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Case report

Possibilities of using ultrasound for diagnosis of invasive pulmonary mucormycosis – A case study

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ABSTRACT

Introduction: Mucormycosis is a rare but highly lethal fungal infection, usually affecting immunocompromised patients.
Aim: To present and analyze the diagnostic capabilities of transthoracic ultrasonography in invasive pulmonary mucormycosis.
Case study: We present a case involving a 41-year-old female patient with pneumonia complicated by multisystem organ failure, who was diagnosed with invasive pulmonary mucormycosis.
Results and discussion: Transthoracic ultrasonography (TUS) revealed a consolidation area of heterogeneous echostructure with an abnormal air bronchogram, possibly suggestive of an invasive pulmonary fungal disorder. The presence of lesions observed with TUS was confirmed by computed tomography (CT). The final diagnosis of mucormycosis was possible after *Mucor* species fungi were detected in bronchoalveolar lavage culture.
Conclusions: (1) TUS is a widely available and inexpensive diagnostic method that is characterized by the absence of adverse effects, and its applicability in the diagnosis of pulmonary disorders other than invasive fungal infections is well documented. (2) Ultrasonographic analysis of lesions facilitates differentiation between bacterial and fungal pneumonia, and the high sensitivity and specificity of the procedure compared to CT scans as a reference method supports the reliability of ultrasound scans in the diagnosis of invasive pulmonary aspergillosis (IPA). (3) The use of TUS in the diagnosis of invasive pulmonary mucormycosis appears warranted, particularly in cases when it is impossible to obtain a proven diagnosis. (4) Ultrasonographic diagnosis of invasive lung disorders, including mucormycosis, requires further studies.

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1. Introduction

Mucormycosis is a rare but highly lethal fungal infection, usually affecting immunocompromised patients. Early diagnosis of the disease, combined with aggressive treatment, is crucial for patient survival.

2. Aim

We present a case of invasive pulmonary mucormycosis complicated by multisystem organ failure, and analyze the capabilities of transthoracic ultrasonography in the diagnosis of mucormycosis.

3. Case study

A 41-year-old female patient with pneumonia complicated by multisystem organ failure was admitted to our Intensive Care Unit (ICU) for further diagnosis and treatment. Her history included approximately a month of a persistent cough with hemoptysis. The patient was previously hospitalized at the Department of Tuberculosis and Lung Diseases. Due to dyspnea, she was transferred first to the Internal Medicine Department, and later to one of the municipal ICUs, where she was intubated and provided assisted respiration due to exacerbating respiratory failure. Diagnostic examinations revealed features of multiorgan failure, and bleeding into the retroperitoneal space with perforation into the peritoneal cavity. Two approaches to laparotomic surgery failed to identify the cause of the bleed. Corticosteroids were introduced into the treatment plan.

Upon admission to our ICU, the patient was in a severe condition; she was under the influence of analgesics and sedatives, yet responsive to voice and capable of performing simple orders. The patient was respiratorily unstable and required ventilatory assistance via a tracheostomy tube. Chest mobility was normal and symmetrical, and respiratory sounds revealed isolated rhonchi. The patient presented with sinus cardiac rhythm with her heart rate maintained within peripheral arteries. Capillary refill time was within normal limits. Arterial pressure (invasive method) was 130/80 mmHg. The abdomen was raised beyond the level of the chest and was swollen, with audible peristalsis. Abdominal integuments featured a post-laparotomy wound fitted with a dressing. In addition, physical examination revealed massive generalized edema, numerous ecchymoses on the skin of the extremities and the trunk, as well as increased muscle tone and increased lower limb tendon reflexes. The urinary bladder was catheterized, revealing clear urine. The patient's own diuresis was preserved. Her body temperature was 35.5°C. The patient interview revealed that she was a bakery worker and had no other known disorders to date.

Upon admission to the ICU, the patient was connected to a respiratory device, and samples were collected for a panel of laboratory and microbiological analyses. Anticoagulation prophylaxis and hemodynamic monitoring of gastrointestinal bleeding were initiated. In addition, due to the massive edema and features of water intoxication, hemodialytic treatment was initiated under hemodynamic monitoring. Empirical antibiotic treatment was enhanced by the addition of colistin, ampicillin/sulbactam, linezolid, levofloxacin, and caspofungin. During her hospitalization, the patient had consultations with a nephrologist, a neurologist, and a pneumologist. Microbial and laboratory diagnostic tests were extended to include screening for hepatitis B and C virus, toxoplasmosis, borreliosis, tick-borne meningoencephalitis, and Epstein–Barr virus. A nasopharyngeal smear was collected for genomic screening for viruses, including type A and B influenza, type A and B respiratory syncytial viruses (RSVs), coronaviruses, adenoviruses, metapneumoviruses, rhinoviruses, parainfluenza viruses (type 1, 2, and 3). The smear was also used for genomic screening for bacteria, including *Chlamydia pneumoniae*, *Bordetella pertussis*, *Legionella pneumophila*, *Mycoplasma pneumoniae*, *Haemophilus influenzae*, and *Streptococcus pneumoniae*. Enzyme immunoassay was performed to determine the levels of cANCA, pANCA, anti-GBM, and anti-Le antibodies, as well as complement components C3 and C4. All results were negative. Bronchoscopy was performed, including collection of a bronchial bioptate. A specimen of nasal septum was collected for histopathological examination, and bronchoalveolar lavage samples were collected for tuberculosis screening. The results ruled out suspected systemic diseases and tuberculosis. Specimens for microbial analysis of fluids and secretions were collected several times, yet all results were negative.

