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CASE REPORT

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Airway-centered invasive pulmonary aspergillosis featuring histopathologic fruiting bodies in an immunocompetent patient with a rare incidental finding of thyroid gland Schwannoma: a case report

Imad Majeed[1*†], Sundal Aziz[2], Zaraq Rashid khan[1] and Forest Arnold[1]

Abstract

Introduction Invasive pulmonary aspergillosis (IPA) is typically associated with immunocompromised patients, but rare occurrences have been documented in immunocompetent individuals. This presents diagnostic and therapeutic challenges due to atypical presentations and less apparent risk factors.

Case presentation A 67-year-old Cambodian American female with a history of stable pulmonary nodules and a left neck schwannoma presented with a two-week history of cough and hemoptysis. Imaging revealed a left lower lobe lung mass suspicious for malignancy. Biopsy and bronchoalveolar lavage confirmed the diagnosis of invasive pulmonary aspergillosis, despite the patient's lack of traditional immunosuppressive risk factors. Her environmental exposures, including a recent trip to Cambodia and a history of gardening, were likely contributing factors. The diagnosis of IPA in this immunocompetent patient was established through a combination of clinical presentation, radiographic findings, and microbiological evidence. Bronchoalveolar lavage and galactomannan testing were crucial in identifying the presence of Aspergillus. Histopathological examination of the biopsy specimen revealed the presence of Aspergillus fruiting bodies, an uncommon finding indicative of invasive disease. The patient was promptly started on voriconazole, the first-line antifungal agent for IPA, which led to an improvement in her symptoms. Moreover, her left neck mass schwannoma in the thyroid bed was also a rare entity.

Conclusion This case highlights the importance of considering IPA as a differential diagnosis in immunocompetent individuals with relevant environmental exposures and preexisting lung conditions, even in the absence of classic immunosuppressive risk factors.

Keywords Aspergillosis, Immunocompetent patients, Thyroid Schwannoma, Fruiting bodies

[†]Imad Majeed are co-first author.

*Correspondence:
Imad Majeed
imadkhan1528@gmail.com

[1]Department of Infectious diseases, University of Louisville Hospital, Louisville, USA
[2]Department of cardiology, Northwest general Hospital, Peshawar, Pakistan

Introduction

There are around 250 species in the genus Aspergillus, and 40 of those species can cause illnesses, most notably invasive aspergillosis and allergic aspergillosis [1]. Aspergillus species are commonly found in the environment, including outdoor areas such as soil and plant debris and indoor environments like hospitals. The main cause of pulmonary disease is Aspergillus fumigatus, which presents a range of clinical syndromes [2]. Invasive pulmonary aspergillosis (IPA) is typically associated with immunocompromised patients, such as those undergoing chemotherapy, solid organ transplantation, or prolonged corticosteroid therapy [3]. In some cases, invasive pulmonary aspergillosis (IPA) has been reported [4, 5] in individuals who appear to have a normal immune system or in those who are mildly immunocompromised, such as patients with alcoholism, chronic liver disease, or diabetic ketoacidosis. Furthermore, IPA is being increasingly identified in patients with advanced COPD, particularly those who are being treated with oral corticosteroids [6, 7]. Aspergillus, a ubiquitous mold found in soil, decaying vegetation, and organic debris, can lead to severe infections in those exposed to large amounts of spores, particularly in individuals with preexisting lung conditions or environmental exposures [2].

Diagnosis requires clinical presentation, radiologic and histopathologic findings. Fever, cough, dyspnea, chest pain, and hemoptysis are the symptoms of invasive aspergillosis [8]. When compared to chest radiography, chest CT is more sensitive. Clinical evidence of invasive lung illness can be demonstrated by CT signs that meet the 2008 criteria. These signs include dense, well-circumscribed lesions, a rising air sign, cavity formation, and a surrounding "halo" of ground-glass attenuation. A review of 235 patients' chest computed tomography (CT) images revealed the following features: macronodules in 94% of cases, halo in 61%, consolidation in 30%, infarct-like nodules in 27%, cavitary lesions in 27%, and indications of rising air in 10% of cases [9]. The histopathologic findings may reveal fruiting structures, which are unusual, as well as sharp branching septate hyphae on GMS stain.

