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Review Article

A Puzzling Febrile Illness with an Unexpected Whitmore Disease Diagnosis

Nayan Bansal[1*], Ashwani Roy[2]

[1]Department of Community Medicine, All India Institute of Medical Sciences, Nagpur, India.
[2]Division of Epidemiology & Communicable Diseases, Indian Council of Medical Research, New Delhi 110 029, India.

Correspondence to: Nayan Bansal, Department of Community Medicine, All India Institute of Medical Sciences, Nagpur, India.

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Abstract

Melioidosis is a potentially life-threatening bacterial infection caused by *Burkholderia pseudomallei*. Although pulmonary infection and bloodstream dissemination are frequently reported, the disease can affect multiple organ systems and produce clinical findings that resemble malignancy, tuberculosis, inflammatory disorders, and other bacterial infections, complicating early recognition, particularly in regions with limited diagnostic facilities. This review aimed to describe the less commonly recognized clinical manifestations of melioidosis, examine associated diagnostic challenges, and discuss their implications for patient management in endemic and non-endemic settings. A narrative review approach was used to examine published clinical reports, case series, and observational studies describing unusual manifestations, with findings categorized according to neurological, musculoskeletal, dermatological, visceral, vascular, genitourinary, and thoracic involvement, as well as disseminated infection, coinfections, imported cases, and unusual exposure histories. Reported presentations included cerebral abscesses, encephalomyelitis, osteomyelitis, pyomyositis, septic arthritis, chronic skin ulcers, inflammatory skin lesions, hepatosplenic abscesses, arterial aneurysms, prostatic abscesses, tubo-ovarian infections, mediastinal lymphadenitis, and ocular disease. Diabetes mellitus was frequently identified as an underlying condition, while diagnostic confusion with tuberculosis, malignancy, fungal infections, and other bacterial diseases contributed to delayed recognition. Microbiological confirmation, appropriate imaging, prolonged antimicrobial therapy, and surgical intervention when indicated were central to effective management. Melioidosis should therefore remain in the differential diagnosis of unexplained abscesses, unusual inflammatory lesions, and complex infections involving multiple organs, as early recognition and reliable laboratory identification are essential for improving clinical outcomes.

Keywords: Melioidosis; *Burkholderia pseudomallei*; Unusual Clinical Manifestations; Neurological Infection; Musculoskeletal Infection; Visceral Abscess; Diagnostic Challenges; Tropical Infectious Diseases; Disseminated Infection.

INTRODUCTION

Melioidosis is an infectious disease caused by *Burkholderia pseudomallei*, an environmental Gram-negative bacterium commonly found in contaminated soil and surface water. The infection is predominantly reported in South Asia, Southeast Asia, and northern Australia. Human acquisition generally occurs through direct contact with contaminated soil or water, inhalation of contaminated particles, or ingestion of contaminated materials. Agricultural activities, flooding, heavy rainfall, and occupational exposure can increase the likelihood of infection.

The disease has traditionally been associated with pneumonia, bloodstream infection, and severe sepsis. However, clinical observations have established that its manifestations extend well beyond the respiratory system. Infection may involve the central nervous system, bones, joints, muscles, skin, liver, spleen, kidneys, reproductive organs, cardiovascular structures, and other anatomical

locations. These presentations can occur independently or as part of disseminated disease [1].

Diabetes mellitus is one of the most frequently identified predisposing conditions. Other associated factors include chronic kidney disease, excessive alcohol consumption, malignancy, immunosuppression, and chronic pulmonary disorders. Nevertheless, infection has also been documented in individuals without recognized underlying medical conditions.

The ability of B. pseudomallei to produce localized abscesses, persistent infections, and multifocal disease creates substantial diagnostic difficulties. Clinical and radiological findings may resemble tuberculosis, pyogenic infections, fungal diseases, inflammatory disorders, and malignancies. In some patients, the initial diagnosis is established only after repeated investigations, surgical sampling, or specialized microbiological testing [2].

The increasing recognition of atypical disease patterns demonstrates the importance of considering melioidosis beyond its conventional clinical presentation. This review examines the major unusual manifestations, associated diagnostic problems, treatment approaches, and clinical implications reported in the medical literature.

