A complicated case of Cryptococcal pneumonia in a renal transplant patient

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Background

Cryptococcal pneumonia is an opportunistic fungal infection seen in immunocompromised patients. Presentation is normally nonspecific with shortness of breath, cough and fever and the most common pathogens are *Cryptococcus neoformans* and *Cryptococcus gattii.* Central nervous system involvement must be determined and anti-fungal treatment is recommended for 6-12 months.

Case

A 42 y/o indigenous woman with a complex medical history was diagnosed with a Cryptococcal lung infection and discharged against medical advice before treatment could be started. She re-presented with unrelated dyspnoea and radiating chest pain that resolved with no significant troponin changes. The patient was admitted to hospital to start treatment for her asymptomatic Cryptococcal lung infection. The chest CT and X-ray showed an increase in density and local inflammation of a round parenchymal density in the upper left lung since the previous admission. Central nervous system infection was excluded and oral fluconazole 400mg daily was started.

Past medical history:

- Kidney transplant secondary to diabetic nephropathy—complicated by delayed graft function and recurrent *E.coli* UTIs
- Type 2 diabetes mellitus—uncontrolled blood glucose levels
- Hypertension
- Hypothyroidism
- Hepatitis B
- Ischaemic heart disease
- Dyslipidaemia
- Hypomagnesaemia
- NSTEACS (2012)

Case Progress

Eight days post admission a follow up X-ray illustrated an increase in lesion size despite anti-fungal treatment. The patients treatment regime was changed to voriconazole 400mg oral twice daily for 1 day then 200mg twice daily as per the infectious disease (ID) team. Bronchoalveolar lavage came back positive for *Cryptococcus gattii*. As her disease had progressed over the two weeks of treatment it was determined that delay in treatment was most likely the cause of lack of improvement than the choice of therapy. Treatment with IV amphotericin B and oral flucytosine was delayed due to the risk of compromising the graft and was initiated on Day 17 due to the severity of the infection.

Complications

- Hospital acquired pneumonia on Day 10 — treated with a 5-day course of ceftriaxone
- Uncontrolled hyperglycaemia throughout admission — daily reviews by the diabetes nurse educator to optimise her insulin regime
- Symptomatic hypoglycaemia with tremors and nocturnal waking to eat to reduce risk of hypoglycaemic attacks — gliclazide was ceased and insulin dose titrated up accordingly

Pharmacist Involvement

- Tacrolimus (CYP3A4 substrate) dose was halved when fluconazole (CYP3A4 inhibitor) was started due to the CYP3A4 interaction — levels continued to be sub therapeutic when voriconazole (strong inhibitor) was started and an increase in dose was recommended with further monitoring
- Atorvastatin (CYP3A4 substrate) was withheld during voriconazole (CYP3A4 inhibitor) therapy due to the CYP3A4 interaction
- Blood pressure was monitored closely due to the potential CYP3A4 interaction between amlodipine (substrate) and voriconazole (strong inhibitor)
- Rounding weight-based doses for amphotericin B vials and flucytosine tablets — 350mg mane and 2250mg twice daily respectively for an approximate weight of 90kg

Case Outcome

The patient was discharged to hospital in the home for continuing amphotericin B infusions and monitoring of her condition. Amphotericin B and flucytosine were concluded after 8 weeks and oral fluconazole 800mg daily was commenced for 8 weeks, then decreased to 400mg daily with the aim of continuing this dose for 12 months. Unfortunately the patient passed away soon after the fluconazole dose was decreased due to cardiac arrest.

Conclusion

Pharmacists can contribute to managing complex infections in transplant patients by carefully monitoring for drug interactions, balancing immunosuppressive therapy and advising on dose changes.

NORTHERN TERRITORY GOVERNMENT