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CASE REPORT

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A rare case of concurrent pneumonia, rib osteomyelitis, spondylodiscitis, paravertebral and epidural abscesses in a patient with chronic granulomatous disease

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Abstract

Chronic granulomatous disease (CGD) is a rare primary immunodeficiency disorder that is characterized by deficiencies in the phagocytes capacity to eliminate ingested microorganisms, which frequently causes bacterial and fungal infections. The extensive involvement of the lungs, ribs, and vertebrae that is complicated by multiple abscesses from aspergillosis is rare. in this study, we report a 13-year-old boy with CGD who experienced concurrent pneumonia, rib osteomyelitis, spondylodiscitis, paravertebral, and epidural abscesses as a result of *Aspergillus flavus* infection with associated computed tomography scan and magnetic resonance imaging findings. Patients with CGD are susceptible to *Aspergillus* infection. Correct diagnosis based on clinical and paraclinical findings as well as choosing the best treatment regimen is essential for achieving a favorable outcome.

KEYWORDS

Aspergillus flavus, chronic granulomatous disease, magnetic resonance imaging, spondylodiscitis

1 | INTRODUCTION

Chronic granulomatous disease (CGD) is a rare primary immunodeficiency disorder caused by the failure of the nicotinamide adenine dinucleotide phosphate oxidase complex to synthesize reactive oxygen substances in activated macrophages, monocytes, and neutrophils.[1] Although it can be diagnosed in both children and adults, the most of those diagnosed are under the age of five.[2] In the United States, the prevalence of CGD is thought to be around 1 in 200,000 live births.[3]

CGD is characterized by recurrent, potentially fatal, fungal and bacterial infections as well as development of tissue granulomas.[3] The most prevalent infections are septicemia, pneumonia, liver abscesses, gastroenteritis, subcutaneous abscesses, perianal abscesses, and suppurative adenitis. The most common pathogenic organisms include *Salmonella*, *Staphylococcus aureus*, *Serratia marcescens*, *Candida*, and *Aspergillus* species.[4,5]

Despite advances in antifungal prophylaxis and treatment, invasive aspergillosis is still the most common infection in CGD patients.[6] It has a significant mortality rate and is the cause of about one-third of fatalities.[7] Patients with CGD infrequently develop osteomyelitis or spinal/epidural abscesses caused by *Aspergillus* species.[8,9] Pneumonia is the most typical type of aspergillosis

in patients with CGD and it is frequently associated with spread to soft tissues, chest wall, ribs, or spine.[8]

In this report, we describe a 13-year-old child with CGD who experienced coexistence of pneumonia, rib osteomyelitis, spondylodiscitis as well as paravertebral and epidural abscesses as a result of *Aspergillus flavus* infection with partial response to antifungal treatment. Detailed imaging characteristics of such a case have not been frequently reported in the literature.

2 | CASE PRESENTATION

A 13-year-old boy who had been diagnosed with CGD at 4 years of age, presented with cough, weakness, lethargy, and gait abnormality. He had several previous admissions for recurrent pneumonia and hepatic abscess to the Pediatrics Department of Mashhad University of Medical Sciences, Mashhad, Iran. The immunologic parameters, including lymphocyte subsets and immunoglobulin levels had been evaluated and the results had shown that IgG, IgA, IgM, and IgE levels, as well as the complement system C3, C4, and CH50 levels, had been within normal ranges for the patient's age. A screening test had been conducted to assess the presence of CGD, which had been confirmed by an abnormal neutrophil nitroblue tetrazolium (NBT) slide test. However, due to regional limitations, genetic testing had not been performed as a diagnostic test.

On physical examination he was afebrile and he had a swelling at the region of upper thoracic vertebrae. The swelling was about 10 × 6 cm with redness and tenderness. Neurologic examination revealed reduced force of lower limbs, but the sensory was normal. The laboratory data showed a white blood cell count of 8400/μL (neutrophils: 65%, lymphocytes: 23%), erythrocyte sedimentation rate of 74, and a C-reactive protein of 120 mg/dL.