LITERATURE REVIEW

Neurological Manifestations

Neurological involvement is an uncommon but potentially disabling complication of melioidosis. Central nervous system infection may present as encephalomyelitis, brain abscess, meningitis, transverse myelitis, brainstem encephalitis, cranial neuropathy, or peripheral neurological dysfunction.

Patients may develop fever, headache, altered consciousness, seizures, limb weakness, sensory abnormalities, and disturbances of bladder function. In some instances, neurological symptoms develop after an infection has already been identified elsewhere in the body. Other patients initially present with neurological abnormalities without an obvious infectious focus. Brain abscesses may appear as ring-enhancing lesions on magnetic resonance imaging and can resemble tuberculous lesions or other intracranial infections. Brainstem involvement may produce multiple cranial nerve abnormalities, cerebellar dysfunction, and visual disturbances. Optic neuritis and facial nerve involvement have also been described.

Diagnosis requires a combination of clinical assessment, neuroimaging, and microbiological investigation. Cerebrospinal fluid examination may provide supportive findings, although a negative culture does not exclude infection. In selected patients, tissue sampling or abscess aspiration may provide a more definitive diagnosis. Treatment generally requires prolonged intravenous antimicrobial therapy, with meropenem or ceftazidime used according to disease severity and clinical circumstances. Intracranial abscesses may require surgical drainage. Neurological recovery varies, and persistent motor impairment or other functional limitations can occur [3].

Musculoskeletal Manifestations

Musculoskeletal melioidosis includes osteomyelitis, septic arthritis, pyomyositis, myositis, spondylodiscitis, and paravertebral abscess formation. These conditions may occur individually or simultaneously. Muscle infection can initially resemble cellulitis, localized inflammation, or necrotizing soft-tissue disease. Patients may present with localized swelling, tenderness, fever, restricted movement, and progressive pain. In certain cases, the infection advances rapidly and produces muscle necrosis requiring surgical treatment.

Bone involvement commonly affects the long bones, vertebrae, and other skeletal structures. Spinal disease may produce vertebral destruction, epidural collections, paraspinal abscesses, and neurological complications. Such findings can be mistaken for spinal tuberculosis, particularly in endemic regions.

Septic arthritis may affect large joints, including the knee, ankle, and hip. Joint aspiration and microbiological examination are essential for establishing the diagnosis. MRI is useful for identifying associated bone, muscle, and soft-tissue abnormalities. Diabetes mellitus is frequently reported among patients with musculoskeletal involvement. Chronic kidney disease, immunosuppression, and occupational exposure to contaminated soil or water are additional associated factors.

Management generally involves prolonged antimicrobial treatment and drainage or debridement when clinically indicated. Delayed recognition may lead to permanent joint damage, functional impairment, or systemic complications.

Cutaneous Manifestations

Skin involvement represents an important component of the unusual clinical spectrum of melioidosis. The disease may produce ulcers, subcutaneous abscesses, cellulitis, nodules, panniculitis, erythema nodosum, and necrotizing fasciitis [4].

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Ulcerative lesions can persist despite conventional antibiotic treatment. Their appearance may resemble chronic bacterial infection, tropical ulceration, inflammatory skin disease, or malignancy. A history of minor trauma, insect bites, or direct contact with contaminated soil may provide useful epidemiological information. Cutaneous abscesses can occur as localized infections or as part of disseminated disease. Cellulitis may be accompanied by thrombophlebitis or venous thrombosis. Severe soft-tissue infection can progress to necrotizing fasciitis and require emergency surgical intervention.

Inflammatory manifestations such as sweet syndrome, panniculitis, and erythema nodosum have also been associated with melioidosis. These findings can create diagnostic uncertainty because the visible skin abnormalities may represent inflammatory responses rather than conventional abscess formation. Localized disease may respond well to appropriate antimicrobial treatment, although extensive or disseminated infections generally require more intensive management. Follow-up is important because persistent infection and relapse have been described.

Visceral Organ Involvement

Visceral melioidosis primarily involves the liver, spleen, pancreas, kidneys, and peritoneal cavity. Abscess formation is a frequent manifestation, although the clinical presentation varies according to the organ affected.

