CASE REPORT

Accidental Detection of Tuberculous Empyema at Health Check-Up

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SUMMARY

Background: Patients with tuberculous empyema (TE) can have a serious impact on lung function as their disease progresses, and, if left untreated, can cause damage to other parts of the body such as the thorax and spine, causing pain and inconvenience to the patient. Early diagnosis and the search for appropriate treatment are key to improving the survival rate of the disease.

Methods: We report a case of a young patient with an unexpected finding of right pleural effusion on physical examination, who was eventually diagnosed with TE using next-generation sequencing of pleural tissue. We analyzed the literature to improve clinicians’ understanding of TE and how to properly diagnose and treat the disease.

Results: Laboratory results of the pleural effusion suggested a possible Mycobacterium tuberculosis infection, but pathogen-related tests were negative, and the diagnosis was eventually successfully confirmed by thoracoscopic pleural biopsy.

Conclusions: The diagnosis of TE should be considered in young patients with pleural thickening of the empyema. Adenosine deaminase may provide diagnostic direction in patients with unexplained thorax abscess. Pleural biopsy, although an invasive procedure, is an essential diagnostic tool in some cases.


KEYWORDS

tuberculous empyema, adenosine deaminase, pleural biopsy, treatment

CASE REPORT

Tuberculosis (TB) is a multisystemic disease and one of the major global public health challenges. Mycobacterium tuberculosis (MTB), the most common agent of TB, can infect organs and tissues outside the lungs (such as the pleura, lymph nodes, and bones), and TB in these areas is called extrapulmonary tuberculosis (EPTB). The most common form of EPTB is tuberculous pleurisy (TP) [1]. The continued progression of TP can lead not only to a decline in lung function but also to tuberculous empyema (TE) [2]. TE is associated with a high mortality rate, so early and accurate diagnosis and treatment and good patient recovery are essential.

The patient is a 30-year-old young man with no underlying medical conditions who was found to have a right pleural effusion during a health check-up at a local hospital more than 10 days ago. After treatment such as
or thoracentesis and drainage at the local hospital, a repeat chest CT indicated no improvement in the lesion. Therefore, on June 1, 2022, he came to our hospital for further treatment. Physical examination after admission: T: 36.5°C, P: 100 beats/min, R: 21 beats/min, BP: 109/96 mmHg, body type was weak, visual examination of the chest showed reduced respiratory dynamics on the right side, palpation showed reduced vocal fremitus on the right side, percussion showed dullness in the right lung and auscultation showed low breath sounds in the right lung. After admission to the hospital, relevant laboratory tests were completed: routine blood tests indicated hemoglobin 98 g/L, procalcitonin 0.11 ng/mL, tumor series indicated neuron-specific enolase 36.4 μg/L, erythrocyte sedimentation rate 68 mm/hour, rheumatic series indicated C-reactive protein 53.7 mg/L, HIV, syphilis, immune series, antinuclear antibody series, viral antibodies, tuberculosis antibodies, and PPD skin test were all negative. Enhanced CT of the chest revealed a right-sided fluid pneumothorax with the incomplete expansion of the lower and middle lobes of the right lung and thickening of the right pleura (Figure 1). On the third day after admission, we performed a second thoracentesis and drainage. Routine laboratory tests for pleural effusion suggested a purulent pleural effusion, predominantly multinucleated leucocytes, with a specific gravity of 1.025 and a positive Rivalta test; biochemical indications were adenosine deaminase (ADA) 50.6 U/L, glucose 3.96 mmol/L, lactate dehydrogenase 503 U/L, total protein 38.5 g/L; X-pert was negative; pathology did not reveal tumor cells, and pathogen culture was negative. The patient presented on day 4 after admission with intermittent fever and no other discomfort. Combined with the current laboratory findings, this suggested that the patient might have an MTB infection. We, therefore, gave the patient empirical anti-tuberculosis treatment with isoniazid (0.2 g PO 1/day), rifampicin (0.45 g PO 1/day), ethambutol (0.75 g PO 1/day), and pyrazinamide (0.75 g PO 1/day). To clarify the cause of the lesion, we performed bronchoscopic alveolar lavage of the basal segment of the right lower lung lobe on day 7 after admission and sent the bronchoscopic alveolar lavage fluid for next-generation sequencing (NGS), but the results did not reveal MTB. On the advice of the thoracic surgeon, the patient underwent a thoracoscopic right pleural biopsy and pleural decortication on day 14 after admission, which revealed a thickening of the visceral and parietal pleura covered with fiberboard. Post-operative histopathological findings were suggestive of chronic granulomatous inflammation (Figure 2), with negative antacid staining, but the NGS of the biopsy tissue was suggestive of MTB. The patient was diagnosed with TE and was treated with a combination of anti-tuberculosis, closed chest drainage, and pleural decortication, and improved without further fever. The patient was discharged after 54 days of hospitalization, and a follow-up chest CT (Figure 3) one month later showed a slight improvement in the lung lesion, but no significant change in the right pleural thickening was observed, and further surgical treatment was required.