In the superior segments of lower lobes of lungs, bilateral peripheral consolidation was observed on axial computed tomography (CT) scan with pulmonary window. Sclerotic and lytic lesions in multiple vertebral bodies were detected on axial and sagittal reconstructed CT scans with bone window. Vertebrae planae were detected at T2, T4, and T5. There was also obvious right-side proximal rib involvement (Figure 1). These findings supported the diagnosis of pneumonia with rib osteomyelitis and multilevel vertebral body spondylitis.

On magnetic resonance imaging (MRI), multiple hyposignal vertebral bodies were detected on sagittal T1W images, which enhanced on post-contrast images (Figure 2). At the T2, T4, and T5 vertebral bodies, vertebrae planae were seen. Subligamentous spread of infection beneath the anterior and posterior longitudinal ligaments was also evident. Posterior epidural abscess and granulation tissue from T3 to T6 had caused spinal canal stenosis and compressive myelopathy which was evident on sagittal STIR image.

Furthermore, axial T2W and post-contrast T1W-fat sat images showed bilateral consolidation, rib osteomyelitis, posterior epidural abscess, and granulation tissue extending to bilateral neural foramina, causing canal stenosis and compressive myelopathy (Figure 2).

Histopathologic examination and fungal culture acquired from abscess aspiration revealed green, powdery surface colonies and septate hyphae with acute angles of approximately 45°, consistent with *A. flavus*.

During his hospital stay, the patient received meropenem, vancomycin, voriconazole, and interferon gamma (IFN-γ) for 6 weeks. Due to patient refusal to surgery and partial improvement of the patient's symptoms, open

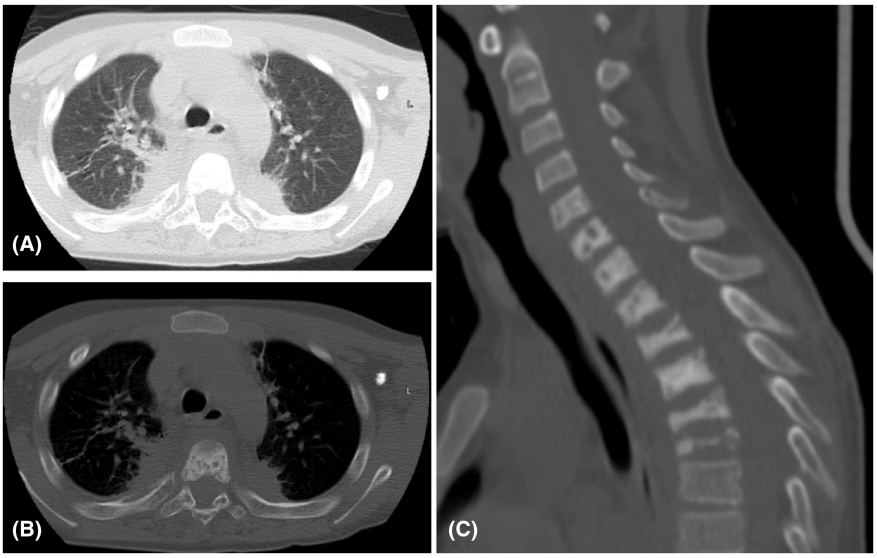

FIGURE 1 (A) Axial CT scan in pulmonary window shows bilateral peripheral consolidation in superior segments of both lower lobes. (B) Axial CT scan image in bone window shows right sided adjacent rib involvement. (C) Reconstructed sagittal CT scan image shows lytic-sclerotic lesions on multiple vertebral bodies and vertebra plana at T2, T4, and T5 vertebrae. These findings are consistent with pneumonia with rib osteomyelitis and multi-level vertebral body spondylitis.

