Author's response to reviews

Title: Chlorambucil-Induced cytomegalovirus infection: A case report.

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Version: 2
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Author's response to reviews: see over
Reviewer's report

Title: Chlorambucil-Induced cytomegalovirus infection: A case report.

Version: 1 Date: 24 February 2014

Reviewer: Changlin Mei

Which of the following best describes what type of case report this is?: Unreported or unusual side effects or adverse interactions involving medications

Has the case been reported coherently?: Yes

Is the case report authentic?: Yes

Is the case report ethical?: Yes

Is there any missing information that you think must be added before publication?: Yes

Is this case worth reporting?: Yes

Is the case report persuasive?: No

Does the case report have explanatory value?: Yes

Does the case report have diagnostic value?: No

Will the case report make a difference to clinical practice?: No

Is the anonymity of the patient protected?: Yes

Comments to authors:
This case report described an aged IMN patient receiving CBL treatment underwent a severe infiltrating pulmonary infection, which was suspected as the results of cytomegalovirus infection. The symptoms were relieved well after antiviral treatment.

Several major issues need to be addressed before this paper can be published.
1. Did authors have additional data to support the existence of CMV infection besides PCR? The diagnosis of CMV infection is critical to this case report, and I need to know more evidence of CMV infection such as the antibodies test for CMV, like IgG and IgM; the existence of virus particles confirmed by EM, if available, will be stronger evidence. Additionally, is this a primary CMV infection or reactivation of latent CMV infection?

All patients with a viral load > 20,000 copies/ml (our patient had 31,400 copies/ml) developed CMV disease. Serological test have no role in diagnosing CMV disease in immunocompromised patients. We assumed a primary CMV infection.

2. How did the parameters for CMV infection change after the treatment of antiviral drug? The copies of virus should also respond to the antiviral treatment if the symptoms were really caused by CMV.

Exactly. Viral load suppression during the first several weeks of antiviral therapy, associated with clinical improvement, was observed.

3. What is the purpose of Figure 2 image listed in the end of manuscript? I did not find the corresponding "Fig 2" in the text. By the way, if authors hope to show the lung infection in Fig 2, images from Lung Window setting will better.

The figure 2 corresponds to a thoracic CAT scan taken a month after the admission. It is a mistake we have not eliminate it.

Quality of written English: Needs some language corrections before being published

Declaration of competing interests: I declare that I have no competing interests'
Reviewer's report

Title: Chlorambucil-Induced cytomegalovirus infection: A case report.

Version: 1.Date: 1 February 2014

Reviewer: Markus Gödel

Which of the following following best describes what type of case report this is?: Unreported or unusual side effects or adverse interactions involving medications

Has the case been reported coherently?: Yes

Is the case report authentic?: Yes

Is the case report ethical?: Yes

Is there any missing information that you think must be added before publication?: Yes

Is this case worth reporting?: No

Is the case report persuasive?: No

Does the case report have explanatory value?: No

Does the case report have diagnostic value?: Yes

Will the case report make a difference to clinical practice?: Yes

Is the anonymity of the patient protected?: Yes

Comments to authors:
The authors of "CHLORAMBUCIL - INDUCED CYTOMEGALOVIRUS INFECTION: A CASE REPORT" state that this is the first reported case of chlorambucil induced CMV infection. I think this is an interesting case report, but I have several major concerns regarding the current manuscript.

- There is no diagnostic proof of CMV-pneumonitis. Due to a relevant CMV copy number and a low procalcitonin value it may be a likely diagnosis, but the patient has also been treated with antibacterial,
antimycotic and antipneumocystic medications. Especially Pneumocystis and atypical bacterial infections like Legionella disease may have been possible culprits.

As bronchoscopy was rejected, cytology or immunohistochemical tests were not possible to asses CMV. We used sputum simple to detect cytomegalovirus-DNA using the polymerase chain reaction (PCR). Our mistake is not mention it on the text.

- Hillmen et al. report a positive CMV-PCR in 7,5% of asymptomatic chlorambucil treated patients, so an asymptomatic CMV reactivation may be a common event and may not be related to the pulmonary symptoms in the described patient.

That is true, but our patient improved once the specific therapy for CMV was established and clinical improvement coincided with a decrease in viral load until full recovery, so a CMV infection was supposed.

- Which antibacterial and antifungal drugs have been used for how long? Maybe the clinical course is persuasive for the diagnosis of CMV pneumonitis

Meropenem, Levofloxacin and Caspofungin were initiated at his admission. At the third day, Vancomycin and Ganciclovir were also begun. All antibacterial and antifungal drugs were discontinued when cultures were negative. However, clinical improvement associated viral load suppression was observed, which was persuasive for the diagnosis of CMV pneumonitis

- This is not the first described case of CMV pneumonitis in a patient on chlorambucil and steroids. Yadegarynia et al. already described a case with pulmonary CMV infection diagnosed via pulmonary biopsy.

We appreciate your contribution. We did not know there was another reported case.

- Figure 2 shows a thoracic CAT scan. Is there any information about pulmonary pathologies form this study?

It is an image taken a moth after, which disclose global cardiomegaly and bilateral diffuse interstitial lung disease with a small bilateral pleural effusion in resolution. Anyway, we have removed it.
- Any CRP measurements?
Viral load monitoring with weekly CMV-PCRs was done for four weeks until it was negative.

- Parts of the manuscript are not written in standard english.

Hillmen et al., Journal of Clinical Oncology 2007
Yadegarynia et al., Iranian Journal of Clinical Infectious Diseases 2009;4(4):238-240

Quality of written English: Needs some language corrections before being published

Declaration of competing interests:
I have no financial interests to declare.