DISCUSSION

We report a case with no underlying disease in which a right pleural effusion was accidentally found during a health check-up. After thoracentesis and drainage, the fluid was found to be purulent and biochemical results suggested elevated ADA and possible MTB infection, but all relevant tests regarding MTB were negative, which made the diagnosis difficult. We were finally able to diagnose it by thoracoscopic pleural biopsy and sending pleural tissue for NGS. The gas in the patient’s chest was considered to be of medical origin, as the patient had no obvious cough or sputum, and no broncho-pleural fistula was seen on bronchoscopy or chest CT. We used this case to discuss TE and hopefully increase clinicians’ awareness of it.

TE is the result of chronic active infection of the pleura, accompanied by an influx of neutrophils and the subsequent development of purulent effusions, which can lead to significant thickening and even calcification of the dirty and mural pleura [3]. TE is defined as having one of the following criteria: 1. pleural effusion smear and/or culture positive for acid-fast bacilli (AFB)/MTB on two or more occasions; 2. CT scan showing radiologic evidence of active pulmonary tuberculosis; 3. accompanied by a positive AFB sputum smear [4]. TE can be caused not only by rupture of caseous material from the superficial parenchymal cavity into the pleural cavity but also by 1. secondary involvement of the para-tracheal lymph nodes; 2. progression of the primary tuberculous pleural effusion itself; 3. direct extension of a paravertebral cold abscess; and 4. hematogenous spread of infection [5]. The extent of pleural lesions usually depends on the amount and virulence of MTB entering the pleural cavity, but the immune status of the patient’s organism is also an important influencing factor. The patient we reported did not have a disease such as HIV that can compromise immunity, but he was wasting quickly. We still considered him to have a lower-than-normal immunity. A study of TE risk factors from China found that gender made a difference in the prevalence of TE, with men more likely to have TE, which may be due to some gender differences in TP [6]. It is now common to classify empyema into 3 stages [5], namely, the exudative stage (stage I), which is characterized by a clear, thin, sterile pleural effusion; the fibrinopurulent stage (stage II), which is characterized by thickening, infection, and purulent pleural effusion; and the organizing or consolidation stage (stage III), which is characterized by the formation of granulation tissue and lung encasement, and this staging also applies to TE. The treatment of TE is to administer pathogen-specific therapy, so it is crucial to look for MTB, an important nucleic acid metabolizing enzyme associated with the level of cellular immunity in the body, with the highest levels in lymphocytes. A meta-analysis assessed...
A Case of Tuberculous Empyema Found by Accident

Figure 1. Enhanced CT of the chest: decreased volume and increased density in the middle and lower lobes of the right lung. The right pleural thickening showed a significant enhancing shadow. Gas and fluid density shadows were visible on the right side.

Figure 2. Pleural biopsy histopathology: biopsy of the right visceral and parietal pleura suggested chronic granulomatous inflammation.

