

Case series

A case series on pulmonary and tissue aspergillosis

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ABSTRACT

Aspergilli species cause opportunistic fungal infection in immunocompromised individuals. Invasive aspergillosis is a highly fatal opportunistic infection that accounts for a major risk to immunocompromised patients. Among these species, *A. fumigatus* is the main opportunistic pathogen followed by *A. niger* and *A. flavus*. In immunocompetent individuals, the effective innate immunity eliminates the inhaled conidia and Allergic bronchopulmonary aspergillosis and aspergilloma are the only infections noted in them. Thus, *A. fumigatus* was considered for years to be an infirm pathogen. With increase in the number of immunosuppressed patients, however, there has been a marked increase in fatal invasive aspergillosis, which is now the widespread mold infection. In this case series, we have described four cases of aspergillosis. Male preponderance is seen, commonly seen in 4th to 5th decade, 3 out of 4 cases are immunocompromised having diabetes, chronic kidney disease, past history of tuberculosis and only one case was not associated with any comorbid illness. In case 4, the recurrence of polypoidal sinusitis itself could be a risk factor causing erosion of nasal mucosa and chronic secretion. The morphological features of intraluminal lesions were of prognostic value. Most of the Aspergillosis patients had a good prognosis with early diagnosis and effective antifungal therapy. It can be deadly if not diagnosed and treated properly. Very rarely aspergillosis may occur in immunocompetent individuals, which urged us to point out these cases. With studies suggesting surging incidence and mortality rates, early diagnosis and treatment are paramount to upgrade patient survival.

Keywords: Sinonasal polyposis; chronic kidney disease; pulmonary tuberculosis; anasarca; polypectomy.

INTRODUCTION

Aspergillus has come up as one of the usual causes of infectious death among severely immunocompromised patients. The mortality rates of 40% to 50% is seen in patients with acute leukemia and hematopoietic stem cells transplantation recipients (HSCTs). Aspergilli are omnipresent in nature. Aspergillosis is caused by inhalation of mycelial fragments or conidia of Aspergillus present in the air, soil or dead and decaying matter. There are around 35 pathogenic Aspergillus species(1). Haematogenous spread of aspergillus leads on to invasive aspergillosis. Some of the risk factors are glucocorticoid use, neutrophil dysfunction, pneumonia, chronic obstructive pulmonary disease, sarcoidosis and tuberculosis patients with weakened immune function or chronic diseases due to AIDS, organ transplantation, chemotherapy or immunosuppressive therapy. *A. fumigatus* accounts for acute pulmonary and allergic aspergillosis and *A. flavus* accounts for hospital acquired infections and is implicated in skin, sinus and ocular infections than *A. fumigatus*. Colonization of upper respiratory tract by *A. niger* causes otitis externa and invasive infection (2).

Design: Retrospective case series

Setting: Tertiary-care hospital

Case 1: A 51 years' old male who is a known case of chronic kidney disease on maintenance hemodialysis presented with breathlessness of 1-month duration associated with orthopnoea, generalized swelling for 1 month, one episode of high-grade intermittent fever associated with chills and rigor and scrotal and penile swelling for 1 month associated with pain and decreased urine output. He is a known alcoholic and smoker. Also, a known case of systemic hypertension on regular medications. On examination, generalized anasarca was present, per abdomen examination revealed collection of free fluid in the peritoneal cavity. Respiratory examination revealed bilateral basal crepitations, scrotal and penile swelling was present on local examination. Bed side USG abdomen showed B/L chronic renal parenchymal disease, B/L moderate pleural effusion, mild hepatomegaly, moderate ascites, diffuse scrotal wall oedema and penile oedema. Screening 2D ECHO showed LVH with pericardial effusion. 5ml of clear serous fluid was aspirated from the right side of the scrotum and fluid was sent for culture and sensitivity. Scrotal fluid was inoculated on SDA and incubated at 25°C. The culture was positive for *Aspergillus terreus*.

