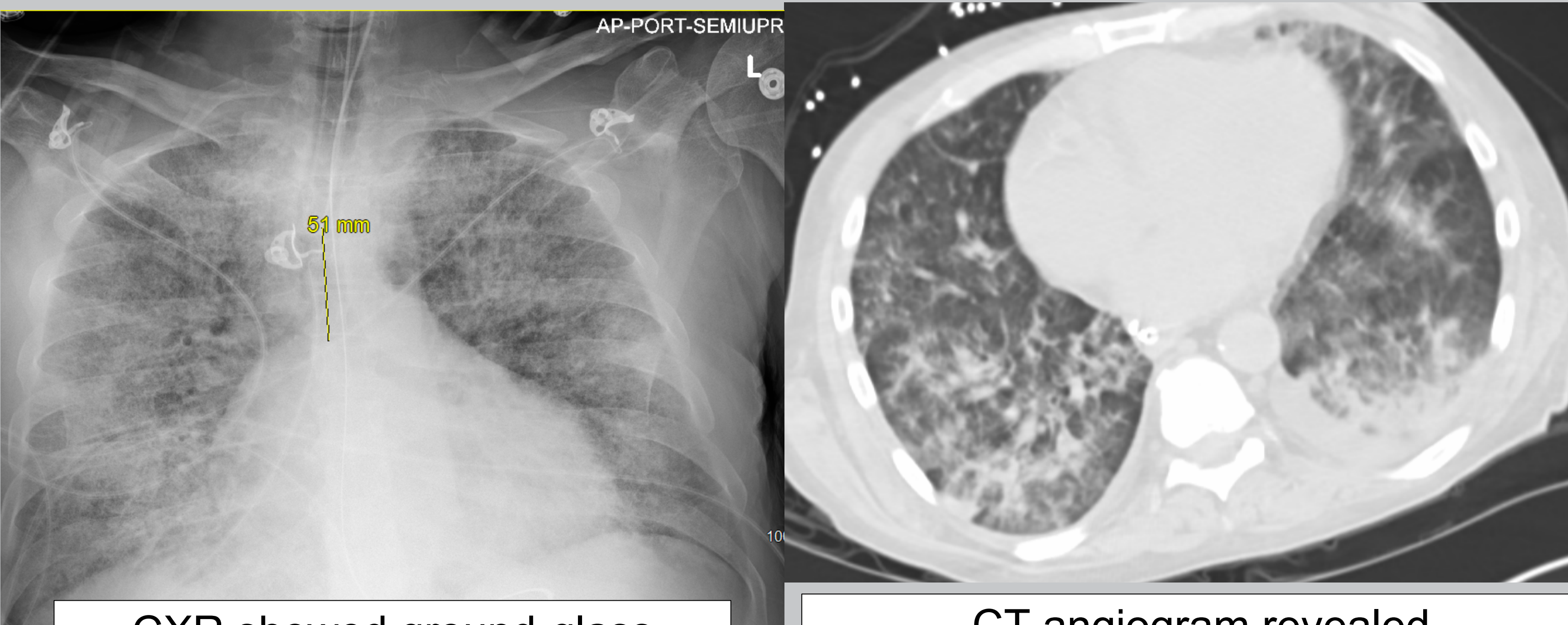


Introduction

- Pneumocystis jiroveci* is a fungus that causes serious pneumonia in immunocompromised individuals.
- Pneumocystis pneumonia (PCP) is most classically associated with AIDS or prolonged steroid use.
- PCP is not typically associated with cirrhosis as a common risk factor.
- We present a case of PCP in a patient with cirrhosis and describe the limited but emerging literature.

Patient Description

|                                    |                                                                                                                                                                                                                                                                                  |
|------------------------------------|----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| Patient: 59-year-old male          |                                                                                                                                                                                                                                                                                  |
| Medical History                    | - Cirrhosis (MELD 30, Child Pugh Class C)<br>- Alcohol abuse (in remission, six months sober at time of presentation)<br>- COPD                                                                                                                                                  |
| Initial presentation               | - Jaundice, ascites, and lower extremity edema without respiratory complaints                                                                                                                                                                                                    |
| Initial Work-up                    | - Labs suggestive of chronic liver failure: total bilirubin of 10.5mg/dL, INR of 2.5, albumin 2.3, AST 54, ALT 20<br>- Positive for spontaneous bacterial peritonitis with neutrophil count of 334 cells/mm^3                                                                    |
| Hospital course                    | - He initially improved clinically on ceftriaxone alone and did not receive steroids.<br>- On hospital day five he developed dyspnea and hypoxia.<br>- Despite broad spectrum antimicrobial treatment, his respiratory condition deteriorated resulting in invasive ventilation. |
| Bronchoalveolar lavage             | Neutrophil predominant WBC count of 410<br>direct smear, culture, and acid-fast bacilli staining were negative<br><i>Pneumocystis jiroveci</i> was detected by PCR                                                                                                               |
| 1,3-β-D-Glucan assay               | Elevated at 373 pg/mL                                                                                                                                                                                                                                                            |
| HIV testing, hepatitis viral panel | Negative                                                                                                                                                                                                                                                                         |
| CD4 count                          | Reduced at 292 cells/mm^3.                                                                                                                                                                                                                                                       |



