Author's response to reviews

Title: Varicella Zoster Virus infection presenting as isolated diplopia: a case report

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Author's response to reviews: see over
Dear Editor, thank you for the interest in our paper. All reviewers’ comments are interesting, and we hope now the paper is substantially improved, and it is suitable for the publication. Please find below our answers to reviewers’ comments.

Best regards,
Raffaella Piasapia

Answers to reviewers’ comments

Reviewer 1
1. We agree with the reviewer, and we modified the text as suggested (see line 48);
2. We modified the text according to the reviewer’s suggestions (see lines 57, 70, 73, 94);
3. We modified according to suggestions (see lines 101, 111, 131).

Reviewer 2
1. We added details about PCR method, as suggested by reviewer (see line 87-90);
2. We agree with the suggestion, and we added a better clarification of time-line. In particular CSF was taken in 2 occasions, on days 1 and 4 (see lines 64 and 73);
3. The intrathecal anti-VZV antibodies were not investigated, as discussed in lines 116-120.

Reviewer 3
1. The reviewer’s remark is very interesting. We also discussed long time on the same point. In the facts, in our patient it is hard to distinguish among a primary Varicella infection, recurrent Varicella, or recurrent Herpes Zoster, in absence of skin lesions, and in absence of a clear serological marker of previous infection. Indeed, a Complement Fixation Test for VZV resulted negative on day 2. After that the PCR performed on CSF resulted positive for VZV-DNA, with a viral load of 30360 copies/ml, we requested a serology for VZV again, with a different method, on day 12: a Chemiluminescence Immunoassay (CLIA) reported IgG 2883, and IgM negative. This result is in contrast with the Complement Fixation result. Moreover, we are not able to demonstrate an increase in VZV-specific antibodies, because no other IgG and IgM detection are available. Because of these reasons, and given that serological testing alone without other virological tests has no value in the diagnosis of VZV infection (see new reference 2, but also Gilden et al, Current topics in Microbiology and Immunology 2009), we decided to not include the CLIA in the report, and preferred the general term “VZV infection”;
2. We agree with the reviewer, and we modified the sentence accordingly (see line 34);
3. We do not agree with reviewer’s comment. Indeed, the distribution of neurological manifestations is similar in primary infection and in reactivations. We added a citation (Koskiniemi et al) where 174 patients, with chickenpox, shingles, or no rash, were described. In this paper, no significant differences are reported in neurological manifestations;
4. We agree with the reviewer that the sentence is unclear, and we modified it (see line 46);
5. We are grateful to the reviewer for the suggestion. We performed the search as suggested, and we found some other case reports, but no substantial contributions to our paper, because the most
relevant articles were already retrieved with initial search, or through the check of bibliographies. Anyway, we changed the method section accordingly (see lines 52-53);
6. The diplopia was isolated, while the syndrome occurred seven days before was very unspecific, and described in lines 59-60;
7. We added normal values where appropriate, according to the reviewer’s suggestion;
8. Please see answer to comment 1 of the reviewer 3.