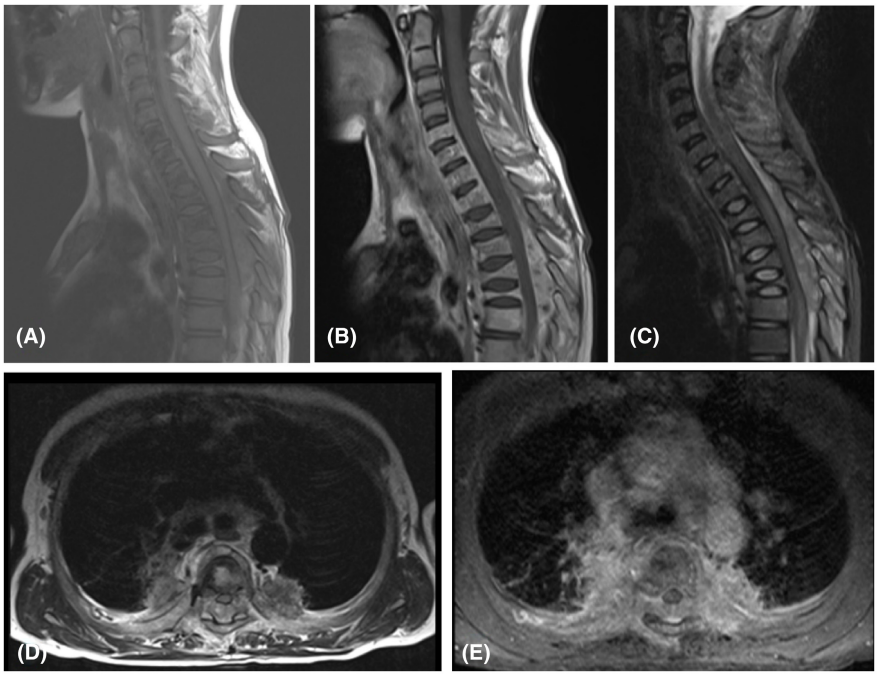

FIGURE 2 Sagittal T1W images without (A) and with (B) contrast show multiple hyposignal vertebral bodies which enhance on post contrast image. Vertebra plana is seen at T2, T4, and T5 vertebral bodies. Subligamentous spread of infection beneath the anterior and posterior longitudinal ligaments is evident. (C) Posterior epidural abscess and granulation tissue from T3 to T6 causing spinal canal stenosis and compressive myelopathy is evident on sagittal STIR image. Axial T2W (D) and post contrast T1W-fat sat (E) images show bilateral consolidation, rib osteomyelitis and posterior epidural abscess and granulation tissue which extends to bilateral neural foramina causing canal stenosis and compressive myelopathy.

surgery was not performed. Following that, 6 months of outpatient therapy with voriconazole and cotrimoxazole was implemented and the patient had partial recovery in the 6-month follow-up appointment. Follow-up examination was done using ultrasonography which showed that the pus collection had significantly shrunk although it was not disappeared. The patient did not show up in the next follow-up sessions.

3 | DISCUSSION

The CGD is an uncommon disease making patients more susceptible to opportunistic fungal and bacterial infections including aspergillosis due to the use of broad-spectrum antibiotics, immunodeficiency, and *Aspergillus* colonization of a pre-existing lung cavity.[10–12]

According to a data analysis from the CGD registry, *Aspergillus nidulans* and *Aspergillus fumigatus* are the most common identified species in the brain, bones, and lungs.[13] Despite the fact that the most frequent obtained pathogen from CGD patients is *A. fumigatus, A. nidulans* seems to be more virulent and has a greater mortality rate.[14] The most typical site for *Aspergillus* osteomyelitis is vertebral bodies. Also, a few cases of Aspergillus epidural abscess have been documented in the literature.[9]

In a study by van den Berg et al. on 429 patients with CGD, 13% (56/429) of them experienced episodes of osteomyelitis. *Aspergillus* species (35% of cases) and *Serratia* species (8%) were the two most common causes. The most commonly affected locations of osteomyelitis were the vertebrae, ribs, talus, tibia, and femur.[15] In another research on 368 patients with CGD, 25% of them suffered from osteomyelitis which was mainly caused by *Aspergillus* species and *Serratia* species.[7]

