Reviewer's report

**Title:** Amyotrophic Lateral Sclerosis-Motor Neuron Disease, Monoclonal Gammopathy, Hyperparathyroidism, and B12 Deficiency: A Case Report and Review of the Literature

**Version:** 1 Date: 23 January 2010

**Reviewer:** Prell Tino

Which of the following best describes what type of case report this is?: New associations or variations in disease processes

Has the case been reported coherently?: Yes

Is the case report authentic?: Yes

Is the case report ethical?: Yes

Is there any missing information that you think must be added before publication?: Yes

Is this case worth reporting?: No

Is the case report persuasive?: Yes

Does the case report have explanatory value?: No

Does the case report have diagnostic value?: No

Will the case report make a difference to clinical practice?: Yes

Is the anonymity of the patient protected?: Yes

Comments to authors:

This paper by Rison and Beydoun presents a patient with a possible motor neuron disease, vitamin B12 deficiency, monoclonal gammopathy and hyperparathyroidism. Afterwards in a review of the literature the correlation and meaning of these diseases is discussed. The rationale for this consideration is to search for alternative and treatable diagnoses in patients with potential amyotrophic lateral sclerosis (ALS). The authors provide interesting informations with relevance for clinical daily routine. With a few exceptions the paper is fairly well written.

Case report

- The nomenclature of hematological diseases should be worked out more
carefully. Lymphomas like the multiple myeloma and its pre-stage the monoclonal gammopathy of undetermined significance (MGUS) do not belong to myeloproliferative disorders. Myeloproliferative neoplasms (MPNs) include chronic myelogenous leukemia, polycythemia vera, essential thrombocythemia, primary myelofibrosis, chronic neutrophilic leukemia, chronic eosinophilic leukemia/hypereosinophilic syndrome and mast cell disease. MPNs can be diagnosed by morphological aspects, cytogenetics and fluorescence in situ hybridization in blood and bone marrow. They cannot be ruled out by immunofixation (page 4, line 16; page 9, line 4; page 11, line 7-8). The serum protein electrophoresis with immunofixation are useful to rule out multiple myeloma or MGUS.

- A normochromic normocytic anemia is a possible, but untypical symptom of vitamine B12 deficiency. Were other reasons for anemia ruled out, like neoplasm, which can be associated with MND? What is the reason of vitamin B12 deficiency? Was a gastroscopy made? How was the methylmalonic acid level?

- The neurologic examination is described very well. There is no sign of upper motor neuron involvement. May be one sentence to classificate the patients symptoms according to the El Escorial criteria would be helpful.

- What is the explanation of hyperparathyroidism and normal calcium level in this patient? Was the kidney function normal? Allthough abnormalities in vitamin D levels in ALS were discussed (at page 14), there is no further information about 25-hydroxy vitamin D level in the case report. Detailed information would clarify the recommendation for a parathyroidectomy.

- At the end a summarized statement would be useful in order to make clear which symptoms can be attributed to a possible MND or which could be caused by vitamin B12 deficiency, hyperparathyroidism and monoclonal gammopathy.

Literatur review:
The literature review includes a lot of interesting facts and details about the correlation between MND and vitamin B12 deficiency, monoclonal gammopathy and hyperparathyroidism. I suggest to substantiate the clinical importance of listed facts in detail instead of copying text passages from several abstracts (e.g. page 10, line 8-10 is a copy of the abstract from the italien paper of Saverio et al.; page 11/12, line 23-24/1-6 is a copy of the abstract from Rudnicke et al.; page 12, line 11-15 is a copy of the abstract of the Japanese paper from Saito et al.. Et cetera on the following pages.

Minor points:
- page 6, line 6: “lambda” instead of “lamba”
- page 6, line 6: Detection of IgG lambda does not mean monoclonal gammopathy. Was the immunofixation positive? What is the Kappa/Lambda quotient?
- page 6, line 9: “Erythrocyte sedimentation rate was slightly elevated .. but an antinuclear antibody screen was negative.” What is the causal relationship between these two facts? Is it not more probable that erythrocyte sedimentation
rate is enhanced because of anemia or monoclonal gammopathy?

- page 7, line 9: “revealed active” instead of “revealed Active”
- page 9, line 12: They are also classified as IgE and IgD.
- page 10, line 18: The nomenclature of lymphomas should be used more correctly. The myeloma and macroglubinemia (Waldenström) are non Hodgkin lymphomas.
- page 11, line 1: “highlite” instead of “hi-lite”
- page 11, line 7: Which kind of monoclonal gammopathy can be found in ALS? Malignant or nonmalignant? A malignant monoclonal gammopathy is a feature of lymphoproliferative disease and not of myeloproliferative neoplasms. Nonmalignant monoclonal gammopathy can also be associated with liver diseases, inflammation or chronic lymphatic leukemia.
- page 11, line 23: “Rudnicki” instead of “Rudnicke”
- page 14, line 15: “were” instead of “was”
- page 16, line 12: “of” instead of “if”
- abbreviations like ALS, MND should be used continuously in the text; e.g. page 10, line 16: MND instead of “motor neuron disease”; LPD instead of “lymphoproliferative disease”, and so on page 8, 11, 12, 13, 14 …

Quality of written English: Acceptable

Declaration of competing interests:

I declare that I have no competing interests.