4. Results

On the 3rd day of hospitalization, transthoracic ultrasonography (TUS) of the lungs revealed a subpleural consolidation area approximately 10 × 30 mm. The area was characterized by a heterogeneous echostructure and echogenicity similar to that of the liver, with an irregular outline and a fragmentarily visible dynamic air bronchogram. The pleural line above the consolidation area was invisible. In the rest of the lung, the pleural line was visible and the pleural sliding sign was preserved. Color-coded Doppler scan revealed no flow within the vessels of the aforementioned consolidation area. Interstitial-alveolar opacities were also revealed bilaterally in the vicinity of the consolidation area. Invasive fungal lung infection was concluded from the ultrasonographic presentation (Fig. 1). On the 5th day of hospitalization, a CT scan of the chest, abdomen, and pelvis was performed with and without contrast administration. Lesions visualized in TUS were confirmed in a thoracic CT scan (Fig. 2). CT of the abdomen and pelvis minor revealed a hematoma within the right pararenal and retroperitoneal spaces, running along the right iliolumbar muscle down into the pelvis minor. Due to the poor overall condition of the patient and the high risk of bleeding, biopsy of the lesion was abandoned. Broad-spectrum antibiotic therapy was continued, including administration of antifungal medications (caspofungin). Despite treatment, no improvement was observed in the patient's condition. The final diagnosis of mucormycosis was possible only after *Mucor* species fungi were detected in bronchoalveolar lavage culture. Amphotericin B was added to the therapy. The treatment led to gradual improvement of the overall condition of the patient,
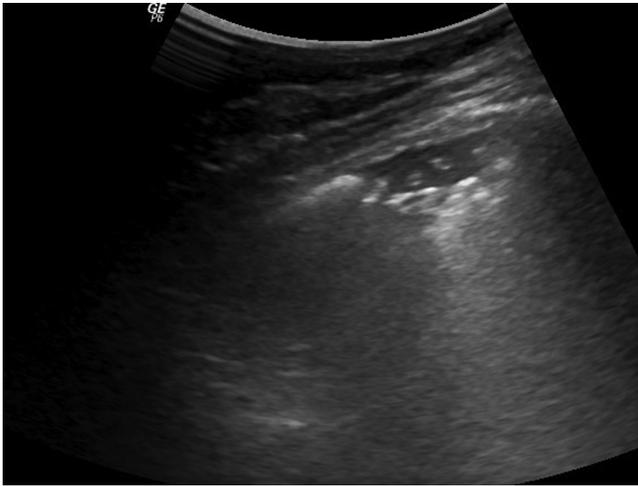
Fig. 1 – Subpleural consolidation area with heterogeneous echostructure and abnormal air bronchogram in transthoracic ultrasonographic examination of lungs.

Fig. 2 – Consolidation area as seen in CT scan of lungs.

including a reduction in inflammatory parameters. The invasiveness of ventilation was gradually reduced, and the patient was eventually allowed to breathe spontaneously. On the 32nd day of hospitalization, the patient was transferred to the rehabilitation department for further care. Follow-up thoracic CT scan revealed complete regression of the previously reported interstitial densities, and a reduction in the size of the focal lesion at the right lung base (decreased to 6 mm).

5. Discussion

Mucormycoses are fungal infections caused by molds of the *Zygomycetes* class. They are widespread in nature, occurring also in foodstuffs such as bread and fruit products. The fungi may enter the human system via the respiratory tract or undamaged skin. Characteristic features of such infections include angioinvasion, vascular thrombosis, and tissue necrosis. The infection may affect a single organ or system, or it may spread in a systemic manner; therefore, the following clinical forms of mucormycosis are identified: pulmonary mucormycosis, nasocerebral mucormycosis, gastrointestinal mucormycosis, dermal mucormycosis, and diffuse mucormycosis.[1,2,8,14] The incidence of mucormycosis differs between the developed and developing countries. In the developed countries, the disease remains rare, occurring mainly in patients with diabetes or in patients with hematopoietic malignancies undergoing chemotherapy and allogeneic stem cell transplantation.[3] On the other hand, in the developing countries, the disease occurs mainly in patients with uncontrolled diabetes or in trauma patients.[3,4] The clinical symptoms are nonspecific, and include fever that is unresponsive to broadspectrum antibiotics, dry cough, hemoptysis, pleural pain, and shortness of breath.[3,5]

