Triple infection with invasive pulmonary aspergillosis, pneumocystis jirovecii pneumonia and COVID-19 in a renal transplant recipient

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Introduction-
Immunosuppression secondary to organ transplantation is a major risk factor for severe manifestations of coronavirus disease 2019 (COVID-19). Opportunistic infections of viral, bacterial and fungal origin are more prevalent in immunocompromised hosts. We report a case of a triple infection with invasive pulmonary aspergillosis (IPA), pneumocystis jirovecii(PCJ) pneumonia and COVID-19 in a renal transplant recipient.

Case presentation-
A 27- year-old renal transplant recipient on immunosuppressive medications for 2 years presented with fever, dry cough and dyspnea for 1 day. fever wasintermittent. He denied contact history of COVID -19 or muddy water exposure. His COVID-19 rapid antigen test was positive and was transferred to high dependency unit. His work of breathing was high with an exertional desaturation to 88% from 95% on room air. Rest of the physical examination was unremarkable.

Full blood count revealed a lymphocyte count of 800 x 103/µL, platelet count of 112 x 103/µL and hemoglobin of 13g/L. C-reactive protein was 134g/L and serum procalcitonin was 0.05ng/mL. Chest radiograph showedperihilar opacities without coexisting pleural effusions. Electrocardiogram was normal. Renal and liver functions were normal. High resolution computed tomography of chest reveled ground glass opacities in bilateral perihilar mid and lower zones. Cavitatory nodules, pneumatoceles, pneumothoraces, reticular opacities and tree in bud appearance were absent. Sputum for PCJ in toluidine blue stain was positive. Sputum studies for tuberculosis, bacterial and other fungal infections were negative. Serum galactomannan titer (GM) was 5.9 indicative of coexisting invasive aspergillosis. Serum cytomegalovirus antibodies were negative. Serum lactate dehydrogenase (LDH), ferritin and d-Dimers were 1500U/L, 4516ng/mL and 422ng/mL respectively. Human im-munodeficiency virus antibodies were negative. Due to aerosol generation and high risk of viral transmis-sion, diagnostic bronchoscopy was not done.

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COVID pneumonia was managed with oxygen therapy via face mask. Prophylactic dose of subcutaneous low molecular weight heparin, intravenous dexametha-sone 6mg daily and intravenous ceftriaxone 1g twice daily were commenced. Oral cotrimoxazole 1920mg thrice daily and voriconazole 200mg twice daily were started for PCJ pneumonia and aspergillosis respec-tively. Mycophenolatemofetil was discontinued and tacrolimus dose was reduced. Renal and liver func-tions were closely monitored during treatment. Af-ter 2 weeks patient had a marked clinical improve-ment with reducing oxygen demands. Cotrimoxazole was continued for 21 days while voriconazole was planned to continue for 8 weeks. After 21 days dexa-methasone was converted to maintenance dose of oral prednisolone.

Discussion

Aspergillus species are ubiquitous saprophytes.[1] Al-though COVID-19 lacks neutropenia, immunosup-pression induced by corticosteroids and immuno-modulatory agents plays a role in the predisposition of IPA in COVID-19 infections.[2] The clinical picture of IPA is altered when it is combined with COVID-19. COVID-19 associated pulmonary aspergillosis (CAPA) noted for lack of typical radiological features such as multiple pulmonary nodules with cavitation, ground glass opacities, wedge shaped infarcts due to angio-invasion, air crescents and reverse halo signs. Typical radiology of IPA may be masked due to overlying COV-ID infection and pulmonary infarctions due to throm-bogenicity. CAPA is categorized into “proven”, “prob-able” and “possible” categories based on diagnostic criteria.3 Our patient belongs to “probable” category since he had positive GM with radiological evidence. But he didn’t fulfill histopathological and microbio-logical criteria. Voriconazole is the preferred agent for the treatment of CAPA although amphotericin B is the alternative.

PCJ is a yeast-like fungus which causes pneumonia in immunocompromised hosts. COVID-19 makes a host susceptible to PCJ in multiple ways. COVID-19 induces macrophage dysfunction leading to defective phago-cytosis of PCJ.4 COVID-19 causes severe lymphocy-topenia. Iatrogenic immunosuppression induced by multiple immunomodulatory agents used in COVID-19also contributes. However a significant overlap may occur with COVID-19, making radiological dif-ferentiation difficult.5 This patient had raised LDH. But it is not specific since COVID-19 itself can result in raised LDH. Diagnosis is confirmed by microbiological tests although the results are frequently negative in a majority. Treatment includes a 21 day course of cotrimoxazole with corticosteroids.

Our patient was a renal transplant recipient requiring long term immunosuppression to preserve the graft. Ideal balance should be struck between immunosuppression and infection control, as imbalance of either would lead to loss of graft or morbidity and even mortality. Commencement of multiple nephrotoxic and hepatotoxic drugs simultaneously was also a challenge in this patient.

Conclusion

Opportunistic infections should be anticipated, investigated and treated promptly in immunosuppressed subjects. COVID-19 infection itself predisposes the host for opportunistic infections. COVID pandemic has emerged as the novel threat to organ transplant recipients. Care should be taken in choosing the ideal antimicrobial and immunosuppressive treatment modality.

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