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CASE REPORT

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Lovebird-induced Aspergillus Infection in a Child with Chronic Granulomatous Disease

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What is known on this subject?

Chronic granulomatous disease (CGD) is characterized by life-threatening bacterial and fungal infections.

What this case report adds?

Here, it is aimed to emphasize that pets may be a possible source of aspergillus infection in people with CGD and that surgically obtained tissue cultures may be required for diagnosis.

ABSTRACT

Chronic granulomatous disease (CGD) is a primary immune deficiency in which the phagocytic system is affected. The disease is inherited X-linked or autosomal recessive and is characterized by life-threatening bacterial and fungal infections. Invasive fungal infections are one of the most important causes of mortality in this disease. Here, we discuss an 8-year-old male patient with CGD considering literature. The patient developed invasive aspergillus infection due to the pet bird. Here, it is aimed to emphasize that pets may be a possible source of Aspergillus infection in people with CGD and that surgically obtained tissue cultures may be required for diagnosis.

Keywords: Aspergillosis, chronic granulomatous disease, diagnosis, treatment

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Introduction

Chronic granulomatous disease (CGD) is a primary immune deficiency affecting the phagocytic system via defects in the subunits of NADPH oxidase system. It is inherited through X-linked and autosomal recessive patterns (1,2). It is characterized by life threatening bacterial and fungal infections which affect the skin, respiratory tract, liver, brain, lymph nodes, and bones. The most common pathogens causing infections are *Staphylococcus* spp., *Klebsiella* spp., *Burkholderia* spp., *Serratia marcescens, Mycobacterium* spp., and *Aspergillus* spp. (2,3,4,5,6,7).

CGD has the highest prevalence of invasive fungal infections among the immune deficiencies. Invasive fungal infections are a major cause of mortality and morbidity in 20-40% of patients. Fungal infections often affect the chest wall and lungs. Most common pathogens are *Aspergillus fumigatus* and *Aspergillus nidulans*. Less frequently, infections with other *Aspergillus* spp. and other fungal strains such as *Mucormycetes*, *Trichosporon* spp., *Histoplasma* spp. have also been reported (8,9,10,11).

Aspergillus spp. are mainly found in soil, air, vegetation, and dead organic materials. The risk factors increasing the susceptibility to Aspergillus infections are warm and humid environment, poor ventilation and hygiene conditions, stored food for a long time, chronic diseases affecting the immune system, and long-term use of immunosuppressant drugs. Aspergillus spp. cause disease not only in humans, even in all domestic birds, waterfowl, wild and ornamental birds (12,13).

Case Reports

An eight-year-old male followed up with a diagnosis of autosomal recessive inherited CGD for seven years admitted to the hospital with a complaint of swelling in the back for a week. He had been suffering from night sweats, loss of appetite, weight loss and disseminated muscle pain for four months. The patient came to out-patient clinic follow-ups irregularly and was last seen 10 months ago. He was receiving co-trimoxazole and itraconazole prophylaxis. A physical examination revealed a pale, cachectic appearance. On the left scapula, there was an 8 x 10 cm sized non-fluctuating solid mass fixed to the underlying tissue. The first laboratory examinations revealed leukocyte as 12570/mm^3, absolute neutrophil as 8740/mm^3, eosinophils as 50/mm^3, hemoglobin as 10.1 gr/dL, etc. as 34.9%, platelet as 336000/mm^3, C-reactive protein as 105 mg/dL, and sedimentation rate as 49 mm/h. The chest radiography showed loss of ventilation in the left middle upper zone of the lung and marked periosteal reaction in the 3rd, 4th, 5th, 6th, 7th, and 8th ribs. Thoracic computed tomography (CT)revealed a subperiosteal abscess affecting 3rd-6th ribs and a solid lesion extending from the lung parenchyma below the skin (Figure 1). Initial culture samples (blood, gastric lavage) were obtained and broad-spectrum antibiotics (teicoplanin and meropenem) were started empirically. Afterwards, based on his anamnesis, probable Mycobacterial and fungal infections were prioritized since the patient's complaints slowly came out of a long time. Four anti-tuberculosis (TB) regimens (isoniazid, rifampicin, pyrazinamide, and ethambutol), caspofungin and voriconazole, were initiated. Following days, he had persistent fever above 39°C and new infiltration developed on the right lung. He rapidly developed into respiratory failure and transferred into an intensive care unit. Mechanical ventilation was initiated. Granulocyte transfusions were administered five times a week based upon critical clinic condition. After remaining on ventilator support for 15 days, the patient was disconnected from the ventilator