Case 2: A 45years' old diabetic female on oral hypoglycemic agents presented to ENT OPD with complaints of recurrent nasal block for 6 months

duration. Patient was apparently normal 1yr back, after that she developed bilateral nasal obstruction which was insidious in onset, gradually progressive in nature aggravated with cold climate and relieved with medications. She also complained of headache on and off over temporal region which was throbbing in nature. Also, gave history of anosmia on and off, recurrent sneezing episode. No H/O epistaxis, post nasal drip, facial pain, nasal discharge, breathing difficulty, throat/ear pain. Systemic examination was normal. Local examination of right and left side of nose showed multiple, pale, glistening polypoidal mass. CT PNS showed bilateral sinonasal polyposis. Endoscopic polypectomy was done. Polypoidal tissue was sent for fungal culture and sensitivity. Tissue was inoculated on SDA and incubated at 25°C. The culture was positive for *Aspergillus flavus*.

Case 3: A 52 years' old male chronic smoker, on oral hypoglycemic agents also an old case of pulmonary tuberculosis presented with complaints of recurrent haemoptysis for 15 days. Cough with expectoration was present on and off for 10 yrs. He completed full course of treatment for pulmonary tuberculosis 10 years back. Systemic examination was normal. Sputum for AFB was negative. CT chest showed Right upper lobe fibrosis with cavitation and patchy nodular opacities were seen. Bronchoscopy was done, tracheobronchial tree was normal. Washings were taken from right upper lobe and sent for CBNAAT, KOH mount and fungal culture and sensitivity. Sample was inoculated on SDA and incubated at 25°C. The culture was positive for *Aspergillus flavus*.

Case 4: A 29 years' old female already operated for left sinonasal polyposis presented to ENT OPD with complaints of left nasal block and discharge for 1 month. Patient was apparently normal 1 month back, then she developed left side nasal obstruction, which was insidious in onset, progressive in nature relieved on medications with hyposmia, snoring, mouth breathing and disturbed sleep. She also complained of mucoid left nasal discharge, whitish color, non-foul smelling and non- blood stained. No complaints of post nasal drip, headache, facial pain, heaviness of head, allergic symptoms, ear block or ear pain. She has past history of endoscopic polypectomy in 2016. Not a known case of diabetes mellitus or hypertension. Local examination of left nose showed a pale polypoidal, greyish white mass completely filling the nasal cavity, insensitive to touch and did not bleed on touch, covered with mucoid whitish discharge. Cold spatula test showed reduced fogging on left side. Cotton wool test showed reduced movement on left side. All baseline investigations done were within normal limits. CT PNS showed left sinonasal polyposis. The patient was diagnosed as a case of recurrent sinonasal polyposis and left recurrent anthrochoanal polyp. Patient underwent left

revision microdebridor assisted endoscopic polypectomy under general anaesthesia on 18.02.2020. Tissue was inoculated on SDA and incubated at 25°C. The culture was positive for *Aspergillus fumigatus*.

DISCUSSION

Aspergillus presents with varied clinical manifestations. The most common primary sites of aspergillosis are lungs, paranasal sinuses, and ear canal (2). It is usually miscounted at first due to its delayed onset and non-specific clinical manifestations (3).

A. terreus is an uncommon fungal pathogen with an aggressive behaviour, and higher mortality rate than other *Aspergillus* species in immunocompromised hosts. *A. terreus* cause infection in humans. Next to *A. fumigatus*, *A. terreus* is the most common cause of IA (4). In a case report by El Saleeby *et al.*, *Aspergillus terreus* was reported in a case of CKD similar to case 1 (5). *Aspergillus* infections of the urogenital tract are very rare (6). In case 1, *A. terreus* was reported in a case of CKD with scrotal swelling who is immunocompromised having diabetes. In a case series by Premamalini *et al.*, *A. terreus* was reported in two cases of *A. terreus* peritonitis and one each of cutaneous aspergillosis and rhinosinusitis among immunocompromised individuals (4). In a study done by Abdelrahman *et al.*, this organism was reported in a case of meningitis in immunocompetent patient (7).