Splenic Involvement

Splenic abscesses are among the recognized visceral manifestations of melioidosis. Patients may experience prolonged fever, abdominal discomfort, anorexia, and constitutional symptoms. Imaging may demonstrate solitary or multiple splenic collections.

Some patients respond to antimicrobial therapy without requiring surgical intervention. However, drainage or surgery may be necessary when abscesses are large, complicated, or unresponsive to medical management.

Hepatic Involvement

Hepatic abscesses may occur independently or alongside splenic lesions. Multiple small collections can produce characteristic radiological appearances sometimes described as honeycomb or necklace patterns. The diagnosis may be confused with conventional pyogenic liver abscesses. In patients from endemic regions, especially those with diabetes, microbiological examination of blood or aspirated material is important.

Pancreatic Involvement

Pancreatic infection is less frequently described. Imaging may demonstrate multiple small abscesses, often accompanied by involvement of the liver, spleen, or other abdominal structures.

Peritoneal Involvement

Peritonitis caused by B. pseudomallei has been reported in patients undergoing peritoneal dialysis and in individuals with intra-abdominal infection. Clinical manifestations may resemble other forms of bacterial peritonitis. Microbiological examination of peritoneal fluid is necessary when the disease is suspected.

Vascular Manifestations

Vascular melioidosis is uncommon but potentially life-threatening. The development of infected arterial aneurysms and pseudoaneurysms has been documented, particularly involving the abdominal aorta and iliac arteries [5]. Clinical symptoms are often nonspecific and may include persistent fever, abdominal pain, back pain, weight loss, and constitutional disturbances. The condition can resemble atherosclerotic vascular disease or other infectious aneurysms.

Diagnosis generally requires appropriate vascular imaging and microbiological confirmation. Treatment involves prolonged antimicrobial therapy and, in selected cases, surgical resection and reconstruction of the affected vessel. The combination of arterial infection, structural damage, and systemic bacterial dissemination can result in substantial morbidity and mortality.

Genitourinary Manifestations

Genitourinary melioidosis includes infections of the prostate, kidneys, epididymis, testes, and female reproductive organs.

Prostatic abscess is an important manifestation, particularly among diabetic men. Patients may present with fever, urinary symptoms, pelvic discomfort, and features resembling complicated urinary tract infection. Renal involvement may occur as pyelonephritis or renal abscess formation. Microbiological testing of urine, blood, and other relevant specimens may help establish the diagnosis.

Female reproductive involvement includes tubo-ovarian abscess and pregnancy-associated infection. Chorioamnionitis has also been described, with potential complications involving premature delivery and maternal

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infection.

Treatment depends on the anatomical site, severity, and presence of drainable collections. Surgical drainage may be necessary for selected prostatic or pelvic abscesses [6].

Thoracic and Cardiac Manifestations

Although pulmonary infection is a conventional presentation, certain thoracic manifestations are less commonly recognized. These include mediastinal lymphadenitis, empyema, pulmonary cavitation, pericarditis, pericardial effusion, endocarditis, and vascular complications within the thoracic cavity.

Mediastinal lymphadenopathy can resemble tuberculosis or malignant lymph node involvement. Endobronchial ultrasound-guided aspiration and microbiological examination may help identify the causative organism.

Cardiac involvement may include pericardial inflammation, effusion, and infective endocarditis. Prosthetic cardiac valves and implanted devices may also become involved.

Empyema and cavitary pulmonary lesions can complicate the disease and may require repeated drainage alongside antimicrobial treatment.

Coinfections

Coinfection represents another diagnostic problem in melioidosis. Concurrent infections involving Leptospira, Mycobacterium tuberculosis, Leishmania, dengue virus, influenza virus, and other pathogens have been described. Leptospirosis and melioidosis share several epidemiological features, including exposure to contaminated environments and overlapping clinical symptoms. Their simultaneous occurrence may produce severe systemic illness.

Coinfection with tuberculosis can be especially difficult to identify because both diseases may cause prolonged fever, weight loss, lymphadenopathy, pulmonary abnormalities, and chronic abscesses.

The possibility of more than one infectious agent should be considered when patients demonstrate an incomplete response to treatment or develop unexpected clinical complications.

Disseminated and Multiorgan Disease

Disseminated melioidosis develops when infection involves several anatomical sites, frequently through hematogenous spread. The central nervous system, lungs, bones, joints, skin, liver, spleen, and kidneys may be affected. Patients can present with prolonged fever, multiple subcutaneous swellings, organ enlargement, joint pain, neurological abnormalities, and constitutional symptoms.

Diabetes mellitus, renal impairment, and immunosuppression are commonly associated with severe disease. However, disseminated infection can also occur in individuals without previously recognized risk factors [7].

The involvement of several organs may delay diagnosis because symptoms are distributed across different clinical specialties. Early blood cultures and microbiological examination of accessible lesions are therefore important.

Other Unusual Clinical Presentations

Several additional presentations have been described, including parotid abscess, cervical lymphadenitis, nasopharyngeal masses, ocular infection, and infections resembling malignant disease.

Ocular manifestations include sclerokeratitis and endophthalmitis. These conditions can threaten vision and may require both systemic and locally administered treatment. Head and neck involvement can produce suppurative lymphadenitis, parotitis, deep-neck infection, and occasionally airway compromise.

Patients with cystic fibrosis may experience recurrent respiratory exacerbations associated with B. pseudomallei. In such cases, the organism may initially be confused with other members of the Burkholderia genus or common respiratory pathogens. Imported infections have also been recognized in patients returning from endemic regions. These observations demonstrate that travel and environmental exposure histories remain relevant even when patients present in non-endemic countries.

Review Methodology

A narrative literature review was used to examine the clinical diversity of melioidosis. The supplied source material describes a PubMed search using the terms “Melioidosis” and “Case Report”.

The original review covered English-language publications from 2000 to 2025 and included case reports, case series, and observational studies with microbiological or serological evidence of B. pseudomallei. Animal studies and preprints were excluded.

Atypical disease was defined as infection involving unusual anatomical locations or clinical syndromes outside the conventional pulmonary and septicemic presentations. The extracted information was organized according to the

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principal organ system involved. Clinical characteristics, associated conditions, diagnostic methods, treatment approaches, and reported outcomes were examined descriptively [8].

The supplied review reports that 238 publications were initially collected, of which 160 articles remained after full-text assessment. The findings are descriptive and should not be interpreted as population-level incidence estimates.

Summary of Clinical Findings

The reviewed reports demonstrate that melioidosis can affect nearly every major organ system. Neurological and musculoskeletal presentations were prominent in the collected literature, followed by cutaneous, visceral, thoracic, vascular, and genitourinary manifestations (Table 1).

Table 1: Distribution of published reports according to the principal clinical manifestation

No.	Clinical category	Representative manifestations	Studies reported
1	Neurological	Brain abscess, encephalomyelitis, meningitis	24
2	Musculoskeletal	Osteomyelitis, myositis, septic arthritis	28
3	Genitourinary	Prostatic abscess, tubo-ovarian abscess	8
4	Cutaneous	Skin ulcers, erythema nodosum, fasciitis	18
5	Thoracic and mediastinal	Lymphadenitis, empyema, vascular complications	14
6	Visceral	Hepatic, splenic, and pancreatic abscesses	14
7	Vascular	Infected aneurysms and pseudoaneurysms	10
8	Coinfections	Leptospirosis, tuberculosis, leishmaniasis	14
9	Disseminated	Multiple-organ infection	12
10	Other presentations	Ocular, head and neck, lymphatic, and malignancy-like disease	18

DISCUSSION

The findings demonstrate that melioidosis cannot be regarded solely as a respiratory or bloodstream infection. Its ability to affect different anatomical structures produces a broad clinical spectrum and creates substantial diagnostic uncertainty. The organism's environmental distribution, capacity for tissue invasion, and potential for persistent infection contribute to its varied clinical behavior.

The geographical distribution of melioidosis is closely related to environmental exposure, particularly in tropical regions. The disease has also been identified in travelers returning from endemic countries, making it relevant to healthcare facilities outside traditionally affected regions [9]. Its clinical and pathological characteristics have been described extensively, including the mechanisms responsible for systemic infection and organ damage .

The estimated worldwide disease burden emphasizes the importance of recognizing infections that might otherwise remain undetected. However, reported case distributions are influenced by differences in surveillance, laboratory resources, and publication practices.

Imported infections provide further evidence of the need to obtain detailed travel and environmental exposure histories. Patients returning from endemic regions may develop unusual manifestations after their arrival in countries where the disease is rarely encountered. Musculoskeletal involvement represents a clinically important component of the disease. Bone and joint

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infections may resemble tuberculosis, conventional bacterial osteomyelitis, or chronic inflammatory disorders. Their recognition requires appropriate imaging and microbiological confirmation.

Vascular complications can be especially serious because infected aneurysms and venous thromboembolic events may produce nonspecific symptoms before substantial clinical deterioration occurs [6]. Reports from regions where melioidosis is underdiagnosed also demonstrate the importance of improving clinical recognition and laboratory identification.

Reproductive and abdominal manifestations further illustrate the diversity of infection. Tubo-ovarian abscesses may initially be investigated as conventional pelvic inflammatory disease, and the causative organism may only be identified after drainage and culture examination. Deep soft-tissue infections, including subgaleal collections, demonstrate that apparently localized lesions may represent an unusual manifestation of an underlying systemic bacterial infection. Renal involvement also deserves attention because urinary abnormalities and renal abscesses can occur alongside other visceral complications [10].

Neurological disease is among the most challenging forms of melioidosis. Cerebral abscesses and calvarial osteomyelitis have been reported in patients with intracranial infection, demonstrating the importance of combining radiological findings with microbiological investigations [11]. Paediatric cases may produce significant neurological disability and require prolonged rehabilitation [12].

Encephalomyelitis and transverse myelitis can resemble inflammatory demyelinating disorders. These presentations may lead to diagnostic uncertainty when conventional investigations fail to identify the underlying infection [13,14]. Cranial neuropathy, including facial nerve involvement, further expands the clinical spectrum [15]. Peripheral neurological complications have also been documented. Guillain–Barré-like presentations may complicate the assessment of patients with active infection and require careful evaluation of the underlying cause of neurological weakness [16]. Persistent infection or inadequate treatment may also be followed by central nervous system complications, including meningitis [17].

Chronic cranial inflammatory manifestations, including pachymeningitis and venous sinus involvement, represent additional diagnostic challenges because their imaging appearances overlap with other infectious and inflammatory conditions [18]. Reports involving both central and peripheral nervous systems demonstrate the possibility of complex neurological disease [19].

Encephalomyelitis and subdural collections have also been described in Indian patients, emphasizing the relevance of this infection in South Asian clinical practice [20]. Other neurological presentations may involve cerebral lesions, psychiatric symptoms, and atypical imaging abnormalities [21,22]. Cerebral melioidosis can occur even in locations where the disease is rarely encountered. Such cases demonstrate why unusual brain lesions should not automatically be attributed to malignancy or other endemic infections [23].

Involvement of the temporomandibular joint and surrounding masticatory structures can produce severe restriction of jaw movement and may resemble deep facial space infection [24]. Similarly, infections involving previously implanted orthopaedic material indicate that the disease may affect patients with a history of surgical intervention [25].

Osteoarticular infections can occur in association with diabetes mellitus and may require combined antimicrobial and surgical management [26]. Septic arthritis is another serious presentation, particularly when the initial symptoms resemble common inflammatory joint disorders [27]. Paraspinal collections may be difficult to distinguish from spinal tuberculosis, particularly when vertebral abnormalities and epidural involvement are present [28]. Septic arthritis of the hip is another uncommon presentation that can cause substantial functional impairment when treatment is delayed [29].

The occurrence of mediastinal lymphadenitis and prostatic abscess demonstrates the importance of considering melioidosis in patients presenting with unusual lymph node enlargement or genitourinary infection [30]. Pregnancy-associated infection also deserves clinical recognition because disseminated disease may have serious consequences for maternal and fetal health [31].

Diagnostic Challenges

The diagnosis of atypical melioidosis is complicated by the absence of a single clinical pattern that reliably identifies the infection. Symptoms frequently depend on the affected organ and the extent of bacterial dissemination.

The major diagnostic difficulties include:

- Nonspecific symptoms during the early stages of infection.

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- Clinical resemblance to tuberculosis and other bacterial infections.
- Radiological findings that overlap with malignancy and inflammatory disorders.
- Limited access to specialized microbiological investigations.
- Delayed recognition of the significance of travel and occupational exposure.
- Difficulty identifying the organism in patients with localized or previously treated infections.

Culture remains central to microbiological confirmation. Appropriate specimens include blood, pus, urine, respiratory secretions, cerebrospinal fluid, and tissue obtained from affected organs. Laboratory personnel must also be informed when melioidosis is suspected because incorrect identification of the organism can create diagnostic and laboratory safety problems.

Predisposing Conditions and Environmental Exposure

Diabetes mellitus is the most frequently reported underlying condition in the supplied clinical literature. Other associated conditions include chronic kidney disease, malignancy, immunosuppressive treatment, chronic pulmonary disease, and excessive alcohol consumption. Environmental exposure is another important component of disease acquisition. Agricultural activities, contact with wet soil, contaminated water, flooding, and skin injuries may increase the likelihood of infection. However, the absence of recognized risk factors should not exclude melioidosis from the differential diagnosis. Infections have also been documented among otherwise healthy individuals.

Treatment and Clinical Outcomes

Management requires prolonged antimicrobial therapy, generally divided into an intensive phase and a subsequent eradication phase. Intravenous ceftazidime or meropenem is commonly used during intensive treatment. Meropenem may be preferred in severe disease and selected neurological presentations. Oral trimethoprim-sulfamethoxazole is commonly used during the eradication phase.

The duration of therapy depends on the affected anatomical site, clinical response, and presence of complications. Deep-seated infections may require extended treatment. Surgical management is necessary in selected patients with intracranial, abdominal, musculoskeletal, vascular, or genitourinary abscesses. Drainage, debridement, and reconstruction may be required according to the extent of tissue damage. Clinical outcomes vary considerably. Patients diagnosed early and treated appropriately may recover, whereas delayed recognition, disseminated infection, and severe underlying disease can contribute to poor outcomes.

Clinical Implications

The findings have implications for physicians, microbiologists, radiologists, surgeons, and infectious disease specialists.

In endemic regions, unexplained abscesses, chronic bone infections, unusual skin lesions, and atypical neurological syndromes should prompt evaluation for melioidosis when relevant exposure or clinical risk factors are present. In non-endemic regions, clinicians should obtain travel histories and consider previous exposure when assessing patients with unexplained infections. Improved communication between clinical teams and microbiology laboratories can facilitate earlier identification.

Strengths and Limitations

The main strength of this review is its broad examination of unusual manifestations involving multiple organ systems. The classification of clinical presentations provides a useful framework for recognizing disease patterns that may otherwise be overlooked. Several limitations should be acknowledged. Most available evidence comes from case reports and small case series rather than prospective studies. Publication bias may therefore favor uncommon or severe presentations. Geographical differences in reporting and laboratory capacity may also influence the apparent distribution of disease. Furthermore, the original review included publications from 2000 to 2025, whereas the requested reference restriction excludes publications after 2020. Consequently, the 31-reference bibliography below cannot independently substantiate every report included in the original 238-publication search. A separate updated literature search and citation audit would be required before submission.

CONCLUSION

Melioidosis presents a broad clinical spectrum that extends beyond conventional pulmonary and bloodstream infections. Its ability to involve the nervous system, musculoskeletal structures, skin, abdominal organs, vascular tissues, and genitourinary tract creates substantial diagnostic difficulties. Unusual manifestations may

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resemble tuberculosis, malignancy, fungal disease, or other bacterial infections, resulting in delayed identification and treatment. Diabetes mellitus remains a frequently reported predisposing condition, although infection can also develop in individuals without recognized comorbidities. Clinical evaluation should incorporate environmental exposure, travel history, anatomical findings, and appropriate microbiological investigations. Culture-based identification remains essential for confirming the causative organism and guiding antimicrobial selection. Prolonged antibiotic treatment, combined with surgical drainage or debridement when necessary, contributes to successful management. Improved laboratory facilities, interdisciplinary communication, and greater awareness among healthcare professionals are necessary to reduce missed diagnoses. Further multicentre investigations are needed to clarify disease patterns, treatment outcomes, recurrence, and long-term complications associated with these uncommon clinical presentations.

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