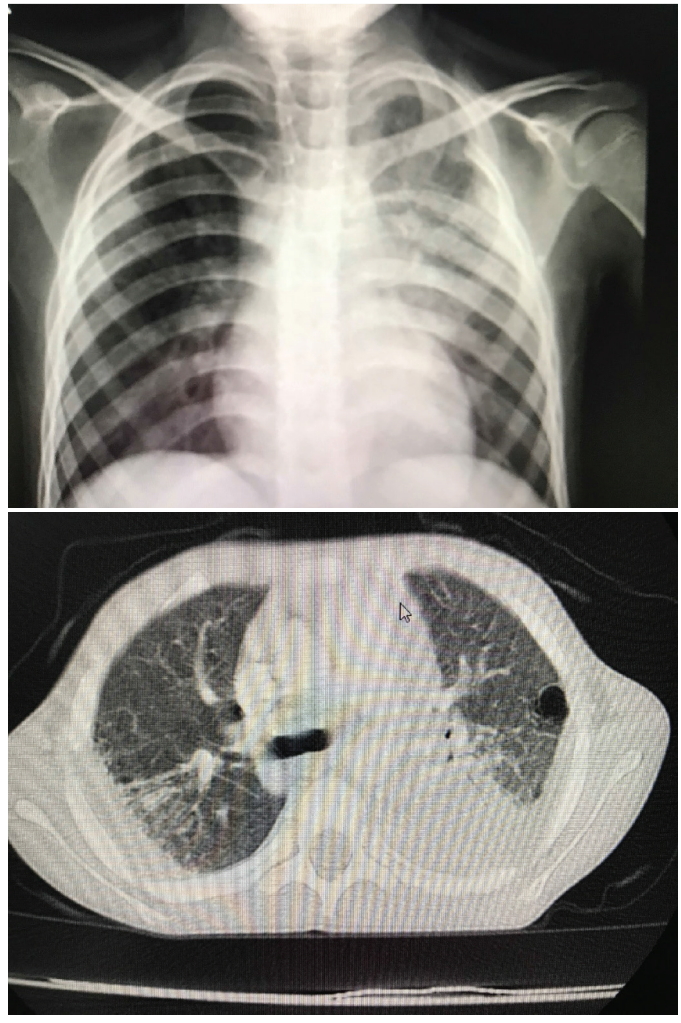


Figure 1. Chest radiography and thorax CT of the patient
CT: Computed tomography

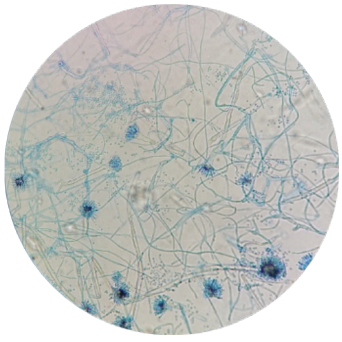
since his clinical findings recovered and the infiltration on the right lung regressed. During this period, the bacteria and fungi were not reproduced in the serial cultures; the acid-resistant bacilli were not detected in the gastric lavage samples; and serum galactomannan antigen was found negative. At the end of the first month of treatment, the chest CT scan showed that the infiltration in the left lung parenchyma was regressed, whereas the lesions in the ribs and subperiosteal abscess persisted. Because of thoracic surgery consultation, partial resection and drainage of the abscess were applied to the left third and fourth ribs, which were in the worst condition. Abscess material was sent for pathology and microbiological examinations (bacteria, fungi and mycobacteria). In addition to morphologically compatible findings with CGD, fungal hyphae and spores were observed with Grocott and periodic acid schiff staining in the histochemical examination, and the acid-resistant bacteria were not detected in Ehrlich-Ziehl-Neelsen staining. The fungal growth was shown in cultures. The typing studies indicated *Aspergillus terreus* that was sensitive to caspofungin and voriconazole. There was no growth in automatized (Bactec) and manuel (Löwenstein-Jensen medium) mycobacteria cultures. Initial antibacterial agents and anti-TB drugs were discontinued. The treatment was rearranged with antifungal drugs.