Invasive pulmonary aspergillosis (IPA) has become an increasingly important cause of morbidity and mortality in patients with suppressed immune systems. IPA can occur in any severely immunocompromised or chronically debilitated host and is associated with fatality rates of 10 to 100% [10, 11]. Rare occurrences of invasive pulmonary aspergillosis (IPA) have been documented in immunocompetent patients. This presents diagnostic and therapeutic challenges due to atypical presentations and less apparent risk factors [12].

In this case, we present a 67-year-old female with a history of stable pulmonary nodules and a left neck schwannoma, who developed IPA despite lacking traditional immunosuppressive risk factors. However, she had significant environmental exposures, including a recent trip to Cambodia and a history of gardening, both of which may have contributed to her acquisition of Aspergillus spores.

Presentation

A 67-year-old Cambodian-speaking female, with a history of stable pulmonary nodules and an establish left sided neck mass, presented with a two-week history of cough and hemoptysis. Her pulmonary nodules and neck mass were first identified in 2019. Since her immigration to the U.S. in 2019, she had two CT scans that showed the pulmonary nodules had remained stable in size of 2.1 cm. Her left neck mass was biopsied positive for benign neural tumor, but her pulmonary nodule was never biopsied due to presumed benign nature on her prior consecutive CT scans.

During our interview, she stated that over the past one year, she had been noticing a gradual increase in the size of her left neck mass. Further she denied any history of fever, chills, chest pain, palpitations, weight loss, or night sweats. She used to live with her daughter and would spend most of her time indoors but had a habit of gardening and farming in her free time. It is worth mentioning that she had a short visit to Cambodia a year prior for her husband's funeral. Her past medical history was unremarkable for conditions commonly associated with IPA. including chronic obstructive pulmonary disease (COPD), asthma, chronic kidney disease (CKD), diabetes mellitus, solid organ or hematologic transplant, HIV infection, previous COVID-19 or influenza infections, or prior use of corticosteroids or immunosuppressants. She also denied any history of autoimmune diseases or cancer. She had been immunocompetent and in good health until two weeks prior to the presentation. Her initial vitals showed temperature of 98.3 F, pulse of 96 bpm, respiratory rate 16, saturation of oxygen 100% and blood pressure of 166/81mmHg. Her systemic examination including neurological, cardiovascular, gastrointestinal and genitourinary findings were insignificant except respiratory examination which showed bilateral end expiratory crackles more on left sided chest.

Upon admission to our facility, on hospital day 01, she remained hemodynamically stable and vitally afebrile. Her initial routine laboratory workup, including complete blood count, and complete metabolic profile were normal. CT chest with contrast was done that revealed Left lower lobe lung mass highly suspicious for malignancy approximately 3.5 cm x 2.7 cm x 3.2 cm (longitudinal by transverse by coronal) in the left lower lobe of the lung with extension into the left lower lobe subsegmental bronchi, minimal upper lobe predominant centrilobular emphysematous changes and a large left thyroid mass measuring approximately 5.2 cm x 3.7 cm x 4.4 cm.

[Figure 1a & b] From her previous records, we know that the pulmonary nodule was 2.1 cm in size and the mass on the left side of the neck was 4.1 cm in size. Further workups were initiated including blood and sputum cultures, HIV screening test, Hepatitis A, B and C, QuantiFERON Tb, and viral respiratory panel that came unremarkable during the following days of hospitalization. During hospital day 02, ultrasound guided left neck biopsy was done, and the specimen was sent to histopathology that confirmed her prior diagnosis of benign neural tumor which was suggestive of schwannoma in the thyroid bed. [Figure 2a & b]

On hospital day 3, bronchoscopy was performed and bronchoalveolar lavage (BAL) cultures including galactomannan, TB and CMV PCR were sent. Needle aspiration biopsy of her left lower lobe pulmonary nodule

Fig. 1 (**a**) shows longitudinal view of the CT chest with left lower lung mass. (**b**) showing cross sectional view of CT chest having thyroid schwannoma with dimensions mentioned

