during which the bulging cyst wall was completely removed and dural repair was performed[7]. Furthermore, a literature review by Kurt et al. in 2021 highlighted that among 6 case reports of cerebrospinal fluid diversion for meningothoraocoele, only 1 was successful. If clinical symptoms do not improve after cerebrospinal fluid shunt surgery, thoracotomy should be considered[8]. In our case, we initially misidentified the pleural effusion as cerebrospinal fluid and drained it, inadvertently performing a shunt that lowered the cerebrospinal fluid pressure and relieved the patient's dyspnea. However, this led to immediate symptoms of postural dizziness and headache caused by intraspinal hypotension. After conducting a thorough review of the patient's past medical history, imaging data, laboratory tests, and thoracoscopy results, we proceeded to perform an MRI scan. The scan revealed that the patient had thoracic scoliosis and discontinuity in the right T4-T8 vertebral bodies. Additionally, we observed that the right pleural effusion was connected to the spinal canal and exhibited the same signal as cerebrospinal fluid. Based on these findings, we ultimately diagnosed the patient with thoracic meningocele. We recommended that the patient undergo further surgical treatment. However, considering that thoracotomy was highly invasive, and its efficacy could not be guaranteed, the patient declined surgery and opted for conservative treatment, including fluid rehydration. Once the symptoms of dyspnea were completely relieved, the patient was discharged from the hospital and continues to be alive to this day.
In the bone manifestation of NF-1, spinal deformities account for approximately 60% of skeletal abnormalities. These deformities include scoliosis, kyphoscoliosis, costal deformities, and vertebral deformities such as spondylolisthesis, scalloping of vertebral borders, thinning of pedicles, enlargement of intervertebral foramen, and vertebral canal[9]. Scoliosis caused by NF-1 can be classified into two types: dystrophic and non-dystrophic. Both types have similar incidence, clinical manifestations, and prognosis. However, dystrophic scoliosis tends to result in more severe curves and rapid progression, requiring early invasive treatment. Non-dystrophic scoliosis typically necessitates spinal fusion when the degree of curvature exceeds 40°[10]. In this case, the patient did not experience any neurological complications due to spinal cord compression. Therefore, we classify her scoliosis as non-dystrophic.

The patient presented with symptoms of chest tightness, shortness of breath, and dyspnea persisting for over a month. A significant amount of 'pleural effusion' was detected on chest CT at a local hospital, leading to their admission to our hospital for further investigation into the cause of the pleural effusion. Pleural effusion caused by lung diseases and systemic diseases typically appears yellow or red. However, if a colorless pleural effusion is detected, CSF should be considered. CSF leakage into the chest cavity is a rare condition that usually occurs after trauma or surgery[11]. It is uncommon for patients to experience CSF leakage without a history of operation or trauma. In this particular case, the patient had a long history of NF-1 disease spanning over 30 years. Among patients with NF-1, there are variations in the clinical presentation, often accompanied by thoracic involvement such as intrathoracic neurofibroma, intrathoracic meningoceles, spinal deformities, cysts, emphysema, subpleural bullae, interstitial pneumonia, and more[12, 13]. Follow-up examinations have shown that lung involvement is more likely to occur in the advanced stages of NF-1, typically in patients in their thirties and forties. Therefore, several studies have emphasized the importance of chest imaging in patients with NF-1[14].

**Lessons Learned**

Pleural effusion is a commonly observed condition in clinical practice, often associated with various underlying diseases. Despite advancements in diagnostic techniques, approximately 20% of pleural effusions still have an uncertain origin[15]. Thoracoscopy, a routine procedure, can be performed to identify the cause of unknown pleural effusions. Studies have shown that thoracoscopy can provide a clear diagnosis for 71–97% of patients[16]. However, in the case of NF-1 patients with intrathoracic meningocele, the blind use of thoracoscopy may pose potential risks, even life-threatening ones.

