

Diagnosis in the mist: Reflections on a misdiagnosed case of invasive pulmonary aspergillosis

Yongfen Zeng¹, Zhuqiang Cheng^{1,*}

¹Department of Pain, Nanjing Jinling Hospital, Nanjing, 210003, China

*Author for correspondence:
Email: zqcheng123@126.com

Received date: July 11, 2025
Accepted date: August 14, 2025

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Abstract

This paper analyzes a misdiagnosed case of invasive pulmonary aspergillosis (IPA) presenting with left upper limb pain as an atypical symptom, exploring cognitive blind spots in clinical diagnosis, limitations in imaging and laboratory examinations, and therapeutic challenges. It emphasizes the importance of multidisciplinary collaboration in complex cases.

Keywords: Multidisciplinary collaboration, Invasive pulmonary aspergillosis, Pain, Atypical symptom

Introduction

In medical practice, making an accurate diagnosis is often akin to finding a path through dense fog—requiring physicians to rely on their professional knowledge, clinical experience, and keen insight to navigate the obscurity and ultimately uncover the truth of the disease. This article aims to provide an in-depth reflection and commentary on the author's recently published case report: "A case of invasive pulmonary aspergillosis with left upper limb pain as atypical symptom" [1]. The report, which details the eventual diagnosis of invasive pulmonary aspergillosis (IPA) in a 75-year-old male patient, presents a highly instructive case of misdiagnosis. By thoroughly analyzing this case, we can extract valuable lessons to enhance our understanding and diagnostic capabilities regarding atypical presentations of invasive fungal infections [2].

The most thought-provoking aspect of this case lies in the patient's primary clinical manifestation of left shoulder and upper limb pain, rather than the typical respiratory symptoms commonly associated with invasive pulmonary aspergillosis [3]. This atypical initial presentation led to multiple misdiagnoses and inappropriate treatments over a 7-month disease course. The patient was successively diagnosed with myofascitis with neuralgia, cervical disc herniation and coronary artery disease, receiving various treatments including shockwave therapy, spinal decompression surgery and even coronary stent implantation, yet the pain symptoms showed no improvement [4]. This diagnostic odyssey reflects clinicians' cognitive limitations when encountering atypical presentations—we often tend to explain symptoms through common diseases while overlooking uncommon diseases' potential atypical manifestations [5]. From a cognitive psychology perspective, this phenomenon closely relates to "confirmation bias" in clinical decision-making, where physicians disproportionately focus on evidence supporting initial hypotheses while disregarding contradictory information [6].

Cognitive Blind Spots in Differential Diagnosis

From the perspective of differential diagnosis, several critical points in this case warrant in-depth discussion. First, when the patient presented with left upper limb pain accompanied by

sensory abnormalities in specific nerve distribution areas (C8-T1 innervation zone), clinicians should have considered the possibility of T1 nerve root involvement [7]. Although cervical disc herniation is indeed a common cause of radicular pain, the surgical site (C4/5) in this patient was clearly inconsistent with the neuroanatomical distribution corresponding to the symptoms, a discrepancy that should have alerted the physician [8,9]. Second, when the patient later developed pinkish sputum, persistently elevated inflammatory markers (C-reactive protein (CRP), erythrocyte sedimentation rate (ESR)) and progressive anemia, clinicians should have broadened the differential diagnosis scope to include infectious or inflammatory diseases [2]. Particularly when conventional anti-infective therapy proved ineffective, special infections such as fungal or tuberculosis infections should have been considered [10]. Studies indicate that atypical manifestations of invasive pulmonary aspergillosis can occur in up to 30%-50% of cases, with skeletal pain and neurological symptoms potentially serving as initial presentations [11].

Insights from Imaging and Laboratory Examinations

Imaging examinations played a pivotal role in the diagnostic process of this case while also revealing certain deficiencies in interpretation. The initial chest CT only indicated lesion in the left lung apex, suggestive of infection, failing to provide more specific diagnostic clues [12]. However, as the condition progressed, subsequent MRI clearly demonstrated the invasion of the left upper lobe space-occupying lesion into adjacent vertebral bodies, appendages, and ribs—a finding that should have been a critical breakthrough point in diagnosis [13,14]. Yet, the clinical team initially interpreted this manifestation as possible pulmonary tumor invasion of the intervertebral foramen, reflecting insufficient recognition of bone destruction caused by infectious diseases [15]. In fact, invasive fungal infections can similarly lead to destruction of adjacent bone structures, a pathological feature that should hold a place in clinical reasoning [16,17].

Laboratory tests in this case revealed characteristic features of chronic inflammatory response (persistently elevated CRP, ESR, and interleukin-6(IL-6)), accompanied by progressive anemia [18,19]. While these nonspecific inflammatory markers cannot directly determine the etiology, they should prompt clinicians to consider possibilities such as chronic infection, autoimmune diseases, or malignancies [2]. Notably, multiple microbiological tests (sputum culture, tuberculosis testing, bronchoalveolar lavage, etc.) yielded negative results in this patient, a phenomenon not uncommon in invasive pulmonary aspergillosis, reflecting the limitations of microbiological test sensitivity [20,21]. Following a multidisciplinary consultation, the outcomes of the lung biopsy and pathological tissue genetic testing indicated the existence of *aspergillus fumigatus*. The definitive diagnosis relied on histopathological examination and molecular testing of lung puncture biopsy specimens, highlighting the irreplaceable value of invasive procedures in diagnosing complex cases [22,23].

Treatment Challenges and Patient Compliance

In terms of treatment, this case also provides important insights. When the final diagnosis was confirmed as invasive pulmonary aspergillosis, the choice of antifungal therapy posed challenges. The initial use of voriconazole caused severe hallucination adverse reactions, necessitating a switch to micafungin sodium [2,24]. This situation reminds us that monitoring adverse reactions to antifungal

drugs is crucial, especially in elderly patients [25]. More regrettably, the patient ultimately refused to continue treatment, leading to disease progression and death. This not only reflects the high mortality rate of invasive aspergillosis (untreated IPA mortality can reach 90%), but also highlights the critical role of patient compliance in treatment success [2,23]. Studies have shown that elderly patients' adherence to treatment regimens is influenced by multiple factors, including cognitive function, social support, and economic burden [12].

In summary, this article provides significant insights for our clinical practice. When encountering complex pain conditions in clinical work, multidisciplinary consultation should be prioritized. Through collaborative efforts, the etiology can be promptly identified, enabling patients to receive optimal treatment timing and therapeutic regimens.

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