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A rare case of invasive aspergillosis complicating rapid progressive glomerulonephritis due to microscopic polyangiitis

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CASE STUDY

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ABSTRACT

Invasive aspergillosis (IA) is a known sequel of severe immunosuppression and usually characterized by diagnostic difficulties because of low yield, sensitivity and specificity of positive respiratory culture results. IA is also associated with a mortality rate exceeding 80 per cent even with early detection and aggressive therapy.

Patients on immunosuppressive therapy for microscopic polyangiitis complicated by non-neutropenic sepsis are susceptible to IA. It is a huge challenge differentiating between a vasculitis flare and an invasive fungal infection. Early bronchoscopy for tracheal aspiration is the diagnostic test of choice. It may however be difficult to perform this invasive procedure in an unstable patient. Prophylactic fungal therapy is recommended in patients at high risk.

A high index of suspicion is pertinent as early therapy may still give a slim chance of survival in some patients. Only a few cases of IA complicating microscopic polyangiitis is reported in the literature. However, to the best of our knowledge there is no reported case of a rapid course with multi-organ failure as seen in this patient.

Key Words
Invasive aspergillosis, immunosuppression, anaemia

Implications for Practice:

1. What is known about this subject?
The diagnosis of invasive aspergillosis is a challenge. A high index of suspicion is necessary in patients with atypical risk due to non-specific presentation.

2. What new information is offered in this case study?
Patients on immunosuppressive therapy for microscopic polyangiitis complicated by non-neutropenic sepsis are susceptible to invasive aspergillosis.

3. What are the implications for research, policy, or practice?
Early bronchoscopy for tracheal aspiration is the diagnostic test of choice and early empiric antifungal therapy may be useful.

Background

Invasive aspergillosis (IA) is a sequel of severe immunosuppression and it is characterized by diagnostic difficulties because of low yield, sensitivity and specificity of positive respiratory culture results.[1] IA is also associated with a mortality rate exceeding 80 per cent even with early detection and aggressive therapy.[2,3] It is therefore pertinent to be wary of aspergillosis complicating less known risk factors which is the premise of this case report.

Case details

A 58-year-old male with recent diagnosis of rapid progressive glomerulonephritis due to microscopic polyangiitis was admitted into the intensive care unit (ICU) of our hospital on account of worsening shortness of breath, palpitations and profound weakness. At presentation, he was afebrile, hypotensive and was in atrial fibrillation with rapid ventricular response.

Initial workup revealed severe anaemia (haemoglobin

5.1g/dL), elevated blood urea nitrogen (97mg/dL), elevated serum creatinine (4.3mg/dL), proteinuria, haematuria, leucocytosis without neutropenia and respiratory alkalosis. He had myeloperoxidase positive antineutrophil cytoplasmic antibodies from records from the hospital he was initially treated. A 2.3cm mass-like opacity was seen in the left mid lung on chest X-ray. Bilateral lung masses/infiltrates were seen on chest CT suggestive of vasculitis and possible superimposed chest infection. These are clearly depicted in Figures 1 and 2.

He had been receiving antibiotics, cyclophosphamide and high dose prednisone (70mg daily for about one week) at a different hospital prior to presentation at our hospital.

He was started on amiodarone drip for rate control, broad spectrum antibiotics for hospital acquired pneumonia including fungal coverage as his clinical condition had rapidly deteriorated with associated type 2 respiratory failure. He received caspofungin 50mg intravenous daily maintenance dose empirically because we had a high suspicion of a co-existent fungal infection even though initial fungal cultures were negative. He also had blood transfusion for severe symptomatic anaemia following the recurrence of gastro-intestinal bleeding from pre-existing gastric ulcers. He was also on intravenous protonix 40mg twice daily. The patient was on several vasopressors (levophed drip at 26mcg/min, dopamine @ 45mcg/min and Phenylephrine drip @ 200mcg/min) because of refractory shock. Our patient could not get haemodialysis because of unstable hemodynamics. He was also on mechanical ventilation because of altered mental status as well as worsening respiratory function with progression to type 2 respiratory failure.