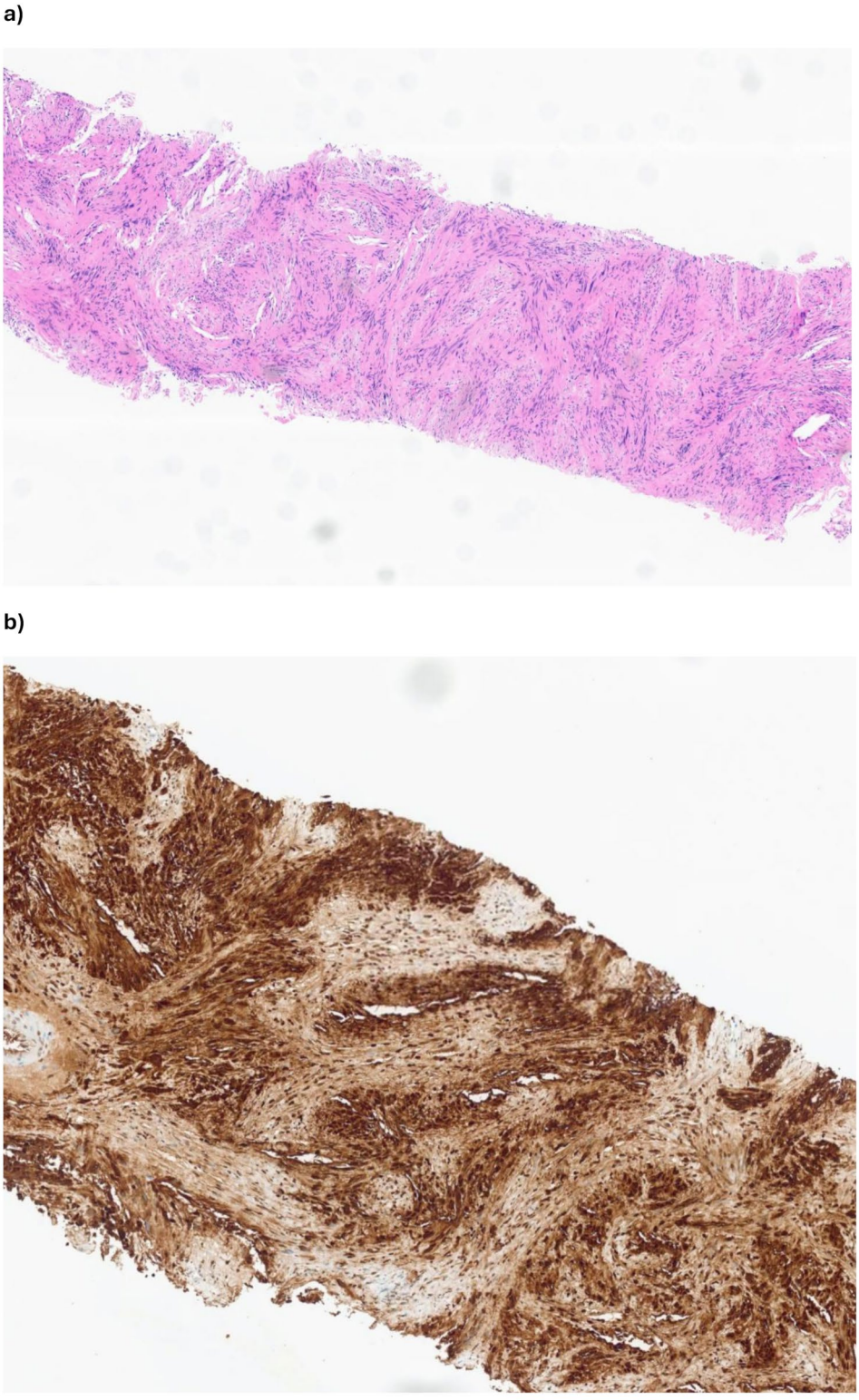

Fig. 2 (**a**) shows the the haematoxylin-eosin staining of this tumor which is predominantly comprised of Antoni A areas of a schwannoma with vague nuclear palisading. Mild nuclear atypia is identified (hyperchromasia and enlargement) that likely represents ancient change. (**b**) shows the S100 immunohistochemical stain that is strongly positive, supportive of a nerve sheath tumor (schwannoma in this case)

