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INVASIVE PULMONARY AND SINUS ASPERGILLOSIS IN A NEUTROPENIC CHILD: A CASE REPORT

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ABSTRACT
Invasive aspergillosis is a major cause of morbidity and mortality in immunocompromised children. It is an opportunistic infection caused by a saprophytic *Aspergillus* species commonly found in the environment. We report a case of invasive aspergillosis with both pulmonary and sinus involvement. The patient is a 15-year-old boy under treatment for idiopathic aplastic anemia (corticosteroids, cyclosporine, and anti-lymphocyte serum). The symptoms began two days prior to admission, with a sudden onset of high fever, dry cough, chest pain, and severe headache predominantly affecting the right side of the face. Laboratory tests revealed severe pancytopenia, a biological inflammatory syndrome, a positive blood culture for beta-lactamase-producing *Klebsiella pneumoniae*, and a galactomannan antigen level of 1.3 ng/mL. Thoracic and sinus CT scans showed bilateral pneumonia associated with right pansinusitis without bone destruction. Clinical, biological, and radiological findings confirmed the diagnosis of invasive pulmonary and sinus aspergillosis. Early diagnosis and treatment of this condition significantly improve both vital and functional prognosis.

KEYWORDS: Aspergillosis, Galactomannan Antigen, Corticosteroid Therapy, Neutropenia, Pneumonia, Sinusitis

INTRODUCTION
Invasive aspergillosis is a major cause of morbidity and mortality in immunocompromised children. It is an opportunistic infection caused by saprophytic Aspergillus species commonly found in the environment.[1] The main risk factor is neutropenia. Its incidence varies depending on the duration and depth of neutropenia, estimated at around 10%.[2] Early diagnosis and treatment improve prognosis. We report a case of invasive pulmonary and sinus aspergillosis in an immunocompromised patient to describe the diagnostic, therapeutic, and evolutionary profile.

CASE PRESENTATION
This is a 15-year-old adolescent followed in the department for idiopathic bone marrow aplasia, undergoing a therapeutic protocol consisting of anti-lymphocyte serum, cyclosporine, and corticosteroid therapy due to the lack of a compatible donor. The patient has been hospitalized multiple times for hemorrhagic and infectious episodes managed with iterative transfusions and antibiotic therapy, with good recovery. The patient is currently readmitted for acute fever.

Clinical fundings
Conscious patient, T°C: 38.7°C, weight: 47 kg, supple neck, no sensory-motor deficits, tenderness on palpation over the right frontal and maxillary sinuses, throat without signs of angina or stomatitis, eupneic with crackles more pronounced on the right, soft and depressible abdomen, no hepatosplenomegaly, free lymph nodes, no cutaneous or mucosal hemorrhages. Ophthalmologic examination: hemorrhage in the anterior chamber and multiple flame-shaped hemorrhages in the retina, more pronounced on the right.

Medical History
Acute fever with sudden onset associated with cough, right-sided chest pain, and severe headache, more pronounced on the right side of the face with photophobia. All symptoms have been evolving for 48 hours prior to admission in the context of general deterioration.

Complementary Test
The biological tests showed a deep bone marrow failure syndrome (see Table 1), a major biological inflammatory syndrome, and the liver and renal tests were normal. Blood culture was positive for Klebsiella pneumoniae, producing extended-spectrum beta-lactamase, sensitive

to imipenem and amikacin. The Aspergillus galactomannan antigen test was positive at 1.3 ng/ml. The search for adenovirus, CMV (cytomegalovirus), and herpes viruses by PCR (polymerase chain reaction) was negative. Deep bone marrow aplasia (Figure 1). The thoraco-abdomino-pelvic CT scan showed a consolidation focus with an air bronchogram in the ventral segment of the middle lobe, two nodules with irregular contours in the dorsal segment of the right lower lobe measuring 5mm and 5.8mm, with a small pleural effusion. The sinus CT scan, motivated by the intense headache, confirmed right-sided pansinusitis without associated bone lysis (Figure 2). These clinical, biological, and imaging data are consistent with probable invasive aspergillosis.

Therapeutic Interventions

The patient was initially started on broad-spectrum antibiotic therapy (imipenem 60mg/kg/day + Amikacin 20mg/kg/day), voriconazole 6mg/kg/12h (loading dose: Day 1), then 4mg/kg/12h, platelet transfusion and phenotyped red blood cell concentrate, dual analgesics (Andol 15mg/kg/6h + Tramadol 1mg/kg/8h), plus a dose of 3mg morphine intravenously.

Follow-up and therapeutic outcomes

The progression was marked by the achievement of apyrexia, regression of retinal hemorrhage, and a decrease in headache. Biologically: a decrease in CRP followed by negativity on day 10 of hospitalization.

Table 1: blood testing results.

Laboratory tests	Results	reference values
WBC (/mm ^{3})	60	3.75-13
PMN (/mm ^{3})	00	1.5-6.3
Hemoglobin level (g/dl)	5.3	12.1-16.6
Platelets (/mm3)	3000	166000-395000
CRP (mg/l)	>320	0.1-2.8
Urea level (g/l)	0.48	0.17-0.49
Creatinine level (mg/l)	16.9	4.6-7.7
Na+/K+ (mmol/l)	135 /3.2	135-145-3.5-5.1
Ca2+ (mg/l)	85	84-102
PT	89%	70-100%
Ferritinemia (ng/ml)	6732	15-80
Fibrinogen (g/l)	4.3	2-4
ALT/AST (ui/l)	31/8	<45
Aspergillus antigen (ng/ml)	1.3	<0.5

WBC: white blood cells **PMN:** polymorphonuclear neutrophils; CRP**:** C reactiv protein; **PT**: prothrombin time; **ALT**: Alanine Aminotransferase, **AST:** Aspartate Aminotransferase.

