Reviewer's report

Title: Case report Erythromelalgia: An Egyptian case report with a new line of treatment and literature review

Version: 3 Date: 7 September 2013

Reviewer: Stephen Waxman

Which of the following following best describes what type of case report this is?: Other

If other, please specify:
report of new purported response to therapy, anecdotal

Has the case been reported coherently?: No

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?: Yes

Is the case report persuasive?: Yes

Does the case report have explanatory value?: No

Does the case report have diagnostic value?: Yes

Will the case report make a difference to clinical practice?: No

Is the anonymity of the patient protected?: Yes

Comments to authors:

Does the case report have explanatory value? It does not provide new insights into pathophysiology. It does present a clear picture of this disorder from clinical perspective.

Does the case report have diagnostic value? Yes, for clinicians who have not seen this disorder.

Will the case report make a difference to clinical practice? Not Clear, anecdotal
Comments to authors:

This article makes an interesting observation. The report is of course anecdotal and should be more clearly labeled as such. The manuscript should be revised as follows:

--1. The article describes anecdotal observations on a single patient (n=1). Chance association of a waxing-waning clinical course or a placebo response can not be ruled out. This must be more explicitly noted in the Abstract and main text.

--2. Moreover, it is not clear whether the apparent response to treatment will be durable over years, or if the patient will relapse. This should be more clearly noted.

--3. The statement that this is the first case of primary EM presenting at age 3 or earlier is not true. The following cases or families include onset at age 3 or less, and should be cited:


-4. Many more Nav1.7 mutations than described in this paper as submitted have been linked to EM. The authors can go the literature and describe them all, or cite this review which lists all of them:


-5. The discussion should point out that some rare pts with EM respond well to treatment with carbamazepine, and their mutations have been shown the sensitive the Nav1.7 channel to this drug (Fischer, T.Z., Gilmore, E.S., Estacion, M, Eastman, E, Taylor, S, Melanson, M, Dib-Hajj, S, Waxman, S.G., A novel Nav1.7 mutation producing carbamazepine-responsive erythromelalgia. Ann Neurol, 65:733-741, 2009). Recent studies have indicated that it is possible to predict the response of patients with EM to treatment with sodium channel blockers on the basis of atomic-level structural modeling (Yang, Y., Dib-Hajj, S.D., Zhang, J., Zhang, Y., Tyrrell, L., Estacion, M., and Waxman, S.G. Structural
modeling and mutant cycle analysis predict pharmacoresponsiveness of a NaV1.7 mutant channel, Nature Comm., 3: 1186, 2012), raising the possibility that, in the future, it may be possible to genotype patients with EM, and prospectively predict the response to various drugs via pharmacogenomics.

**Quality of written English:** Acceptable

**Declaration of competing interests:**

I declare that I have no competing interests