The patient's home condition was re-questioned for a predisposing factor for invasive fungal infection. His parents admitted that he had been keeping a love bird (*Nymphicus hollandicus*) for a year. The feathers of the bird were brought and inoculated on Sabouraud dextrose agar medium and incubated at 25 °C and 37 °C for 5-7 days. Lactophenol cotton blue was prepared from the colonies that grew when the incubation period was over, and the length of the conidia for, the shape and width of the vesicle, and the shape of the conidia were examined under the microscope (Figure 2). The same microorganism, *A. terreus*, was detected in the feathers of the bird (Figure 2). The demonstration of the same strain in the patient and the bird suggested that the infection might be transmitted from the animal. When this situation was shared with the family, the bird was taken to the veterinarian, treated and removed from the house.

We observed that the infiltration in the parenchyma completely regressed in control imaging under antifungal treatment. His general condition and oral intake improved and he began gaining weight. At the end of the third month of his treatment, he was discharged with voriconazole and itraconazole and co-trimoxazole, which he received as prophylaxis.

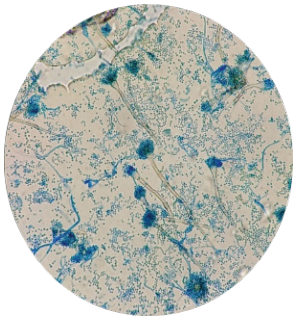
Discussion

Invasive pulmonary aspergillosis is one of the most important causes of death in patients with a suppressed immune system and CGD (14). Aspergillus causes airborne infections through its conidia, the respiratory tract being the most frequently affected area (14). Additionally, there may

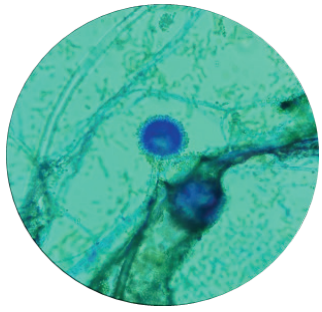


Aspergillus terreus

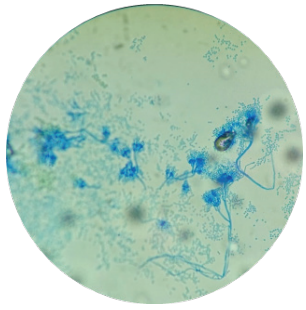
- The following culture growths were detected in the sampling made from the feather of the same patient, which he has fed at home.
- Domestic Bird Feather
- ***Aspergillus terreus***



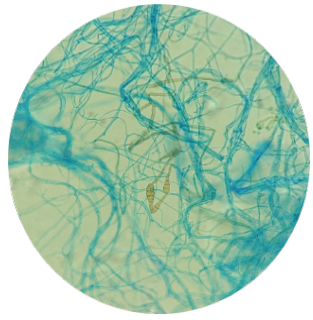
- Domestic Bird Feather
- ***Aspergillus terreus***



- Domestic Bird Feather
- ***Aspergillus niger***



- Domestic Bird Feather
- ***Penicillium* spp.**



- Domestic Bird Feather
- ***Alternaria* spp.**

Figure 2. Lactophenol cotton blue microscopy image of mold fungus growing in tissue biopsy culture

be widespread involvement in the central nervous system, liver, kidney, eye, and heart (3,14).

