Multiorgan Failure Resulting from Disseminated Adenovirus Infection in a Patient with a History of Mantle Cell Lymphoma on Rituximab

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Refs and COI

INTRODUCTION

- Adenovirus infections are a ubiquitous cause of acute upper respiratory disease.
- Usually self-limited, however in a subset of immunocompromised patients they have been associated with multiorgan failure and death.
- We present a case of multiorgan failure secondary to disseminated adenovirus infection (DAI) in a patient on rituximab.

CASE REPORT

- 75-year-old male with a history of mantle cell lymphoma presented with cough and dyspnea.
- He completed chemotherapy 3 months prior and has been receiving rituximab maintenance therapy since.
- On presentation he was noted to be hypoxic with adenovirus detected on respiratory droplet PCR, chest imaging was notable for bilateral ground glass opacities [Figure 1].
- Initially placed on nasal cannula but was quickly escalated to high-flow and over the first few days of hospitalization he developed hemorrhagic cystitis and elevated liver function tests, leading to concern for DAI.
- Serum adenovirus PCR was sent on hospital day (HD) 5 and detected at 5.7 log copies.
- Over subsequent days he developed ileus, acute kidney injury requiring renal replacement therapy, worsening hypoxemic respiratory failure, and altered mental status.

Figure 1: Timeline of Events

12/10: Saw PCP for lump in neck
12/22: CT 12x6cm conglomeration of lymph nodes
1/4: Mass biopsied, revealed Mantle Cell Lymphoma
1/19: Started C1 chemotherapy with BRCA 500 (Bendamustine, Rituximab, Cytarabine)
6/7: Completed C6 BRCA 500
7/19: EOT PET CT shows CMR
8/26: Maintenance Rituximab started

10/1: Presented to ED, found to be adenovirus positive, placed on 5L and treated with Vancomycin and Ceftriaxone
10/3: Placed on HFNC, Bactrim added
10/4: Pulmonary consulted, dexamethasone 6mg daily started for viral ARDS as well as for possible PJP
10/5: 1,3 Beta-D-Glucan positive, developed hematuria
10/6: Serum quantitative adenoviral PCR sent, steroids held due to concern for disseminated viral infection
10/7: FiO2 increased to 80%, upgraded to ICU, steroids restarted as hypoxic respiratory failure primary issue
10/8: Started on CBI for persistent hematuria, given IVIG
10/9: Creatinine starts to rise
10/11: Increasing abdominal distension, imaging c/w ileus
10/12: CRRT started, adenoviral PCR results from 10/6 at 548,000 copies/mL (5.7 log copies/mL)
10/14: Given Cidofovir and Probenecid
10/15: GCS started to decline, started on vasopressors
10/16: Made DNR/DNI, transitioned from HFNC to BiPAP
10/18: Transitioned to full comfort measures, repeat adenoviral PCR undetectably high (>7 log copies/mL, resulted 4 days after patient passed away)

10/01	10/02	10/03	10/04	10/05	10/06	10/07	10/08	10/09	10/10	10/11	10/12	10/13	10/14	10/15	10/16	10/17	10/18	
0701	0701	0701	0701	0701	0701	0701	0701	0701	0701	0701	0701	0701	0701	0701	0701	0701	0701	
Nasal ...	Non-re...	High f...	High f...	High f...	High f...	High f...	High f...	High f...	High f...	High f...	High f...	High f...	High f...	High f...	Bi-PAP	Bi-PAP	Bi-PAP	Oxygen Device
		60	70	70	45	80	60	60	60	60	70	60	60	65	60	80	80	FiO2
5	15	35	35	35	40	40	40	50	50	60	60	60	60	60	70	45		Flow Rate

Figure 2: Representative CT Slices obtained on admission showing diffuse ground glass opacities with areas of increased focal consolidation

DISCUSSION AND CONCLUSIONS

- DAI is a rare, but likely underdiagnosed, cause of mortality, especially in immunocompromised patients.
- The most frequent manifestations of DAI include pneumonia with acute respiratory distress syndrome, hemorrhagic cystitis, interstitial nephritis, hepatitis, colitis, and encephalitis.
- Mortality is extremely high, up to 83% in immunocompromised patients, and >70% in all comers with significant viremia.
- DAIs are previously well described in stem cell transplant patients where the data suggests that treatment with cidofovir may be beneficial.
- In patients without a history of stem cell transplantation the literature is limited, though IVIG has been used in some case reports with positive outcomes.
- In our patient, IVIG was given on HD 7 after the development of hemorrhagic cystitis raised concern for DAI.
- He failed to demonstrate clinical improvement, however, and on HD 13 the decision was made to give cidofovir despite acute renal failure.
- Unfortunately, he continued to deteriorate and expired on HD 17.
- DAI should be considered in patients with respiratory failure, hemorrhagic cystitis, then progressive multiorgan dysfunction including liver disease, especially when there is an antecedent viral syndrome.
- Serum PCR testing is available, but result time may be prolonged, and therefore should be sent early in the course of illness.
- Unfortunately, the available therapies have unclear efficacy and come with significant adverse effects, therefore mortality remains extremely high.
- Increasing awareness and obtaining timely diagnosis is the first step in identifying patients who may benefit from targeted therapies.