Patient had rapid progressive decline in his clinical state with multi organ failure. He died on the 7th day of admission despite aggressive management in the ICU. Repeat blood cultures and tracheal aspirate results came back positive for Aspergillus fumigatus 4 days after the demise of the patient even though initial studies were negative. Autopsy also proved the diagnosis of invasive aspergillosis.

Discussion

Aspergillus is a fungus that belongs to the family of molds referred to as ascomycete.[4] Aspergillus may cause a wide range of pulmonary diseases some of which may be life threatening especially in the presence of underlying lung disease and compromised immune status.[5]

IA was first described in 1953 by Rankin.[4] The incidence of IA is on the increase because of wide spread use of immunosuppressants, chemotherapeutic agents and transplantation.[4,6] Risk factors include prolonged and severe neutropenia, hematopoietic stem cell and solid organ transplantation, advanced acquired immune deficiency syndrome (AIDS) and chronic granulomatous disease.[5] The diagnosis of IA remains a great challenge especially in severely immunocompromised patients. A high index of suspicion is usually necessary in patients with atypical risk as the presentation may be non-specific and may be misconstrued for some other disease process such as pneumonia.[4-7] Diagnosis is also difficult because of lack of clear diagnostic criteria.[6-8] Hence, a holistic approach ranging from radiologic findings to pathologic findings and host's immune state should be considered in entertaining a possible diagnosis of IA.[7,8] In most cases the primary site of infection is the lungs but it may spread and involve several organs.[7,8]

Corticosteroids use at a high dose and for a prolonged period of time is a documented risk factor for IA.[6,7] The mechanism is thought to be the inhibitory effect of corticosteroids on the function of neutrophils, macrophages and lymphocytes in the killing of Aspergillus. Corticosteroid use may also directly stimulate the growth of Aspergillus.[6,7]

Our case had only a short course of high dose steroids and not much has been reported about IA complicating vasculitis on therapy.[9] It is a huge challenge differentiating between a vasculitis flare and an invasive fungal infection being the cause of rapid clinical deterioration as seen in our case presentation. Early bronchoscopy for tracheal aspiration is the diagnostic test of choice.[10] It may however, be difficult to perform this invasive procedure in an unstable patient. Prophylactic fungal therapy is recommended in patients at high risk even if they are not neutropenic as in our case presentation.[11,12]

Therefore, patients on immunosuppressive therapy for microscopic polyangiitis complicated by non-neutropenic sepsis are susceptible to IA. There are a few cases of IA complicating microscopic polyangiitis reported in the literature.[9,11] However, to the best of our knowledge there is no reported case of a rapid course with multi-organ failure as seen in our patient.

Conclusion

Patients on immunosuppressive therapy for microscopic polyangiitis complicated by non-neutropenic sepsis are susceptible to invasive aspergillosis.

The diagnosis of invasive aspergillosis is a great challenge due to the non-specific nature of the symptoms and lack of clinical suspicion in patients without classical risk factors. A high index of suspicion is required as early therapy may still give a slim chance of survival in some patients.

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PEER REVIEW

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CONFLICTS OF INTEREST

The authors declare that they have no competing interests.

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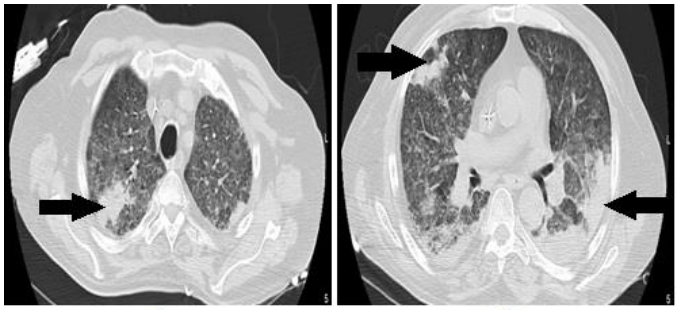
PATIENT CONSENT

The authors, *Paladugu K, Mene-Afejuku TO and Newman TG)*, declare that:

1. They have obtained written, informed consent for the publication of the details relating to the patient(s) in this report.
2. All possible steps have been taken to safeguard the identity of the patient(s).
3. This submission is compliant with the requirements of local research ethics committees.

Figures 1 and 2: Multiple lung masses - neoplastic, inflammatory or infectious process, Interstitial septal thickening



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