Outcome

- Treatment with trimethoprim/sulfamethoxazole was not initiated due to severe renal impairment.
- Therapy was initiated with clindamycin and primaquine, but his condition continued to decline ultimately resulting in his passing

Description of cases of Pneumocystis pneumonia in cirrhosis

| Author   | Date | Age/sex | Prior steroid exposure (duration if applicable)         | Etiology of cirrhosis | Additional conditions                                          | Treatment for PCP                                 | Death (y/n) |
|----------|------|---------|---------------------------------------------------------|-----------------------|----------------------------------------------------------------|---------------------------------------------------|-------------|
| Ikawa    | 2001 | 40M     | Y (10 days and 22 days with a 7 day interim in between) | alcohol abuse         | cytomegalovirus pneumonia, esophageal candidiasis, lymphopenia | none                                              | Y           |
| Faria    | 2007 | 44F     | present in 6 of 7 cases (median duration: 16 days)*     | alcohol abuse         | cytomegalovirus isolated in 3 of 7 cases*                      | trimethoprim/sulfamethoxazole (TMP/SMX)           | Y           |
|          |      | 49M     |                                                         | alcohol abuse         |                                                                | TMP/SMX                                           | Y           |
|          |      | 50M     |                                                         | alcohol abuse         |                                                                | TMP/SMX                                           | Y           |
|          |      | 53M     |                                                         | alcohol abuse         |                                                                | TMP/SMX                                           | Y           |
|          |      | 56F     |                                                         | alcohol abuse         |                                                                | TMP/SMX                                           | Y           |
|          |      | 58F     |                                                         | alcohol abuse         |                                                                | TMP/SMX                                           | Y           |
|          |      | 61M     |                                                         | alcohol abuse         |                                                                | TMP/SMX                                           | Y           |
| Dodi     | 2010 | 54F     | Y (9 days)                                              | alcohol abuse         | cytomegalovirus pneumonia, hepatorenal syndrome                | TMP/SMX                                           | Y           |
| Yee      | 2017 | 52M     | N                                                       | hepatitis c           | hepatitis c, lymphopenia                                       | primaquine, clindamycin, corticosteroids, TMP/SMX | N           |
| Hadfield | 2019 | 63M     | N                                                       | alcohol abuse         | COPD                                                           | TMP/SMX                                           | Y           |
| Akhter   | 2020 | 67F     | N                                                       | hepatitis c           | COPD                                                           | steroids, antibiotics (unspecified)               | N           |
| Dugan    | 2020 | 64M     | N                                                       | NASH                  | COPD, lymphopenia, histoplasma capsulatum pneumonia            | TMP/SMX                                           | Y           |
| Chung    | 2020 | 43M     | Y (26 days)                                             | alcohol abuse         | n/a                                                            | TMP/SMX                                           | Y           |
| Meyers   | 2022 | 59M     | N                                                       | alcohol abuse         | COPD, lymphopenia                                              | clindamycin, primaquine                           | Y           |

Discussion

\*Not specified which cases had the exposures and/or conditions

- Despite immunocompromise, PCP is rare; however, there are multiple possible mechanisms to explain why patients with cirrhosis may develop PCP outside of previously described risk factors which include AIDS, prolonged systemic steroids and other immunosuppressive therapies.
  - Decreased hepatic clearance of pathogen associated molecular patterns causes systemic inflammation. TNF-alpha is a key mediator of the initiation of CD4+ cells against pneumocystis. Cytokine dysregulation could contribute to infection.
  - Additionally, decreased immune cell counts likely contribute; this was reflected in our review as lymphopenia was seen in 27% of cases.
- While nine patients received treatment with steroids for alcoholic hepatitis, none of the steroid treatment exposures were significant enough to be considered risk factors for PCP. This implies an innate state of immunocompromise rather than iatrogenic.
- CMV pneumonia was present in three cases, one of which also had esophageal candidiasis, and an additional case had Histoplasma capsulatum pneumonia. These opportunistic co-infections highlight the severity of immunocompromise.
- In conclusion, this case and review are important reminders of the severe immunocompromised state caused by cirrhosis. Opportunistic infections such as PCP should be considered.