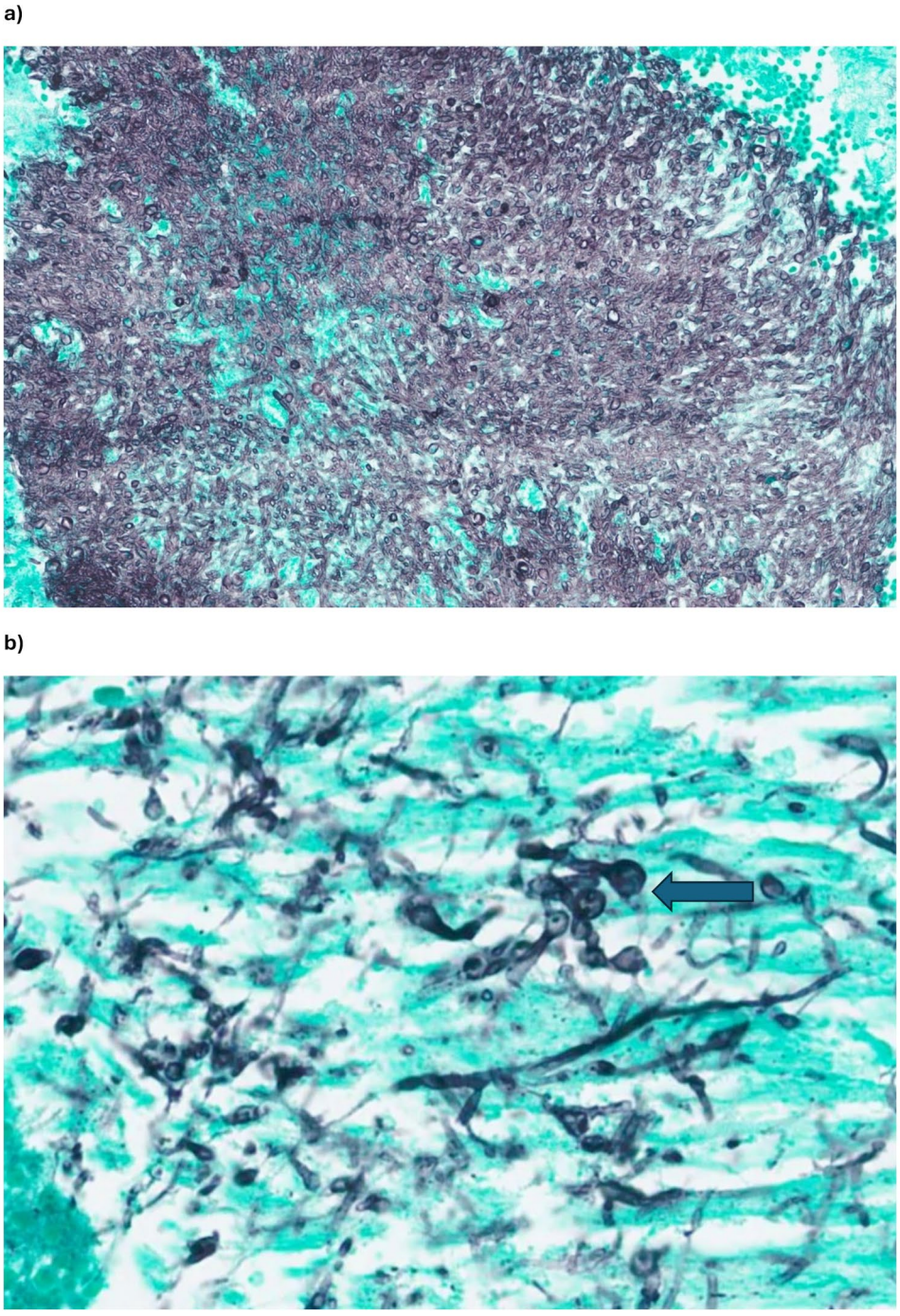

Fig. 3 (**a**) shows a microscopic view of fungal elements stained with Gomori methenamine silver (GMS). The fungal structures, highlighted in black, are clearly visible against a lighter background. These elements exhibit septate hyphae with branching at acute angles, characteristic of Aspergillus species. (**b**) shows microscopic image, taken at 400x magnification, demonstrates fungal structures visualized using the GMS (Gomori Methenamine Silver) special stain. The fungal fruiting bodies appear as distinctive black structures, with one specifically indicated by an arrow, providing clear evidence of fungal presence in the specimen