As is the case with all invasive fungal diseases, the diagnosis of mucormycosis is difficult and highly imperfect. Therefore, the final diagnosis is often made only following an autopsy examination.[6,13] According to the guidelines proposed by the European Organization for Research and Treatment of Cancer (EORTC), diagnostic probability may be classified as either 'proven,' 'probable,' or 'possible.' In the case of mucormycosis, the diagnosis is proven when fungal hyphae are detected in microscopic analysis or culture. Direct histological examination of the tissue collected in biopsy or thin-needle aspiration remains the gold standard in the diagnosis of mucormycosis, as identification of characteristic hyphae in the sample allows for confirmation of the disease.[7] However, it should be kept in mind that a biopsy is an invasive procedure that is not always feasible.[9] Therefore, a proven diagnosis of mucormycosis may be unavailable. In such cases, the decision to initiate or abandon the treatment usually depends on the clinical presentation of the patient, including the risk factors and performance status, as well as the overall results of laboratory and imaging examinations.[7] In the case of invasive fungal infections of the lungs, this decision is based mostly on the results of imaging studies. High-resolution thoracic CT scans are crucial, as they are capable of revealing focal lesions with halo or reversed halo signs, enlarged lymph nodes, and pleural effusion.[10] These changes are reduced upon follow-up, leading to the development of necrosis.[11] Even if it is impossible to perform the biopsy of the suspected focal lesions, one should always strive to determine the etiology of the infection with diagnostic material collected from the sites of suspected infection. In the case of invasive fungal infection of the lungs (IFIL), this may involve a nasopharyngeal smear, a sputum sample, or bronchoalveolar lavage. According to the EORTC criteria, the detection of hyphae in either direct examination or in the fungal culture, combined with identification of characteristic lesions in CT scans in patients of high-risk groups is sufficient to diagnose a probable invasive fungal infection.

The applicability of TUS in the diagnosis of disorders such as pleural effusion, pulmonary embolism, pneumonia, and pulmonary edema is well documented.[12,15–17] The usefulness of TUS in the diagnosis of IFIL is currently a subject of studies.

A report on the first application of TUS in the diagnosis of invasive pulmonary aspergillosis (IPA) was found in the available literature, with the sensitivity and specificity of the method being estimated at 73.3% and 100%, respectively, relative to CT as the reference method.[12–17] The author of the article proposed the diagnostic criteria of invasive pulmonary aspergillosis. These are modeled after the diagnostic criteria for bacterial infections developed by Ressig et al., including:[13]

(1) **parenchymal criteria**: subpleural consolidation of pulmonary parenchyma, fluid bronchogram, superficial fluid alveologram,
(2) **pleural criteria**: fluid within the pleural cavity, localized or at the lung base,
(3) **vascular criteria**.

According to the author of the article, parenchymal and vascular criteria are the most important in the diagnosis of IPA.[12–17] Heterogeneous echostructure of the lesion, presence of static or fluid bronchogram, and abnormal vascularity or the absence of visible vessels with amputation sign at the lesion base were most suggestive of the diagnosis of IPA. At the same time, the criteria allowed for exclusion of the bacterial etiology of the reported lesions. These were expanded by the assessment of lung tissue adjacent to the consolidation, due to the fact that interstitial or interstitial-alveolar opacities and/or B-, Z-, or I-line artifacts were observed in 90% of patients diagnosed with IPA.[12–17] Such a high incidence suggests that this might be another criterion suggestive of an IPA diagnosis; however, further evaluation is necessary, as no such criterion was used to date in the diagnosis of bacterial pneumonia.

6. Conclusions

1. TUS is a widely available and inexpensive diagnostic method, and it is characterized by the absence of adverse effects. Its applicability in the diagnosis of pulmonary disorders, such as bacterial pneumonia, pulmonary edema, and pulmonary embolism is well-documented and confirmed by experts.
2. Ultrasonographic analysis of lesions facilitates differentiation between bacterial or fungal pneumonia, with lesions already visible at the early stages of infection. The high sensitivity and specificity of the procedure compared to CT scans as a reference method supports the reliability of ultrasound scans in the diagnosis of IPA.
3. The use of TUS in the diagnosis of invasive pulmonary mucormycosis appears warranted, particularly in cases when it is impossible to obtain reliable materials for mycological analyses, or when the collected material lacks diagnostic features.
4. Ultrasonographic diagnosis of invasive lung disorders, including mucormycosis, requires further studies to be conducted in a larger group of patients.

Conflict of interest

None declared.

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