Reviewer’s report

Title: Central nervous system Gadolinium accumulation in patients undergoing periodical contrast MRI screening for hereditary tumor syndromes

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Reviewer: Hartmut Neumann

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This is a study on VHL and TSC patients for potential toxicity of Gadolinium which is used for regular screening in order to detect tumors which should be removed in time according to guidelines for prevention medicine. Such tumors may develop in the CNS but also in visceral organs.

Included are 28 VHL and 24 TSC patients. Main outcomes are enhanced accumulation in dentate nucleus and globus pallidum in 100% VHL patients after 16 years.

The number of patients and the length of follow up are of interest.

Concerns:

Not reported are clinical signs of toxicity; this is seemingly absent but showed be added.

Methods regarding Gadolinium uptake are clear.

Unclear to me remains the number of injections of Gadolinium. At least the number of MRI dates should be given. Most patients know that quite exactly, in others the intervals may allow to conclude how many MRIs have been done.

We must be aware that patients with VHL may have lost one kidney because of cancer and that TSC patients may have lost a kidney because of angiomyolipomas. Also we need to know if more than the mentioned TSC case has polycystic kidney disease. This must be reported.

Regarding kidney function measurement according to MDRD formula, this is ok. But it has to be mentioned that normal function is 90 ml/min and more. 60-90 ml/min is so-called stage 2 and means already impaired renal function. We need to know how many cases had stage 2. They should also say that stage 3 is 30-59 and that the given case had stage 3 of chronic renal failure.
Table 1: Show only the line 28 VHL and 24 TSC cases.

Under the line: Seemingly no signs of symptomatic toxicity, but clear signs of cumulation of Gadolinium by time.

These results lead to reconsideration of the policy of prevention medicine in VHL and TSC. So far, patients felt comfortable, if they had regular screening, and best quality of imaging, and best method for detection of tumors is contrast enhanced MRI.

Where should we go? This paper says that all sites of potential tumors should be documented after a single shot of gadolinium. That is fine and important.

But we must reconsider the length of intervals and potential alternatives of imaging. 1. The authors should comment, if gadolinium-free MRI is diagnostic for CNS lesions. 2. For visceral tumors, ultrasonography should be considered as a relevant alternative. 3. Regarding intervals of imaging, it must be considered how many operations the patients had and if based on these, as I think, astonishing low numbers of operations the intervals of imaging can be stretched.

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