was taken and was also biopsied. On hospital day 5, her BAL fungal culture including galactomannan came positive for invasive Aspergillosis while her TB and CMV PCR came negative. Needle aspiration biopsy also came positive for Aspergillosis. [Figure 3a & b] Subsequently, she was counselled regarding her new diagnosis and the anticipated treatment and its side effects. The patient was started on per oral Voriconazole 800 mg as a loading dose twice daily on first day and then 400 mg maintenance

dose twice daily. She was asked for a follow-up visit to our clinic for 1 month and her symptoms have improved.

Discussion

Invasive pulmonary aspergillosis (IPA) typically affects immunocompromised individuals, but the case presented here illustrates that IPA can occur in immunocompetent individuals, posing unique diagnostic challenges. This case is significant as it demonstrates that environmental exposure may be a key risk factor for IPA even in the absence of classic immunosuppressive conditions.

IPA is primarily seen in patients with compromised immune systems due to chemotherapy, corticosteroid use, organ transplantation, or conditions like neutropenia and advanced HIV infection [2, 3]. However, IPA has been increasingly recognized in non-immunocompromised patients with other underlying risk factors, including chronic lung diseases such as chronic obstructive pulmonary disease (COPD), where the use of corticosteroids can predispose patients to IPA [6, 7]. In this case, the patient lacked such underlying risk factors. She had no history of COPD, asthma, diabetes, kidney disease, or corticosteroid use, all of which are commonly associated with IPA [3, 10].

One of the most striking aspects of this case is the patient's environmental exposure, which likely contributed to her development of IPA. The patient had recently traveled to Cambodia, a tropical environment where exposure to fungal spores, including *Aspergillus*, is more common due to the warm and humid conditions conducive to fungal growth [13]. Furthermore, her history of gardening and farming may have also contributed to her inhalation of *Aspergillus* spores. Exposure to considerable quantities of Aspergillus spores, particularly in individuals with preexisting pulmonary conditions like stable nodules, may play a role in the development of invasive disease. However, this association should be viewed cautiously and warrants further investigation, as current evidence does not robustly support this interpretation.

Gardening and agricultural work are known risk factors for *Aspergillus* exposure, as spores are abundant in soil, decaying vegetation, and organic matter [14, 15]. The inhalation of *Aspergillus* spores can occur even in immunocompetent individuals, especially if they are exposed to high concentrations of spores over a prolonged period or if they have preexisting pulmonary conditions, as in the case of this patient. Previous case reports have documented IPA in patients with chronic lung diseases such as COPD, even when they are not overtly immunosuppressed [6, 12]. In the current case, her stable pulmonary nodules may have provided a nidus for fungal growth following spore inhalation.

Diagnosing IPA in immunocompetent patients presents a clinical challenge because the disease can manifest with non-specific symptoms, such as cough, hemoptysis, and respiratory distress, which may mimic other pulmonary conditions like bacterial pneumonia or malignancy [16]. In this case, the patient was presented with a cough and hemoptysis, but no other systemic symptoms, which further delayed diagnosis. However, bronchoalveolar lavage (BAL) and galactomannan testing proved crucial in identifying the presence of *Aspergillus*, supporting the diagnosis of IPA. Galactomannan is a useful biomarker for detecting *Aspergillus* infections, and its presence in BAL fluid strongly suggests IPA, particularly when combined with histopathological evidence of the fungus [14].

Clinical, radiographic, and microscopic evidence are all considered in the diagnosis of Aspergillosis in humans [17]. In our case, she presented with intermittent symptoms and her CT chest with contrast was indicative of pulmonary nodule that was increased in size from her prior imaging. Moreover, microscopic examination of transbronchial, and bronchoalveolar specimen revealed acute branching hyphae with fruiting bodies on GMS stain. Fruiting bodies were also an uncommon microscopic finding [17]. If present, they are the hallmark for histopathologic diagnosis of angio-invasive aspergillosis [18].