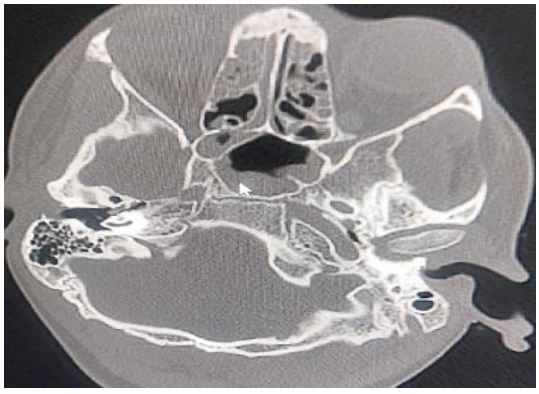

Image A: ***Right pan sinusitis without associated bone lysis.***

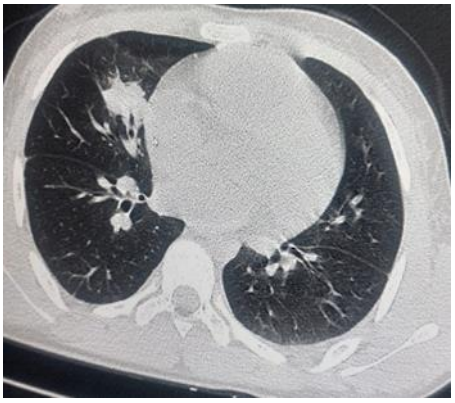

Image B: A pneumonia appearance with pulmonary consolidation, air bronchogram, and nodules.

Figure 1 (A and B): CT scan images of thoracic and sinus sections.

DISCUSSION

Aspergillosis refers to a group of diseases that depend on host-related factors and the immune response. Among the risk factors for this opportunistic infection are prolonged neutropenia and immunosuppressive treatment (cyclosporine, corticosteroids).[3] Our patient exhibited all of these factors. The diagnosis of invasive aspergillosis remains a challenge for clinicians. The mortality rate is high despite the introduction of new diagnostic methods. Early diagnosis and treatment improve prognosis. The presence of multiple risk factors for aspergillosis should lead to diagnostic suspicion and prompt treatment, according to the Italian review by Vito Terlizzi et al.[4]

The clinical manifestations of aspergillosis depend on the affected site and the clinical response of the patient. The upper airways, pulmonary parenchyma, and contiguous structures are most commonly affected, although the infection can be disseminated in 10% of cases. The main clinical signs of invasive aspergillosis are fever, cough, chest pain, dyspnea, and/or hemoptysis. Sinus cavity aspergillosis may be the primary site of the disease or manifest as a disseminated infection originating from a pulmonary source, according to the review by Cadena et al.[5]

The diagnosis of invasive aspergillosis relies on a combination of clinical, microbiological, and radiological findings. According to the EORTC/MSG diagnostic criteria, invasive aspergillosis in children is classified as proven, probable, or possible. The measurement of Aspergillus antigen galactomannan in blood and bronchoalveolar lavage fluid provides important diagnostic support with high sensitivity and specificity in neutropenic children, according to the review by Athanasia Apsemidou et al. The presence of (1; 3)-β-D-glucan in serum indicates fungal invasion but is not specific to Aspergillus spp. PCR testing for Aspergillus is not validated in recommendations for the pediatric population.[6] Conventional radiography rarely differentiates aspergillosis from other infections. Computed tomography (CT) is the gold standard examination. It may show infiltrates in the form of ground-glass lesions, the halo sign indicating angioinvasion, nodules that may develop into cavities, and pulmonary consolidation lesions, sometimes accompanied by pleural reaction. Nonspecific signs are frequently observed, according to the study by Jeffrey D. Jenks et al.[7] Invasive pulmonary and sinus aspergillosis can occur in immunocompromised or immunosuppressed patients. The diagnostic approach is identical to that of pulmonary aspergillosis alone and relies on the clinical, microbiological, and radiological criteria of EORTC/MSG. The prognosis is severe in cases of bone lysis and requires prompt treatment, according to the review by Matthew William McCarthy et al.[8]

The most common form of invasive aspergillosis is pulmonary aspergillosis, with a mortality rate ranging from 30% to 60%. Early treatment, starting at the first clinical signs, improves survival. Voriconazole, at a dosage of 6mg/kg/12h on the first day, then 4mg/kg/12h, is the first-line treatment. Isavuconazole gives similar results to voriconazole with fewer side effects. Monitoring plasma voriconazole concentration is necessary for efficacy and toxicity surveillance. The normal plasma concentration of voriconazole is 2 to 5mg/L. Liposomal amphotericin B is positioned second due to its nephrotoxic toxicity in the treatment of invasive aspergillosis.[9]

CONCLUSION

Invasive pulmonary and sinus aspergillosis is a rare and severe opportunistic infection occurring in immunocompromised and/or immunosuppressed individuals. Early diagnosis and treatment improve survival prognosis. Neutropenia, corticosteroid therapy, and cyclosporine are additive risk factors for opportunistic infections, including aspergillosis. Therefore, any infectious episode in an immunocompromised (neutropenic) patient should raise suspicion for aspergillosis. The dual localization of aspergillosis is a rare entity. Large-scale studies are needed to assess the clinical, diagnostic, and evolutionary profiles.

Conflicts of interest: The authors declare no conflicts of interest.

Consent: Informed consent from the parents was obtained for publication.

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