A 31 year-old male with history of newly diagnosed Hodgkin’s lymphoma presented with shortness of breath, persistent fever and seizure-like activities. Initial CT scan revealed diffuse lymphadenopathy with normal lung parenchyma. After initiation of chemotherapy, patient developed hypoxia and diffuse interlobular septal thickening on CT scan (Fig. 1). Initial evaluation including bronchoalveolar lavage were unremarkable. Lung biopsy showed non-specific focal fibrosis (Fig. 2). However, further evaluation with immunohistochemistry revealed positive immunostaining for cytomegalovirus (CMV) (Fig. 3). CMV pneumonitis was confirmed with other supportive evidence with viral culture and high serum CMV PCR titer. After an appropriate therapy with Foscarnet, patient was able to wean from oxygen and subsequent CXR showed dramatic improvement after 1 week of treatment (Fig 4).

### Differential diagnosis

Differential diagnosis of ground-glass opacity in patients undergoing chemotherapy are broad, including, but not limited to lymphangitic spread of tumor, infections, pulmonary edema, diffuse alveolar hemorrhage and drug toxicities. Detailed history and careful evaluations are warranted to guide our decision and an appropriate treatment.

SeroLogic evaluation for infection including CMV PCR, EBV PCR, Beta-D Glucan HSV, HZV titer, HIV and cultures should be sent as soon as suspected since they are easy to be obtained and could be monitored for treatment responses.

The patterns of ground-glass appearance (centrilobular vs crazy paving) on CT scan may guide the differential diagnosis.

#### Centrilobular patterns

- **Ground-glass opacity**
- **Hypersensitivity pneumonitis** (environmental, drugs)
- **Nodules**
  - Infectious bronchiolitis (bacterial, viral, fungal)
  - Respiratory bronchiolitis
  - Diffuse panbronchiolitis
  - Milky TB (random)
  - Metastasis (random)
- **Tree-in-bud**
- **Mucus impaction**

#### Interlobular septal thickening

- **Smooth** Pulmonary edema
- **Nodular**
  - Lymphangitic spread of cancer
  - Sarcoïdosis

#### Patterns of CMV pneumonitis

- **Ground-glass opacity**
- **Pneumonitis** (Crazy paving pattern)
- **Alveolar proteinosis**
- **PJP pneumonitis**
- **Pulmonary edema**
- **Alveolar hemorrhage**
- **Adenocarcinoma in situ**
- **Lipoid pneumonia**

### CMV pneumonitis

#### Definition

<table>
<thead>
<tr>
<th>CMV Infection</th>
<th>Definition</th>
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<tbody>
<tr>
<td>Asymptomatic viremia</td>
<td>Virus isolation or detection of viral proteins (antigens) or nucleic acid in any body fluid or tissue specimen regardless of symptoms or signs</td>
</tr>
<tr>
<td>CMV disease</td>
<td>Evidence of CMV infection with attributable symptoms or signs</td>
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<tr>
<td>CMV syndrome</td>
<td>Fever, malaise, weakness, myalgias, and arthralgias, leukopenia, thrombocytopenia without end-organ involvement</td>
</tr>
<tr>
<td>CMV pneumonitis</td>
<td>Upper respiratory symptoms and tissue invasion</td>
</tr>
</tbody>
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#### Symptoms

- Low-grade fever, shortness of breath, nonproductive cough, and changes in measured pulmonary function

#### Diagnosis

1. Bronchoscopy with transbronchial biopsy
   - Identification of CMV inclusions (gold standard)
   - Positive CMV-specific immunohistochemistry staining

2. Qualitative CMV PCR from blood
   - CMV PCR results are often available prior to the biopsy results
   - May influence the decision to initiate antiviral therapy

#### Treatment

- **IV Ganciclovir** 5 mg/kg IV every 12 hours, with dose adjustment for renal dysfunction
- Once the patient has demonstrated clear clinical improvement, IV ganciclovir can be transitioned to oral Valganciclovir.
  - Foscarnet 60 mg/kg IV every 8 hours (severe disease or resistant CMV)
  - Cytomegalovirus immune globulin (Cytosar)

#### Side effects

- Ganciclovir:
  - Severe leukopenia, neutropenia, anemia, thrombocytopenia, panhypopituitarism, and bone marrow failure
- Valganciclovir:
  - Granulocytopenia, anemia, thrombocytopenia, and panhypopituitarism
  - Foscarnet:
  - Nephrotoxicity

#### Conclusion

Timely bronchoscopy with possible transtracheal lung biopsy should be considered before further deterioration of clinical status.