Classically, Aspergillus hyphae are characterized as acute branching septate hyphae; nevertheless, it can be challenging to distinguish these hyphae from those of other fungi, such as Pseudallescheriaboydii, the Fusarium Spp., and Candida spp. Therefore, confirmation often necessitates a microbiological isolation by culture, which can be challenging to achieve due to Aspergillus's widespread nature. In our case, her blood cultures came back negative, the cultures from BAL were positive for Aspergillosis. Aspergilli fruiting bodies (Conidia) emerge from mycelia in environments with high oxygen tension or because of severe infections. Unfortunately, histopathological sections hardly reveal them [17]. Some species of Aspergillus can be subtyped in situ based on the shape of their fruiting bodies, which consist of a vesicle and one or two layers of phialides that produce conidia. Contrarily, culture confirmation is necessary for precise species diagnosis [17].

The patient's prompt initiation of voriconazole, the first-line antifungal agent for IPA, was appropriate and essential for managing her infection. Voriconazole has been shown to significantly improve outcomes in IPA, especially when initiated early in the disease course [19]. Despite the unusual presentation in this case, the patient responded well to voriconazole, reflecting the importance of early and appropriate antifungal therapy even in immunocompetent patients.

Of note, our case was also unique for incidental finding of schwannoma in the thyroid bed. Although, there are no clear correlation between airway centered

aspergillosis and thyroid schwannoma in the available literature, our patient does have the co-occurrence of both findings since 2019 when she first moved to US from Cambodia. Moreover, she also endorsed an increase in the size of the left sided neck mass which was confirmed through her recent imaging. Schwannomas are common in the head and neck region but are unusual in thyroid gland. It is uncommon to see schwannomas in the thyroid bed [20, 21]. There are very few cases reported in the English-language literature, with most of those cases mimicking a thyroid nodule [22].

This case underscores the need for clinicians to maintain a high index of suspicion for IPA, even in patients who are not traditionally considered at risk. Environmental exposure, particularly in patients with preexisting lung conditions or significant spore exposure, should be considered a potential risk factor for invasive fungal infections. Clinicians should consider IPA in the differential diagnosis of patients presenting with pulmonary symptoms and relevant environmental exposures, regardless of their immune status. A limitation of this study was that, instead of a BAL PCR test for aspergillosis, a BAL galactomannan test was performed to evaluate the underlying diagnosis.

Conclusion

This case underscores the significance of considering aspergillosis as a differential diagnosis in immunocompetent individuals without a history of prior lung conditions or other chronic diseases, who may present with intermittent symptoms. The diagnosis of aspergillosis necessitates a comprehensive clinical evaluation, including relevant environmental exposure, radiographic, and histopathologic evidence. Furthermore, the histopathologic specimen should be examined for the presence of fruiting bodies, which is an uncommon finding and indicates invasive aspergillosis. In this instance, the patient presented with multiple uncommon findings, including a thyroid bed schwannoma.

Abbreviations

CT	Computed tomography
IPA	Invasive pulmonary aspergillosis
BAL	Bronchoalveolar lavage
CMV	Cytomegalovirus
PCR	Polymerase chain reaction
Tb	Tuberculous
Bpm	Beats per minute

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Author contributions

IM: analyzed and interpreted patient data and procedures along with the writing of the manuscript. SA: interpretation and analysis of radiological imaging with the assistance of writing the manuscript and final review. ZK: procedure with final review of the manuscript. FA: final review of the manuscript. All authors read and approved the final manuscript.

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Data availability

Data sharing is not applicable to this article as no datasets were generated or analyzed during the current study.

Declarations

Competing interests

The authors declare no competing interests.

Ethics approval

Not applicable.

Consent to participate

Not applicable.

Consent for publication

Written informed consent was obtained from the patient herself for the publication of this case report and any accompanying images. A copy of this written consent is available for review by the Editor-in-Chief of this journal.

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