Invasive aspergillosis could be treated well with second-generation triazoles like posaconazole and voriconazole.[16] In a study that looked at 20 patients with *Aspergillus* osteomyelitis, voriconazole was effective in 55% of the cases that had not responded to amphotericin B therapy.[17] Although the ideal treatment duration for *Aspergillus* osteomyelitis is still unknown, a longer course of therapy (>6 months) is usually needed.[18]

Surgery might be considered in specific cases with deterioration of symptoms and/or patients who fail to respond adequately to medical therapy.[18] In a study of 12 patients with Aspergillus osteomyelitis, surgery enhanced survival considerably.[19] Furthermore, *IFN-γ* has also been beneficial in treating cases with severe invasive aspergillosis or osteomyelitis. Al-Tawfiq et al. reported notable improvement when they used the combinational therapy of itraconazole and *IFN-γ* in a patient with CGD and

vertebral osteomyelitis who presented with quadriplegia 14 months after treatment with surgical drainage, caspofungin, itraconazole, and voriconazole.[20]

Our patient presented with cough, weakness, lethargy, and gait abnormality. On imaging he had pulmonary and vertebral involvement. We treated our patient with meropenem, vancomycin, voriconazole, and IFN-γ which ameliorated the symptoms in a 6 months period. Follow-up sonographic examination also revealed significant abscess shrinkage. Unfortunately, complete resolution was not evident as the patient did not appear in the next follow-up sessions. Chang and colleagues treated their patient with voriconazole and IFN-γ for an 8-months period which resulted in the resolution of paraspinal abscess.[8] Like our case, their patient did not undergo surgery. İkincioğulları et al. treated a patient with pneumonic consolidation and paravertebral abscess and osteomyelitis due to *A. flavus* and *S. aureus* whose blood culture was positive for *Acinetobacter baumannii*.[21] Although, the patient received vancomycin, meropenem, amphotericin B, itraconazole, and granulocyte transfusion and underwent lung segmentectomy, she died on the postoperative day 19 due to acute respiratory distress syndrome. First-generation azoles, such as itraconazole have been demonstrated to have higher rates of resistance development and adverse effects, compared to newer triazoles such as voriconazole; therefore, the latter are preferred.[22] Amphotericin B has been previously used as a first-line agent for invasive aspergillosis in patients with CGD; however, due to nephrotoxic effects and suboptimal results, it has been substituted by newer options, such as voriconazole.[8,23]

4 | CONCLUSION

In conclusion, we described a case of a 13-year-old boy with CGD who had *A. flavus*-related pneumonia, rib osteomyelitis, spondylodiscitis, and paravertebral and epidural abscesses. The significance of this case report is due the substantial involvement of the lungs, ribs, vertebrae, and several abscesses in the aspergilloma field, as well as the paucity of imaging descriptions of similar patients in the literature.

AUTHOR CONTRIBUTIONS

Nahid Tavakolizadeh: Conceptualization; writing – original draft. **Amir Mahmoud Ahmadzade:** Conceptualization; writing – original draft. **Behnam Beizaei:** Conceptualization; writing – original draft. **Mostafa Izanlu:** Conceptualization; resources. **Farzaneh Khoroushi:** Conceptualization; resources. **Behzad Aminzadeh:** Conceptualization; resources; writing – review and editing.

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None.

CONFLICT OF INTEREST STATEMENT

The authors declare that they have no conflict of interests.

DATA AVAILABILITY STATEMENT

The data that support the findings of this study are available from the corresponding author upon reasonable request.

ETHICAL APPROVAL

This study was approved by institutional review board committee.

CONSENT

Written informed consent was obtained from the patient's parents to publish this report in accordance with the journal's patient consent policy.

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