In case 1, commonly 4th decade are affected with male predominance similar to a study done by Akhaddar *et al.*, (8). But in a case report by Kamble *et al.*, paranasal sinusitis by *Aspergillus* species was reported in a 11 year old male (9). In a case report by Humphrey *et al.*, invasive *Aspergillus* sinusitis in human immunodeficiency virus infection was reported in a female patient (10). Aspergillosis is acquired by inhalation of aerosols containing spores, haematogenous seeding and perioperative inoculation in postoperative invasive aspergillosis (1). Patients who undergo multiple instrumentation of urethra due to bladder outflow obstruction are more prone for colonization of *Aspergillus* spores and presence of urinary reflux may lead on to testicular involvement.

Aspergillosis of the paranasal sinuses is infrequent and is usually caused by *A. fumigatus* or *A. flavus* (1). *Aspergillus flavus* was reported in a case of nasal polyp by Sumangala *et al.*, which is similar to case 2 (11). However, there is a difference in the genetic preponderance in both the case reports. In a case report by Taj-Aldeen *et al.*, aspergillosis was reported in a 29 year old woman, unlike case 2 where it is reported in a 45 years' old female (12). In case 2, the patient is immunocompromised having diabetes, whereas in a study done by Anna Maria *et al.*,

aspergillosis was reported in a immunocompetent patient (13).

Pulmonary aspergillosis (PA) is a rare disease (14). In a study conducted in Nigeria, the CPA was found in 14.5% of smear negative TB and HIV-negative patients. Indonesia is leading in the case load of tuberculosis with estimated total TB incidence of 312 per 100,000 population in 2019 with high mortality rates. The total prevalence of CPA was approximately 83,000 with new incidence of 17,561 after pulmonary tuberculosis every year as per the data on TB surveillance from Indonesia (15). In a case report by Nejad *et al.*, it was given that history of treated pulmonary tuberculosis will also be an underlying symptom of opportunistic aspergillosis by *Aspergillus flavus* which is similar to case 3 (16). The genetic preponderance and age group in both the studies are similar.

Both innate immune responses and inflammatory cells limit fungal growth and prevent disease in the majority of individuals. Aspergillosis of the sino-pulmonary tract is relatively a common finding. In case 4, the recurrence of polypoid sinusitis itself could be a risk factor causing erosion of nasal mucosa and chronic secretion as *Aspergillus* cannot penetrate undamaged or intact skin and mucus membrane as it lacks keratolytic enzymes. There is a difference in the age group of the study population between case 4 and a case report by Cagigal *et al.*, (17). Due to non-specific nature of symptoms, the diagnosis is more challenging in immunocompetent hosts. As illustrated in our case, invasive aspergillosis is difficult to diagnose but high index of suspicion made us identify this case. Early diagnosis, steroids, antifungal therapy, surgical debridement along with proper control of the underlying disease indicates successful treatment (18). Early diagnosis is essential to prevent intracranial seeding of the infection.

More meticulous and long-term surveillance may be needed for tracing the changing course of the emerging infections by this mold and early diagnosis is very important in attaining good results. In invasive aspergillosis, amphotericin B is used as the first line of treatment, Combination therapy of voriconazole and echinocandin can be used in salvage therapy (19).

CONCLUSION

In conclusion, the spectrum of Aspergillosis in immunosuppressed as well as in immunocompetent patients is evolving and these trends in the frequency might have implications for the index of suspicion for diagnosis as well as for the choice of empirical and pre-emptive antifungal therapy. Proper identification of molds is more critical for effective early antifungal therapy. In patients with prolonged ICU care, Aspergillosis must be considered as a possible

differential diagnosis, irrespective of the immune status of an individual if they fail to respond adequately to standard treatment.

The limitation of this study is that this was a retrospective case series, bounded by the ingrained deficiencies of the retrospective design.

CONFLICT OF INTEREST

Authors declare no conflict of interest.

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