Author's response to reviews

Title: Persisting right sided chylothorax in a patient with chronic lymphocytic leukaemia: a case report

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Author's response to reviews: see over
Re: Revised Manuscript. “Persisting right sided chylothorax in a patient with chronic lymphocytic leukaemia: a case report”

Dear Madame, dear Sir,

Please find enclosed our revised manuscript. We have addressed all comments raised by the reviewers. As mentioned in your e-mail the patient’s ethnicity has been included in the abstract and in the case presentation section. The language has also been revised as suggested. All changes are listed in the point-by-point response below.

We feel that our manuscript especially the Discussion section has been improved by these changes and hope that you might find it acceptable for publication.

Sincerely Yours

Bernd Spriewald
Reviewer #1

1. Other cases of CLL/lymphoproliferative disease + chylothorax have already been reported in the English literature. Considering the rarity of this association, a review of the described cases, evaluating the eventual differences in diagnosis, therapy and evolution, would be very interesting and it would improve the quality of the discussion section.

As suggested by the reviewer the previous cases of chylothorax in CLL patients have been discussed more intensely.

On page 7 line 10 the following passage has been included: “…replacing the normally present T-cells. This is in accordance with findings of two previous cases reported by Doerr et al. and Zimhony et al. [11, 12], whereas Rice et al. found predominantly T-cells in the chyle of their CLL patient [6]. Therefore immunophenotyping of chyle may have limited value in diagnosing chylothorax in CLL patients. …”

On page 9 line 5: “A similar observation was reported by Zimhony et al. [12]. The chylothorax of their patient with CLL did not improve after chemotherapy and mediastinal irradiation and required pleurodesis to resolve pleural effusion. However, mediastinal irradiation can be effective in CLL associated chylothorax, as demonstrated by Ampil et al., who reported of a female CLL patient developing chylothorax under continuous treatment with chlorambucil and prednisone. Following mediastinal irradiation with 1000 cGy over 5 days the chylous effusion resolved during the nearly five years of follow up [17]. “

On page 9 line 15: “One other case of CLL associated chylothorax, reported in the literature had also received successful ligation of the thoracic duct, albeit in combination with pleurodesis [11]. Despite her age of 93 years the patient recovered well after surgery, indicating that thoracic duct ligation is well tolerated.”
On page 9 line 25: "Another therapeutic option for chylothorax is pleurodesis. Mares and colleagues reported a case series of talc pleurodesis for chylothorax caused by lymphoma including one patient with CLL and colon carcinoma. In contrast to our case the patients in their series had end stage lymphoma. Although the CLL patient was not specifically pointed out, pleurodesis was described as successful in all cases. However, a high short term mortality due to the underlying disease was noted [19]. Similarly the CLL-patient reported by Rice et al., who was treated symptomatically by repeated thoracentesis and total parenteral nutrition died shortly after developing chylothorax [6]. Also the CLL patient reported by Aranda et al., who was started on chlorambucil and prednisone for CLL treatment and repeated thoracentesis after developing chylothorax, died shortly thereafter [20]. This indicates that CLL patients developing chylothorax late in their disease course may have a limited prognosis. Whether the prognosis for these patients might improve with modern immuno-chemotherapy remains to be seen. It is also interesting to note, that patients with a longer reported survival had either successful thoracic duct ligation, mediastinal irradiation or pleurodesis [11, 12, 17]. In our opinion this allows the conclusion that definitive resolution of the chylothorax should be aimed for. “
Reviewer #2

1. Unclear abstract: First-line treatment consisted of conservative treatment in addition to four cycles of an immuno-chemotherapy. What does it mean? It need to be divide in CLL treatment and chylothorax treatment.

As suggested by the reviewer, in the Abstract the initial therapy has been described in more detail. On page 2 line 7 “First-line treatment consisted of conservative treatment in addition to four cycles of an immuno-chemotherapy consisting of fludarabine, cyclophosphamide and rituximab.” has been changed to

“As first line treatment four cycles of an immuno-chemotherapy consisting of fludarabine, cyclophosphamide and rituximab were administered. In addition, the patient received a total parenteral nutrition for the first two weeks of treatment. …“

2. “Since chylothorax is an overall infrequent condition the best therapeutic approaches is still under debate [1, 5, 7, 8]. In particular in lymphoma associated chylothorax the impact of modern immuno-chemotherapy including the anti-CD20 antibody rituximab is not yet established. “

Chylothorax and CLL is very rare condition and there is not possibilities to make estimation of impact of any type therapy.

We agree with the reviewer that due to the rarity of chylothorax in CLL a statistical assessment of the various therapeutic options for chylothorax or a randomised study is not feasible. Since the reviewer objects to the term “the impact of modern immunotherapy is not yet established” the sentence “… In particular in lymphoma associated chylothorax the impact of modern immuno-chemotherapy including the anti-CD20 antibody rituximab is not yet established. …” (page 3 line 17) has been changed to

“… In particular in lymphoma associated chylothorax the use of modern immuno-chemotherapy including the anti-CD20 antibody rituximab has not yet been described. …”
3. In the manuscript You wrote anti lymphoma therapy. It is not anti lymphoma therapy. It is standard CLL therapy. Also, You can calculate Cumulative Illness Rating Scale for patients

Chronic lymphocytic leukaemia is a non-Hodgkin’s lymphoma. The term anti lymphoma therapy has been used to indicate that the findings of our case report may also be of value for other non-Hodgkin's lymphoma, since FC-R is also used in follicular lymphoma for example. However, as the reviewer indicated the term anti-lymphoma therapy may be misinterpreted and has therefore been removed.

On page 8 line 20 and 24 the term “anti lymphoma therapy” has been changed to “immuno-chemotherapy” and on page 9 lines 5 and page 10 line 21 into “anti-CLL therapy”.

The Cumulative Illness Rating Scale mentioned by the reviewer is generally used to integrate comorbidity into clinical studies. On an individual basis it might be helpful in therapeutic decision making. However, we feel that this index will not add additional information in the current case presentation.

4. Discussion need to be more dedicated to compare results of other authors who described CLL and chylothorax. Their therapeutic approach and results what is different? You can briefly describe theoretical part of chylothorax.

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