Reviewer's report

Title: Pseudo - subarachnoid haemorrhage due to chronic hypoxaemia: Case report and review of the literature

Version: 2
Date: 9 September 2014
Reviewer: Nina Tsakadze

Reviewer's report:

Thank you for the invitation to review the manuscript "Pseudo - subarachnoid haemorrhage due to chronic hypoxaemia: Case report and review of the literature" by Maximilian Patzig, Christoph Laub, Hendrik Janssen, Lorenz Ertl and Gunther Fesl.

The subject of pseudo-SAH is important as head CT is typically the very first imaging test performed in patients with acute onset of headache, and SAH is certainly on top of differential in such cases. Pseudo-SAH is a phenomenon observed on CT head in which cisterns and sulci appear to be hyperattenuated relative to brain parenchyma giving radiographic appearance of the SAH in the absence of blood in subarachnoid space. The condition was first described by Spiegel et al (Can Assoc Radiol J, 1986) in 10 patients with cerebral edema secondary to brain tumor or stroke, found to have increased density in tentorium and interhemispheric fissure on head CT. The term “pseudo-SAH” was introduced by Azvarami et al (Eur J Radiol, 1998), who observed similar findings on head CT in 100 comatous patients with brain edema. Later this phenomenon was described in several other conditions such as cerebral anoxia/hypoxia, meningitis, leukemia, gliomatosis, intracranial hypotension to name a few. The rare causes of pseudo-SAH include bee sting or valproic acid toxicity.

The mechanisms behind the neuroradiographic phenomenon of pseudo-SAH may be caused by several different factors, or their combination. In most commonly reported causes - cerebral edema, brain anoxia, or combination of two - those are engorgement of pial vessels, displacement of hypoattenuated CSF from subarachnoid spaces, and brain edema itself, which causes decreased density of brain parenchyma. In meningitis there is blood-brain barrier disruption with high protein content of the CSF, giving sulci and cisterns hyperattenuated appearance on head CT and creating basis for pseudo-SAH pattern. In the presented case report additional factor may have been polycythemia and increased hemotocrit, aggravating hyperattenuation of the pial vessels and cisterns. While this appears to be the first report of pseudo-SAH in chronic hypoxia with PubMed search, there have been several previous reports on this phenomenon in more acute anoxic/hypoxic encephalopathy, including Yuzawa et al (AJNR, 2008), Agha and Al Hakam (Maedica, 2011), Al-Yamany et al (Can J Neurol Sci), Ahn et al (Hong Kong J Emerg Med, 2012) to name a few. Specifically, Yuzawa at all (AJNR, 2008) summarized data on 45 non-traumatic patients resuscitated after cardio-pulmonary arrest (CPA) and found pseudo-SAH
in 20% of cases. Therefore, this phenomenon does not appear to be as rare as previously thought. Moreover, Yuzawa et al (AJNR, 2008) found that pseudo-SAH appeared by Day 3 after CPA and persisted in unchanged pattern for as long as 268 days demonstrated by consecutive serial head CT was done 6 times over this interval. Henceforth, this radiographic phenomenon is hardly limited to acute hypoxia/anoxia only, although majority of previous reports indeed describe more acute cases. Going back to the current manuscript, we may speculate, that if the reported patient had CT head done few months prior, he most likely would have had the same findings. We just do not have previous imaging for comparison. While the reported case indeed describes a rare combination of mechanisms such as polycythemia with increased hematocrit and compensatory vascular proliferation secondary to chronic hypoxia – all of which may have contributed to radiographic pattern of pseudo-SAH, I would refrain from defining it as the first report pseudo-SAH in chronic hypoxia, and would suggest to give more credit to previous authors.

What are other factors helping in differentiating pseudo-SAH from true SAH? MRI is certainly helpful, and new sequence described in the paper is worth consideration. In addition, determining Hounsfield units (HU) may also be helpful. While pseudo-SAH has HU in the range of 21 to 44 (mean 29-33), SAH is characterized by much higher values with HU 60-70 (Yuzawa et al, AJNR, 2008).

And as always, clinical picture and clinical course are of paramount importance. While SAH usually presents with thunderclap headache, this is not typically the case with other conditions associated with pseudo-SAH. Therefore, as always, history of illness remains critical for any clinician.

I would also like to comment on the classification of headache subtype in the reported case. While headache phenotype may have been similar to tension type headache (which is one of the primary headaches), presence of chronic hypoxia with polycythemia and increased hematocrit, as well as compensatory vascular proliferation, - may all predispose (each individually or in combination) to the development of secondary headaches, and should be classified as such. This was most likely secondary headache with phenotype of tension type headache.

And last but not the least, while the subject of the paper and case itself are interesting and appealing, the manuscript is not an easy read, primarily due to the fact that it appears to be written by a non-English speaker(s). It needs to be rewritten to make it more readable and easily understandable by English speakers. Authors may want to consider help of someone for whom English is the first language.

With all of the above, I recommend major and minor revisions to this manuscript, after which it can be re-submitted. Those are summarized below:

Major Essential Revisions:
1) Language and style to make article more easily readable
2) More accurate review of literature on the subject with in depth analysis of
previous publications
3) Classification of headache subtype

Minor Revisions:
1) In my opinion manuscript may benefit with mention of CT characteristics of pseudo SAH, such as HU

**Level of interest:** An article of importance in its field

**Quality of written English:** Not suitable for publication unless extensively edited

**Statistical review:** No, the manuscript does not need to be seen by a statistician.

**Declaration of competing interests:**

None of the above