Author's response to reviews

Title: Immunohistochemical investigations in an uncommon variant of scleromyxoedema: Case report

Authors:

Frank Breuckmann (Frank.Breuckmann@ruhr-uni-bochum.de)
Marcus Freitag (M.Freitag@derma.de)
Sebastian Rotterdam (S.Rotterdam@derma.de)
Markus Stuecker (M.Stuecker@derma.de)
Peter Altmeyer (P.Altmeyer@derma.de)
Alexander Kreuter (A.Kreuter@derma.de)

Version: 2 Date: 1 July 2004

Author's response to reviews: see over
Dear Ladies and Gentlemen

Thank you for the email containing questions, comments and critical remarks regarding our manuscript. We have incorporated the reviewers’ recommendations in our manuscript and would like to submit a revised version of our consideration for publication in your journal.

We would like to address the reviewers’ comments point by point.

Reviewer # 1 (R. Dawe):

1. The reviewer remarked that the title accurately reflects the main focus of your case report on the immunohistochemical investigation results. Nevertheless he wondered whether it was worth also addressing treatments in slightly more detail and modifying the title to make it clear that treatments, as well as investigations, are discussed? According to the reviewer's request we revised our title of the manuscript to „Immunohistochemical investigations and introduction of new therapeutic strategies in scleromyxoedema: Case report“.

2. The reviewer wondered whether a table summarising the treatments previously reported (including numbers of patients treated and a summary of results) could usefully complement
the text. Unfortunately, although we included reference 16 (Krasagakis, et al.) in our first version ECP seems to be missing from our list.

In order to avoid wasting space, we propose not to recite data given in the text within an additional table. Nevertheless, we completed the list of previous therapeutic approaches within the conclusion section integrating ECP by Krasagakis et al.

3. The reviewer would consider shortening those aspects of the conclusions which essentially repeat what we have reported under results. He thinks the report would be enhanced if under conclusions we concentrate more on our hypotheses.

According to the reviewer’s comment, we shortened the corresponding aspects within the conclusion section and tried to include more details about theories of aetiology, pathogenesis and choice of treatment.

_Reviewer # 2 (P. Terheyden):_

1. The reviewer remarked that our case might represent a typical case of scleromyxoedema (distribution, firm papules and stiffness of skin) and that we should eliminate all phrases like “uncommon variant”, “lichen myxoedematous”, etc.

   Following the reviewer’s request we changed the corresponding phrases of our manuscript, even though ‘more typical’ forms of scleromyxoedema were given in the literature.

2. The reviewer remarked that the authors should be aware of the fact that scleromyxoedema has an unpredictable course hampering all analyses and studies published so far. The continuous deterioration before MTX cannot be proved and stabilisation of disease would be a success. Therefore, “therapy-resistant” is not the adequate term and is confusing.

   The course of scleromyxoedema seems to be unpredictable and even spontaneous remission has been described. Our patient experienced a chronic progressive course for more than two years. Even though we cannot ensure continuous clinical deterioration, at the time of the initiation of therapy, there was no hint for a beginning stabilisation or even improvement of symptoms. However, we deleted „therapy-resistant“ from our manuscript and added clinical history as mentioned above.

3. The reviewer criticised that although impressing, unless serial documentations of dermal thickness were obtained, ultrasound imaging is not necessary to be illustrated by a separate figure. Could the subjective impression of amelioration be confirmed by ultrasound (reduced thickness, altered dermal echogenic pattern)?

   Unfortunately, subjective impression of amelioration could not be confirmed by means of ultrasound measurement. We added that fact to our manuscript and deleted ultrasound imaging as a separate figure.
4. The reviewer remarked that representative stainings of immunohistological investigation should be illustrated together with a detailed methodological description and at least the accumulation of MIB1+ and tryptase+ cells in mucinous deposits must be given and data should be discussed, e.g. mast cells are suspected to play an important role in many mucinoses together with activated fibroblasts. The reviewer stated that a longitudinal analysis of immunohistological findings before, during and after treatment would be extremely interesting. According to the reviewer’s request we added immunohistochemical illustrations of MIB-1 and tryptase stainings and an additional reference. Unfortunately, we were not able to provide a longitudinal analysis of the different stainings due to missing consent of the patient to perform additional experimental biopsies. However, we added this information within the conclusion section of our manuscript.

Reviewer #3 (K. Krasagakis):

1. The reviewer remarked that it is not clear why the case represents an uncommon variant of scleromyxoedema. 
   Please refer to reviewer #2, remark 1.

2. The reviewer remarked that Figure 2 is not necessary. Findings of ultrasonography are presented sufficiently otherwise in the paper.
   Please refer to reviewer #2, remark 3.

3. The reviewer remarked that immunohistochemical findings and methodological descriptions should be shown in a greater extend, since this has been suggested as a major point of the paper, and that it is preferable to demonstrate some of the findings of the immunohistochemistry as figure, especially those related with mast cell tryptase and Ki-67. According to the reviewer’s request, we integrated extensive methodological descriptions and tried to precise the histological findings within the case presentation of the revised version of our manuscript. For histological figures please also refer to reviewer #2, remark 3.

4. The reviewer remarked that the paper could also gain in quality, if it could be provided a stain for B cells in the inflammatory infiltrate, or a stain for kappa chains. Following the reviewer’s request, we performed additional B cell immunostaining of the corresponding sections and completed the results/conclusion and tables.

5. The reviewer criticised that the authors should not use abbreviations for the description of the findings of serum electrophoresis. Following the reviewer’s request, we avoided abbreviations in the description of serum electrophoresis results.
6. The reviewer wondered whether we could better describe the findings of blood smear cytological evaluation and the reactive lymphoid infiltration providing evidence for MGUS. According to the reviewer’s request, we gave further descriptions of the above-mentioned laboratory examinations. Blood smear cytological evaluation revealed beginning qualitative but still no quantitative changes as defined by leukocytic aberrations pointing towards a leftward shift. Bone marrow biopsies displaying reactive lymphoid infiltration including minimal extension of plasma cells with monoclonal immunoglobulin production provided evidence for monoclonal gammopathy of undetermined significance (MGUS) without distinct morphological characteristics of a plasmocytic plasmocytoma or plasmoblasts.

7. The reviewer remarked that phrases such as "stable clinical outcome without improvement", "insufficient low dose methotrexate" or "our patient experienced an adequate acceptance" or "no further improvement could be evaluated while skin status appeared to be stable", "to interrupt the obvious therapy-resistant potency of this interesting case" need to be improved. Following the reviewer’s remark we replaced imprecise phrases by more specific descriptions throughout the manuscript.

We are thankful for the reviewers’ critique. The commentary has helped us to improve our manuscript substantially. We therefore anticipate that you will find the revised version acceptable for publication in your widespread journal.

Yours sincerely

F. Breuckmann et al.