Although *A. fumigatus* is the most common type of opportunistic infection in humans, infections might occur with *A. flavus*, *A. niger*, *A. nidulans*, *and A. terreus* (1,3,14).

A. terreus is common in our environment like other species and causes invasive and disseminated infections as well as respiratory tract involvement (15). *A. terreus*-related infections occur worldwide, however they are more common in some geographical regions such as Innsbruck, Austria and Houston, USA (15). In an international prospective multi-center study, the prevalence of *A. terreus*-related infection among all fungal infections was reported as 5.2% (15). Our patient was diagnosed with immune deficiency and the involvement of the lungs and ribs due to *A. terreus* was detected.

For the diagnosis of invasive aspergillosis, both histopathological evidence and growth in a sample culture taken from a sterile tissue is required. In cases where biopsy is impossible, serum biomarkers such as galactomannan, beta-D-glucan, as well as direct staining and culture of the fungus from sputum and/or bronchoalveolar lavage fluid can be used (14). Galactomannan was found negative in our patient, and there was no growth in the tracheal aspirate and in the blood cultures. For this reason, material was taken from the lung tissue and cultured, and *Aspergillus* species was demonstrated in tissue cultures.

Effective treatment of invasive aspergillosis is possible with early antifungal initiation, immunomodulation, and, in some cases, surgical intervention (15). Given that Aspergillus infections are extremely fatal in immunocompromised patients, it is recommended to immediately initiate empirical antifungal treatment when suspected, and to revise the treatment based on an antifungal sensitivity test in confirmed cases. In proven Aspergillus infections, treatment should be continued according to the antifungal sensitivity test (14). We also started antifungal treatment in our patient empirically, without waiting for the culture results and continued in the same way when it was seen that he was responsive to the treatment he received according to the antifungal sensitivity test when there was a growth in the tissue culture. Despite contrasting reports, interferon-gamma (IFN-γ) has been found to be beneficial in these patients as an immunomodulator of both severe infections and prophylaxis (1). We could not apply IFN-γ for our patient because our order was not obtained due to a problem. Since we could not get enough clinical and radiological response despite regular antifungal treatment, partial resection of the two worst ribs and abscess drainage was performed.

Aspergillosis can be seen not only in humans but also in poultry. Particularly, all domestic birds, waterfowl, wild and ornamental birds can be affected by the disease. Young animals are more susceptible to disease, for which infections are acute and severe while the mortality rate is high. In older animals, the disease is characterized by atypical symptoms, and has a chronic and milder course. It has been reported that there occur frequent diarrhea, hair irregularity/loss, and weakening. The prognosis in animals is not known clearly due to inadequate and ineffective approaches in diagnosis and treatment (12,13). It can be transmitted from animals to humans. Although our patient was susceptible to aspergillosis because of his known immune deficiency, the inquiry of home conditions revealed his contact with a domesticated bird at home for a year that had long-term diarrhea and feather loss.

As a result, invasive aspergillosis is most commonly seen in individuals with a suppressed immune system and can be mortal. Considering the differential diagnosis, early and effective treatment is life-saving. While the treatment continues, home conditions and the existence of pets should be questioned. Families with immunocompromised individuals should be advised not to keep pets at home.

Ethics

Informed Consent: The patient's consent and signature were stored with hand writing.

Peer-review: Externally and internally peer-reviewed.

Authorship Contributions

Concept: Ç.A., S.Y., Design: Ç.A., Data Collection or Processing: Ç.A., A.G., S.K., Analysis or Interpretation: A.G., S.K., Literature Search: H.N., Writing: Ç.A., H.N., S.Y.

Conflict of Interest: No conflict of interest was declared by the authors.

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