Author's response to reviews

Title: Unsuspected Pulmonary Alveolar Proteinosis in a person with AIDS: A case report

Authors:

Dimple Tejwani (dtejwani@bronxleb.org)
Angel E. DeLaCruz (adelacru@bronxleb.org)
Masooma Niazi (mniazi@bronxleb.org)
Diaz-Fuentes Diaz-Fuentes (gfuentes@bronxleb.org)

Version: 2 Date: 18 May 2010

Author's response to reviews: see over
Dear Editor-in-Chief:

We are enclosing the revised version of the manuscript entitled: Unsuspected Pulmonary Alveolar Proteinosis in a person with AIDS: A case report.

The authors Dimple Tejwani, Angel E. DeLaCruz, Masooma Niazi and Gilda Diaz-Fuentes have revised, read and approved the revised manuscript. The requirements for authorship have been met, and each author believes that the manuscript represents honest work.

Revisions

Response to the comments of reviewer #1:

1- The case report offers a concise synopsis of PAP, despite minor grammatical errors it is easy to read and understand. – All grammar revised. We hope is to your satisfaction

2- Although secondary PAP has been described in association with both HIV and CMV infection the radiological features on CT are very suggestive for Pneumocystis pneumonia, it would strengthen the case if more emphasis was placed on the exclusion of Pneumocystis in this patient, e.g. mentioning that specific stains for P jirovecii were negative on the biopsy specimen. It would be useful to include duration of time on PCP treatment and when the biopsies were preformed. I am unclear if the patient required mechanical ventilation and if he did were high pressures required?

Response : The patient’s condition continued to deteriorate despite treatment. On the third day after admission, he required noninvasive positive pressure ventilation (FiO\textsubscript{2}, 50%) to maintain O\textsubscript{2} saturation at 92%. Because of a persistent air leak, the patient required two chest tubes in each lung, and on day 6 after admission, he underwent bilateral sequential video-assisted thoracoscopic surgery and lung biopsy. The biopsy revealed foamy macrophages, and PAS-
The biopsy revealed foamy macrophages, and PAS-positive, diastase-resistant, and mucicarmine-negative material. *Pneumocystis* organisms were not detected by direct immunofluorescence with monoclonal antibodies. Histopathology revealed CMV inclusion bodies and proteinaceous material filling the alveoli. On day 10 after admission, ganciclovir was initiated and the other antibiotics were discontinued (Figures 3 and 4). The serology test for CMV was positive, and ophthalmology evaluation for CMV retinitis was negative.

3- The most unusual part of this case are the bilateral pneumothoraces and pneumatoceles which to my knowledge have not been previously described in secondary PAP and the authors could have placed more emphasis on this.

Response: A high-resolution CT study reported that secondary PAP was significantly more diffuse than autoimmune PAP. Pneumothoraces associated with secondary PAP have been rarely reported, usually in association with PCP. In addition, a report suggests that emphysematous bullae in patients with PAP could lead to pneumothoraces.

**Response to the comments of reviewer #2:**
There are no time frames given. Please see the revised case presentation. Time frames are provided.

**Response to the comments of reviewer #3:**

I have two concerns about the case presentation that lead to some doubt as to the correct diagnosis and need to be addressed

1) Is the histology obtained from lung biopsy absolutely characteristic of alveolar proteinosis, and could it not be anything else? The lung biopsy figure legend indicates only that the histology revealed “proteinaceous material filling up the alveoli”. Were special stains done to look for, and exclude the presence of, pneumocystis organisms? Were special stains done to look if the material was PAS positive, as it would be with PAP? Were any immunohistochemical stains done?

Response: The biopsy revealed foamy macrophages, and PAS-positive, diastase-resistant, and mucicarmine-negative material. *Pneumocystis* organisms were not detected by direct immunofluorescence with monoclonal antibodies. Histopathology revealed CMV inclusion bodies and proteinaceous material filling the alveoli.

2) It is not uncommon to find CMV in specimens such as lung biopsy where the microorganism may simply be present but not causing inflammation and not contributing to the disease process in any way. Was there any evidence of an inflammatory process in association with the isolated organism, rather than it being simply an "innocent bystander"? Were any CMV serological studies done or CMV viral loads performed? Clearly the presence of the organism in no way
proves that it had any relationship to the presence of PAP
Response: The serology test for CMV was positive, and ophthalmology
evaluation for CMV retinitis was negative. Patient improved with treatment for
CMV

Sincerely yours,

Gilda Diaz-Fuentes, MD, FCCP
Chief Pulmonary and Critical Care Division
Bronx-Lebanon Hospital Center, NY
Address: Pulmonary Division,
1650 Grand Concourse, Bronx, NY 10457
Phone: (718) 466-8160
Fax: (718) 466-8184
E-mail: gfuentes@bronxleb.org