In this case, it has been determined that the patient has had NF-1 for over 30 years. When a significant amount of fluid is detected in the patient's pleural cavity, it is important to immediately consider the possibility of cerebrospinal fluid. Although cases of intrapleural meningocele are extremely rare, this should not be overlooked. Unfortunately, we did not consider this possibility and instead conducted thoracoscopy to search for the cause of the 'pleural effusion'. However, no large pleural effusion was found during the thoracoscopy, and biopsy ruled out any pleural lesions. To confirm the diagnosis, we performed thoracentesis on the patient once again, sent the fluid for routine biochemistry testing, and conducted an MRI examination. Eventually, the diagnosis of intrathoracic meningocele was confirmed.
Additionally, if CSF effusion is suspected, a beta-2-transferrin test should be performed[17]. β-2-Transferrin is a glycoprotein produced by neuraminidase in the brain and is predominantly found in CSF. It is present in only small amounts in cochlear perilymph, aqueous humor of the eye, and vitreous body. Laboratory techniques such as immunofixation, immunoblotting, gel electrophoresis, and isoelectric focusing are commonly used to determine β-2-transferrin content, all of which have high accuracy and specificity (over 90%) for CSF diagnosis. Moreover, studies have demonstrated that β-2-transferrin can be reliably detected in CSF samples stored at room temperature or refrigerated for 14 days[18]. Hence, β-2-transferrin serves as a reliable marker for determining CSF presence. However, in our case, although we strongly suspected the effusion to be CSF, we did not conduct a β-2-transferrin test on the extracted fluid. Instead, we opted for MRI scanning as it provides a clear visualization of the lesion site’s relationship with the spinal cord and nerves. Furthermore, MRI enables the comparison and identification of fluids and can differentiate intrathoracic meningocele from tumors like neurofibroma and neuroblastoma, thereby aiding in accurate diagnosis.

Conclusions

In patients with NF-1 complicated by spinal deformity, there is a high incidence of intrathoracic meningoceles. However, draining fluid and prematurely adopting a thoracoscope can be dangerous, leading to postural headache, intracranial hypotension, pneumocephalus, and even death. The treatment approach may vary depending on the characteristics of the lesions, and multidisciplinary collaborations can greatly enhance the prognosis of these patients.

Abbreviations

NF-1
Neurofibromatosis type 1
CSF
Cerebrospinal fluid
CT
Computed tomography
MRI
Magnetic resonance imaging

Declarations

Acknowledgements

Not applicable.

Authors' contributions
JRB, NYC and WJL wrote and revised the manuscript. LFM and QH conceived and directed this study. All authors read and approved the manuscript and agree to be accountable for all aspects of the research in ensuring that the accuracy or integrity of any part of the work are appropriately investigated and resolved.

**Funding**

There is no relevant funding in this study.

**Availability of data and materials**

Not applicable.

**Ethics approval and consent to participate**

This study was approved by the Human Research Ethics Committee of Northern Jiangsu Province Hospital.

**Consent for publication**

Written informed consent for publication of data was obtained from the patient. A copy of the consent form is available for review by the Editor of the journal.

**Competing interests**

None.

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**References**


**Figures**

![Figure 1](image)

**Figure 1**

Chest computed tomography revealed a large low-density image in the right thoracic cavity, extending into the spinal canal, along with a defective thoracic vertebra.
Figure 2

The thoracoscope confirmed the presence of a drainage tube within the thoracic cavity. The figures indicated minimal fluid accumulation and smooth pleurae, and a tissue biopsy was conducted.
Figure 3

(A1-A2) Both the sagittal and horizontal axial views of the thoracic vertebrae demonstrate a discontinuity between the T4-T8 vertebrae. (B1-B2) The MRI reveals that the thoracic vertebrae are protruding towards the right. (C1-C2) A right thoracic meningocele has developed, there is a connection between the 'pleural effusion' and the spinal canal.