Author’s response to reviews

Title: Rapid Diagnosis of Propionibacterium acnes Infection in Patient with Hyperpyrexia after Hematopoietic Stem Cell Transplantation by Next-Generation Sequencing: A Case Report

Authors:

Mingzhi Ye (yemzhina@163.com)
Wei Wei (weiwei3@genomics.cn)
Zhikai Yang (568329311@qq.com)
Yingzhen Li (liyingzhen@genomics.cn)
Shaomin Cheng (chengshaomin@genomics.cn)
Kang Wang (wangkang1@genomics.cn)
Tianliangwen Zhou (408915649@qq.com)
Jingmeng Sun (840796596@qq.com)
Sha Liu (972930260@qq.com)
Na Ni (nina@genomics.cn)
Hui Jiang (jianghui@genomics.cn)
Hua Jiang (weimeitiantang1213@163.com)

Version: 1 Date: 27 Sep 2015

Author’s response to reviews:

In the Case presentation part

1. the author use the phrase "CIS" retinoid acid

   Is this 13-cis-retinoid acid (isotretinoin)? We suggested changed to a common medical phrase with better understanding.

   A1: Thank you for pointing this out. We have corrected it.

2. The author had mention some discrete old rashes on skin. In about 15-20% of patients of JMML are neurofibromatosis which usually carried freckes under arms or in the groin
region. The author should state about the past medical condition. Is the skin lesion as a character of JMML? (discolored but not raise)

A2: Thank you for pointing this out. The old rashes on skin were a character of JMML, which should fade away after chemotherapy. However, our patient’s rashes developed to blacken, which seemed to progress to hyperpigmentation. We considered the possibility of skin infection, although the bacterial identification in the skin lesion was negative. And through the treatment of antibacteria agents, the old rash faded, so we thought that the old rash fading related to the treatment response against infection.

3. Dose the patient had Noonan syndrome which may render a favorable prognosis

A3: Thank you. According to the patient’s symptom and vital signs, we didn’t diagnose he have Noonan syndrome.

4. The author should explain the purpose G test which was target for broad spectrum detection of fungal infection.

A4: As suggested, we have modified this section.

5. The patient was treated with meropenem and vancomycin initially. Are these antibacteria agents for prophylaxis purpose before HSCT as a common regime

A5: Thank you. Because the patient was receiving a myeloablative conditioning regimen and his symptom indicated respiratory infection which might be life-threatening, we chose meropenem and vancomycin to treat him. So, these antibacteria agents before HSCT were not for prophylaxis purpose, but for anti-infective purpose in our case.

6. There is no mention about (capofungin acetate)CAS which appeared on the figure (we suggested added it in the antifungal agent part for detailing.)

A6: Thank you for pointing this out. We have modified it.

7. The author should explain why fever, mild expectoration and some discrete old rashes would make you think of tuberculosis bacillus infection. Is the fever with the characteristic of recurrent spiking fever with poor response to antibiotic use or?

A7: Thank you. During the treatment, several broad-spectrum antibiotics had been used regularly, but with poor response. The patient’s symptoms of fever, chills and cough didn’t lighten. And the chest X-ray images just showed slightly increased lung-markings. So we considered the possibility of occult infection, such as tuberculosis bacillus infection, which was not rare in Chinese. We agreed that the characteristic of recurrent spiking fever indicated poor response to antibiotic use. Therefore, we should switch drugs frequently.
8. We suggested the author to state possible risk factor in this patient as the reason for possible survey including sputum collection and lumbar puncture. Such as HIV? malnutrition? underling malignancy state?steroid use? A8: As suggested, we have modified this section (in page 8).

9. The author had mention about the chest CT change (pneumonia in the posterior basal segment of the lower lobe of right lung) The author should discuss that is the pneumonia predisposed by Propionibacterium acnes or caused by other possible pathogen.

A9: Thank you. Because no positive results were obtained by culture and PCR based methods. And the detection of potential pathogens based on NGS technology showed uniquely corresponding to Propionibacterium acnes (P. acnes), which is confirmed to be the infectious agent by quantitative real-time polymerase chain reaction validation result. It is highly possible that this patient is infected by the opportunistic P. acnes.

9.Did the old rash fading related to the treatment response? Is the rash related to Propionibacterium acnes infection?

A9: Thank you. As been mentioned in A2, The old rashes on skin were a character of JMML, which should fade away after chemotherapy. However, our patient’s rashes developed to blacken, which seemed to progress to hyperpigmentation. We considered the possibility of skin infection, although the bacterial identification in the skin lesion was negative. And through the treatment of antibacteria agents, the old rash faded. So we thought that the old rash fading related to the treatment response and Propionibacterium acnes infection.

10. Acute GVHD usually occur within 100 days after HSCT, is the infection pattern in this case as acute GVHD, please state how to exlude the possibility( normal liver function)

A10: Thank you. In our case, the infection pattern wasn’t acute GVHD because of his normal liver function, proper bowel movement and fading rash.

11. After the complication of GVHD developed, what’s the outcome of the patient( survival or expired due to other complication?)

A11: Due to juvenile myelomonocytic leukemia recurrence, the patient died on July 4th, 2015, which indicating we should pay more attention to infection, GVHD and the other complication in JMML children.

In the figure part:

In the figure 1. We suggested that the author added "day of hospitalization" in the clinical course part which can help the reader better understanding the timeline.

Figure 1: As suggested, we have modified this section.
In the figure 2, We suggested better figure resolution if there is other additional pictures; it will be better to localized the lesion site and the improved lesion site after treatment for better identification if the author failed to provide better picture.

Figure 2: As suggested, we have modified this section. We are sorry for failing to provide better picture.

In the figure 3. We suggested the author reorganized the CXR figure order 2014/06/17 as Panel A and 2014/07/07 as Panel B which better correlated with timeline. The author should stress out the Figure 3D about the CT change in the lung. Why showed the Figure of brain MRI? if there is any positive finding associated with this infection, please state it in the context. If not, please delete the figure.

Figure 3: As suggested, we have Intermodulated position between Panel A and Panel B. We also stressed out the Figure 3C and 3D about the CT change in the lung. Because there was not any positive finding of brain MRI associated with infection, we have deleted the Figure 3E and 3F.