Figure 3. Repeat chest CT: volume reduction in the lower and middle lobes of the right lung was less severe than before and the increased density was less than before. Pleural thickening on the right side was not significantly altered from before. Gas and fluid decreased on the right side compared to before.
the value of ADA in pleural effusions in the diagnosis of tuberculous pleural effusions, with a sensitivity and specificity of 92% and 90%, respectively [7]. High levels of ADA in pleural effusion predicted an increased risk of TE [6]. Although elevated pleural effusion ADA levels are sometimes seen in patients with empyema, malignancy, or rheumatoid pleurisy, patients with exudative and lymphocytic pleural effusions without other tests to make a definitive diagnosis in the setting of high TB burden may be empirically started on anti-tuberculosis therapy [7]. It has been suggested that in patients with isolated pleural effusions, the MTB sputum culture positivity rate is only 4%, but the sensitivity by thoracoscopic pleural biopsy is close to 98% [8]. In this patient, we performed a thoracoscopic pleural biopsy after a negative pathogen-related test result and sent it for histopathology and antacid staining. Because MTB takes a long time to culture, the acidic and anaerobic pleural environment of patients with empyema may hinder MTB growth, resulting in positive smear results but negative culture results, and in some cases, the diagnosis can only be confirmed after pleural biopsy [9]. However, our patient also had a negative smear result, so we chose to send the tissue for NGS and the results soon returned suggesting the discovery of MTB. Pleural biopsies include closed pleural biopsies and thoracoscopic pleural biopsies. Although obtaining pleural tissue samples is invasive, it has irreplaceable diagnostic value in patients with stage II/III TE. A study has considered that the detection rate of pleural tissue specimens is higher than that of pleural effusion in both Xpert and mycobacterial cultures in patients with TP. The most effective way to obtain pleural tissue is usually through thoracoscopy under the direct visualization of the physician [10]. The definitive diagnosis of TP depends on the presence of tubercle bacilli in the sputum, pleural effusion, or pleural biopsy samples [11]. Based on all our laboratory findings, we considered that this patient had developed TE due to a long period of undiagnosed asymptomatic TP.

Treatment of TE usually requires prolonged intermittent drainage and may prolong hospitalization, leading to costly medical treatment. Untreated or inadequately treated TE may lead to more serious complications (e.g., empyema necessitatis, rib and bone destruction, and chest wall masses) [6]. For the treatment of empyema, different treatments (e.g., appropriate antibiotic therapy, pleural drainage, pleural decortication, video-assisted thoracic surgery (VATS), and thoracotomy) are used depending on the stage and combined in the most appropriate way and at the best time so that the best outcome can be achieved [12]. A thick and calcified pleural wall can prevent the penetration of anti-tuberculosis drugs into the empyema space, which in turn can lead to the prevalence of drug-resistant bacteria. Early drainage of pus can improve long-term outcomes, with the retention of a pleural catheter reducing the degree of pleural thickening and the risk of complications such as surgical intervention [13,14]. Anti-tuberculosis and drainage treatment at an early stage can therefore improve the prognosis of patients. Surgery is still the most studied treatment for stage II or III empyema, which has several advantages: 1. facilitates the diagnosis of the disease stage; 2. reduces infection; and 3. re-expands the compressed lung and prevents subsequent chronic respiratory lesion [15]. It is now believed that lung resuscitation cannot be effectively achieved in patients with a disease duration of more than 1 month; if conservative treatment has failed after 1 to 2 months, the pleura fibroboard must be completely stripped by VATS, and once the disease has progressed beyond 3 months there is difficulty in stripping the pleura fibroboard; if a thick pleural peel is encasing the lung, an open access lung debridement is usually required [5]. Our treatment of this patient was therefore focused on anti-tuberculosis and drainage of effusion, and pleural decortication was performed thoracoscopically. After treatment, the patient’s right lower and middle lung lobes are reduced in size slightly compared to before, but the thickened pleura did not change significantly, so we still recommended further surgical treatment to avoid serious complications.

CONCLUSION

Despite the availability of anti-TB drugs and advanced surgical procedures in clinical practice, TE remains a serious problem in countries with a high TB burden. The diagnosis of TE cannot be excluded in young patients with empyema once pleural thickening is detected. Elevated ADA in pleural pus helps to make an early diagnosis. Pleural biopsy, although an invasive procedure, can differentiate between benign and malignant pleural lesions. Treatment of TE requires a specific combination of polychemotherapy, thoracentesis and drainage, and surgical treatment. Early and accurate diagnosis and appropriate treatment according to its staging can reduce the occurrence of serious complications of TE, improve the patient’s prognosis and reduce the burden on the patient.

Acknowledgment:
We would like to thank the other members of the Department of Respiratory Medicine, Affiliated Hospital of the North China University of Technology for the constructive criticism.

Source of Support:
This work was supported by the Hebei Province Science Development Program [20201246] and the Respiratory and Critical Care Endoscopic Diagnosis and Interventional Treatment Team and the interventional treatment of central airway tumors with rigid bronchoscopy combined with an argon knife and cryo [GZ2021057].
Ethical Approval:
This study was approved by the ethics committee of North China University of Science and Technology Affiliated Hospital. All procedures performed in studies were in accordance with the ethical standards. Informed consent was obtained.

Declaration of Interest:
No conflicts of interest.

References: