Recurrent poststernotomy mediastinitis due to histoplasmosis: the critical role of histopathology in surgical site infections

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This report describes the first case of surgical site infection due to *Histoplasma capsulatum*. A 4 year-old presented with recurrent thoracotomy surgical site infection (SSI) requiring multiple debridements until the correct diagnosis was performed. This case illustrates the critical role of histopathology in early recognition of unusual pathogens causing SSIs. *Ann Pediatr Surg* 12:22–24 © 2016 Annals of Pediatric Surgery.

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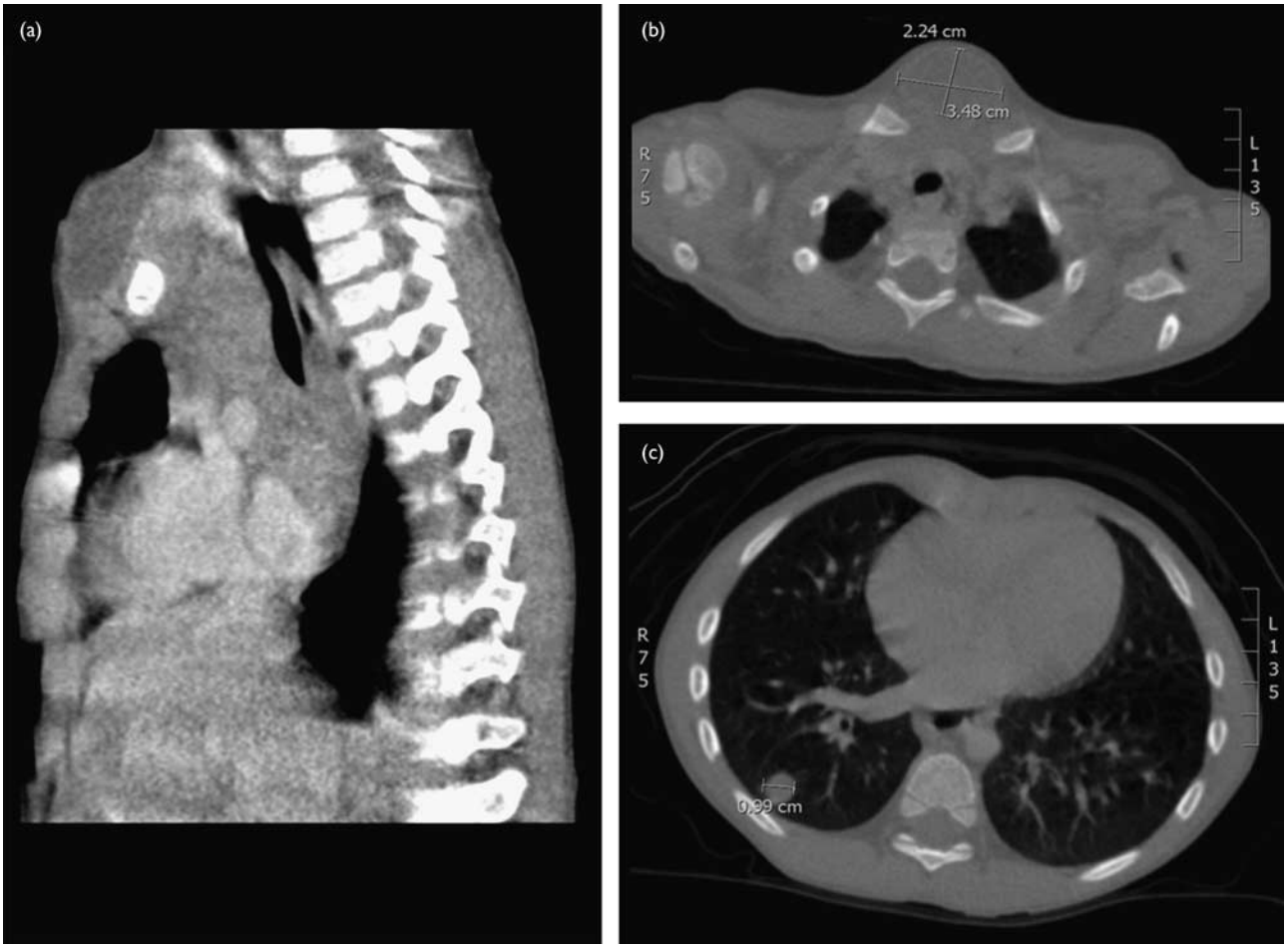
Introduction

Skin and soft tissue infections are rare manifestations of *Histoplasma capsulatum*, a dimorphic fungus endemic in the USA, mainly in the Ohio and Mississippi River valleys [1]. We report the first case of surgical site infection (SSI) due to histoplasmosis in a 4-year-old with a history of total anomalous pulmonary venous return.

Fig. 1



Helical computed tomography (CT) of the chest performed with intravenous injection of omnipaque 300. (a) Low-attenuation rim-enhancing fluid collection at the sternoclavicular junction and in the superior aspect of the sternum abutting the sternotomy wires, measuring 2.2 × 3.5 cm. (b) Pretracheal and subcarinal lymphadenopathy. The subcarinal density measure up to 3.5 × 2.5 cm. (c) Right lower lobe lung nodule measuring 1.0 cm in diameter.

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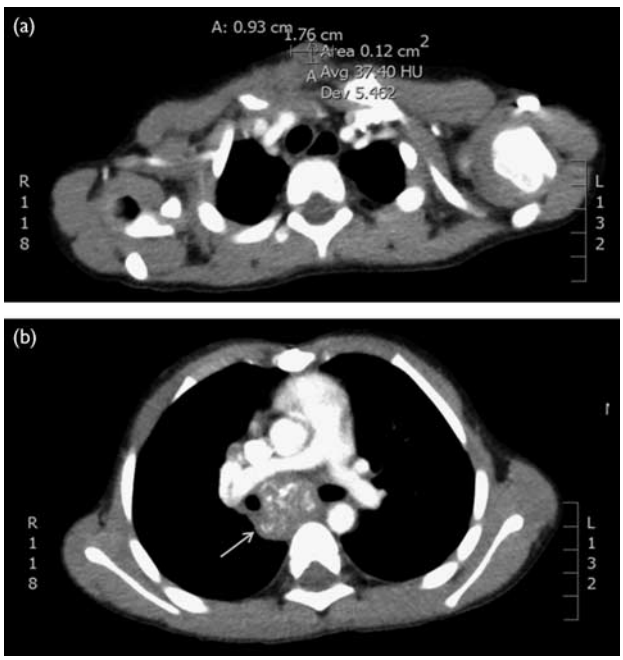
Case report

A 4 year-old with a history of total anomalous pulmonary venous return presented with recurrent thoracotomy surgical site infection over a 12-month period. A chest computed tomography (CT) revealed a rim-enhancing fluid collection anterior to the superior sternum, pretracheal and subcarinal lymph nodes, and a 1 cm right lower lobe lung nodule (Fig. 1). He was taken to the operating room for surgical debridement, including the removal of the superior wires of the sternotomy wound. He was treated with a 4-week course of cefdinir and clindamycin with complete healing of the wound. Bacterial and fungal cultures from the purulent content of the abscess were negative. Serum histoplasma antigens were negative.

Five months later, he returned to the emergency room with a recurrent swelling and erythema of the suprasternal notch area. Chest CT showed a soft tissue abscess in the subcutaneous tissues of the sternoclavicular junction, with an adjacent prominent lymph node (Fig. 2). He underwent surgical debridement with the removal of the remaining wires. Routine bacterial, fungal, and mycobacteria cultures obtained in the operating room were negative. A 4-week course of intravenous cefepime was given as an outpatient, followed by 6 weeks of oral levofloxacin and clindamycin. Histoplasma serology was performed to confirmed the diagnosis of pulmonary histoplasmosis (Histoplasma yeast antibody titer 1 : 256 [negative reference value $< 1:8$]). A follow-up chest CT performed after completion of the therapy showed complete resolution of abscess, and enlarging of the subcarinal soft tissue mass with central necrosis extending into the right hilum (Fig. 3). Itraconazole was started for mediastinal histoplasmosis.

Fig. 2



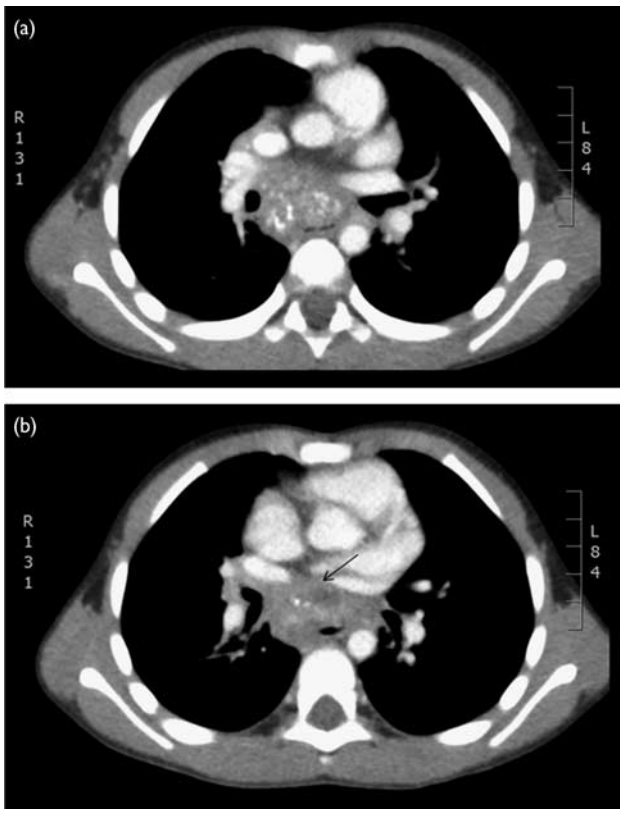
Helical computed tomography (CT) of the chest performed with intravenous injection of omnipaque 300. (a) Low-attenuation rim-enhancing fluid collection at the sternoclavicular junction measuring 1.76×0.93 cm, with an adjacent prominent lymph node. (b) Bulky partially calcified lymphadenopathy in the prevascular region (arrow).

Within 3 weeks of starting itraconazole, he developed recurrent swelling of the sternotomy wound (Fig. 4). A partial upper sternotomy, with drainage of the right and left pleural spaces and mediastinum, was carried out. Surgical pathology showed extensive necrosis with poorly formed granulomas containing few yeast forms, highlighted with Grocott's methenamine silver (GMS) stain consistent with histoplasmosis. AFB stains were noncontributory. Routine bacterial, fungal, and mycobacteria cultures were again negative. In view of these findings, antifungal therapy was instituted with ambisome for the initial 3 weeks, followed by oral itraconazole to complete 1 year of treatment. Follow-up evaluation 7 months after discontinuation of antifungal therapy showed complete resolution of the SSI.

Discussion

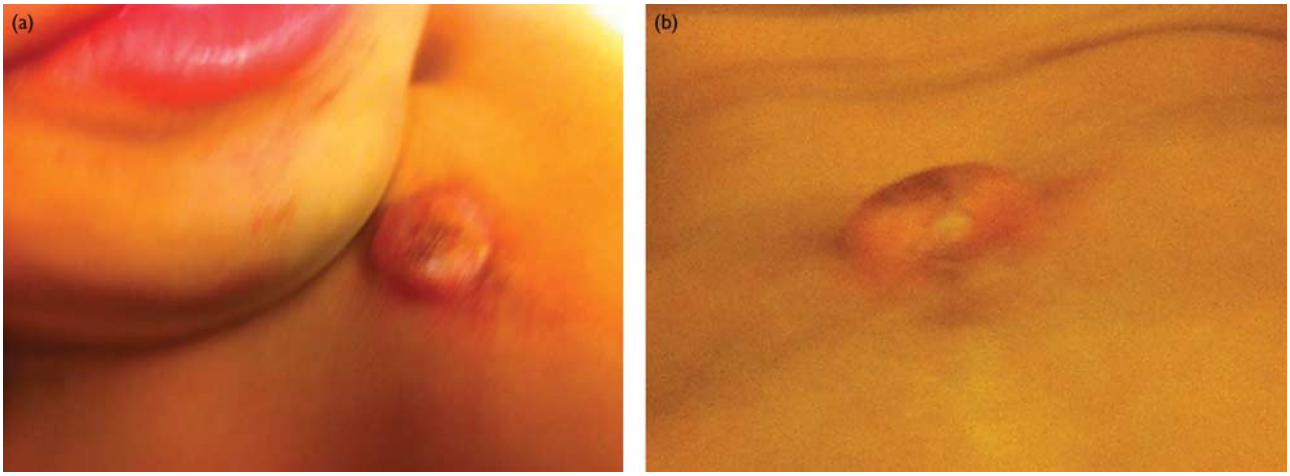
H. capsulatum variety *capsulatum* has a worldwide distribution. Endemic areas, such as the Ohio, Mississippi, and St Lawrence River valleys in the USA, have subtropical climates. The natural inhabits of *H. capsulatum* is soil rich in organic matter, particularly with birds and bat droppings [2]. Histoplasmosis is primarily a pulmonary disease. Nevertheless, most patients with histoplasmosis experience asymptomatic hematogenous dissemination, which is controlled by activated macrophages in the presence of a normal immune response [2].

Fig. 3



Helical computed tomography (CT) of the chest performed with intravenous injection of omnipaque 300. (a) Bulky partially calcified lymphadenopathy in the prevascular region unchanged from previous scans. (b) Mediastinal granuloma with a small hypoechoic area within the anterior aspect of the subcarinal lesion measuring $\sim 0.6 \times 1.2$ cm likely representing necrosis (arrow).

Fig. 4



(a) Nontender sternal mass, measuring 2.0 × 2.5 cm in diameter with an umbilicated center and faint erythema at the thoracotomy site. (b) Flesh-colored tissue mass with a pustule at 6 o'clock.

Mucocutaneous manifestations of disseminated infection are unusual in the USA, developing in less than 10% of HIV/AIDS patients [3]. These have a wide range of clinical manifestations, including molluscum-like papules, cellulitis, purpuric lesions, panniculitis, and plaques with or without crusts, pustules, and nodules. Primary cutaneous infection is extremely rare, with a handful of cases described in the literature [3–5]. These lesions might present with regional adenopathy, which resolves within the course of weeks or months [3]. To the best of our knowledge, this is the first report of SSI associated with histoplasmosis.

Diagnosis of histoplasmosis is based on the clinical presentation and access to tissue biopsy. When feasible, diagnosis involves a combination of histopathology, culture, and antibody and antigen detection. The diagnostic method to evaluate cutaneous involvement with *H. capsulatum* is a full-thickness punch biopsy [6]. As described for the patient in the present report, histopathology reveals necrotizing granulomas with intracellular yeast measuring 1–5 μm in diameter found inside macrophages and neutrophilic granulocytes. Fungal cultures obtained in two surgical procedures performed 5 months apart yielded negative culture results in this case. Insensitivity and delayed growth are well known limitations of this diagnostic methodology [7]. Cultures from extrapulmonary tissues yield positive results in only 37% of the cases [7]. Serological testing provides the basis for the diagnosis of histoplasmosis, particularly for patients with chronic infection, when sensitivity approaches 100% [7]. On the other hand, the persistence of elevated antibody titers for several years after exposure complicates the interpretation of positive serology in symptomatic patients [7].

Diagnosis in the child described was performed by the characteristic findings on chest CT, elevated antibody titers, and the presence of granulomas and yeast forms on histopathology. Infection most likely spread from a mediastinal node to the surgical site. Despite extensive surgical debridement and removal of the wires, infection could not be controlled until appropriate antifungal therapy was instituted. Yet, the gross anatomy of the skin manifestations, as shown in Fig. 4, are more consistent with a granulomatous process than with a bacterial infection by pathogens commonly associated with SSIs, such as staphylococci, streptococci or Gram-negative bacteria. A high index of suspicion prompted the request of histopathology, and the recognition of the fungal nature of this patient's SSI.

In summary, this case illustrates the critical role of histopathology in the diagnosis of histoplasmosis in an immunocompetent patient with recurrent SSI. An early diagnosis could have avoided multiple surgical debridements and prolonged courses of intravenous and oral antibiotic therapy.

Acknowledgements

Conflicts of interest

There are no conflicts of interest.

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