Author's response to reviews

Title: Gardening can affect your lungs- Aspergillus ARDS in an immunocompetent patient

Authors:

Nina Jung (jungnin@med.uni-marburg.de)
Silke Mronga (mronga@med.uni-marburg.de)
Susanne Schroth (schroth@med.uni-marburg.de)
Timon Vassiliou (Timon.Vassiliou@med.uni-marburg.de)
Frank Sommer (sommerf@med.uni-marburg.de)
Eduard M Walthers (walthers@med.uni-marburg.de)
Christian Aepinus (aepinus@staff.uni-marburg.de)
Andreas Jerrentrup (jerretr@med.uni-marburg.de)
Claus F Vogelmeier (vogelmei@med.uni-marburg.de)
Angelique Holland (holland@med.uni-marburg.de)
Rembert Koczulla (koczulla@med.uni-marburg.de)

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Author's response to reviews: see over
Dear editor, dear reviewers!

Thank you for the constructive critical appraisal of our manuscript. We appreciate the extensive effort that has been made. In the following, we provide a one-to-one reply.

Reviewer 1:

This is a case report of a severe lung infection attributed to Aspergillus fumigatus. It is an interesting case. My only comment is that a Minor Essential Revision should be performed: The manuscript must be corrected by an English speaking person because there are many language mistakes.

Thank you very much. A native speaker corrected the manuscript.

Reviewer 2:

I carefully read the case report and I think that, although interesting, it is not clear and acceptable for publication in its present form. In particular, the final diagnosis is not clear to me: the authors conclude that the patient suffered from Aspergillus sepsis (which is really uncommon!!), while reported diagnostic tests are consistent with Aspergillus pneumonia.

Thank you very much. In the present case, we saw a patient who suffered from proven pneumonia (clinics, chest x-ray, CT scan). We found Aspergillus in BAL fluid of the patient, galactomannan test on blood was positive. We did not perform galactomannan test on BALF. The patient fulfilled all the criteria for septic shock: SIRS, pneumonia, refractory hypotension[1]. Beside the aspergillus, we could not detect other microbes that caused the septic situation. We added a sentence to the manuscript.

Furthermore, when talking about a potential relationship between gardening and Aspergillosis, the variable “time” is essential: a long term exposure to spores due to working or hobbies is more reasonable than a single exposure (like that one reported in this paper).

We fully agree that in the context of gardening a long-term exposure to Aspergillus is more likely than a single exposure. However, long-term exposure to the spores (from a clinical point of view) would be more likely to be associated with allergic disease. Since the patient suffered from severe Aspergillus pneumonia, we would like to assume that there might be a "single" exposure to Aspergillus (for example, during the regrouping of the bark chip mulch). However, long-term exposure (or multiple exposure) to spores cannot be excluded in the case described herein, the infection/colisation/exposure being controlled by the immune system for a certain time and finally leading to pneumonia for unknown reasons.

A possible higher susceptibility based on literature data and the history of the patient was discussed. Smoke and second-hand smoke might be a factor which increases susceptibility of aspergillus infection[2]. We included a part in our discussion section.
Other Major Compulsory Revisions

1) Line 56: why the first reference cited is reference number 3?
   Thank you, we restructured reference list.

   However, the article is about a single case report: this is very far from “demonstration”.
   I don’t agree with the first sentence, that should be rewritten in the sense of a “possible
   and hypothetical correlation” between gardening and aspergillosis risk.
   Thank you. We replaced the phrase “it was demonstrated” with “it was hypothesized that
   there might be a possible correlation.”

2) Several data are missing: drug dosages, treatment duration, etc.77
   Thank you. We added missing drug dosages and treatment duration.

3) Was galactomannan test on blood? Did they have the test performed on BAL?
   We found Aspergillus in BAL fluid of the patient. galactomannan test on blood was positive.
   We did not perform galactomannan test on BALF.

4) What about sensibility test? How can they prove that the good results were due
to the combination caspo+vorico? I would like to see the MIC results. How long
did they treat the patient with vorico alone?
   No susceptibility testing of the isolates was performed. In 2013, the susceptibility of
   Aspergillus isolates was not routinely analyzed by our laboratory. Furthermore, according to a
   study performed by the Robert Koch Institute Berlin[3], resistance to voriconazole in clinical
   isolates of Aspergillus fumigatus was as low as 0,9% in Germany. Therefore, it is quite likely
   that the isolate was susceptible to voriconazole. Of cause, we cannot prove that the clinical
   cure/success described herein is related to the combination therapy. However, a recent, as yet
   unpublished randomized trial showed a trend toward improved six-week survival with the
   combination of voriconazole and anidulafungin compared with voriconazole monotherapy in
   invasive aspergillosis[4].

5) Lines 98-99: the expression “to treat aspergillus” is not appropriate: this is not a
target therapy. Is it empirical? Pre-emptive?
   Please excuse the imprecise explanation. We corrected it to “Without initial proof, we started
   empirical antifugal treatment.”

6) Did they have any other isolates (including bacterial) from BAL?
   That is an important point. Thank you for mentioning it. No bacteria were cultured from the
   BALF. We included a sentence in the case presentation.

   Douglas IS, Jaeschke R et al: Surviving Sepsis Campaign: international guidelines for
   228.
2. Zmeili OS, Soubani AO: Pulmonary aspergillosis: a clinical update. QJM 2007, 100(6):317-
   334.