Author's response to reviews

Title: Rapidly progressive dementia and Parkinsonism as a gliomatosis cerebri's initial clinical presentation in a 82 year old patient. A case report

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Version: 6 Date: 14 January 2008

Author's response to reviews: see over
Dear Professor Kidd,

Please, find enclosed a manuscript by Dr Duron Emmanuelle et al. that we would like to resubmit as a Case Report entitled:

“Gliomatosis cerebri presenting as rapidly progressive dementia and Parkinsonism in an 82 year old patient. A case report”

Duron Emmanuelle MD\textsuperscript{1}, Lazareth A MD\textsuperscript{1}, Gaubert Jean-Yves MD\textsuperscript{1}, Raso Carole MD\textsuperscript{1}, Hanon O MD, PhD\textsuperscript{1}, Rigaud Anne-Sophie MD, PhD\textsuperscript{1}.

From: 1. Department of Geriatry, University Hospital Broca, AP-HP, France.

We hope that you will consider it suitable for publication.
Looking forward to hearing from you.

Sincerely yours,

Dr Emmanuelle Duron, MD

As suggested by the referees recommended revisions have been made. We confirm that the manuscript or part of the data have not been published or is not being simultaneously submitted elsewhere. All the authors have agreed to its submission.
Referee # 1 (David S Geldmacher)

Thank you for your constructive comments and suggestions. Each of your comments is addressed and is followed by a description of the modifications.

Comment:
The results of the CT brain scan are not reported. The usefulness of MR image would be enhanced if multiple levels were included
Response
We added a CT scan image (Figure 1) and another MR image.

Comment
The statement that rapid progression and executive dysfunction are not suggestive of dementia with Lewy body is not supported by the literature. Several cases of very rapidly progressive DLB have been reported. The discussion would be enhanced by mention of this well recognized phenomenon and clinical differentiating factors from the reported case.
Response
The discussion was modified with mention of these cases of very rapid progressive DLB. We added that “the lack of recurrent hallucinations, delusions and fluctuating cognition and the absence of response to treatment did not favour this diagnosis in our patient”.

Comment
The anatomic explanations are unduly simplified. Disruption of the connecting fibers in the white matter is an important contributor to parkinsonism. The implication that it is ironic that parkinsonism is frequently due to non-basal ganglia lesions fails to reflect that neuronal tumors are nearly nonexistent and the basal ganglia are neuron rich structures.
Response
We mentioned the role of white matter lesions and added a figure (Figure2) showing the implication of the lenticular nuclei. Furthermore, the term “Ironically” was removed.

Comment
“Tumoral” would be better substituted with “neoplastic” or “tumor related”.
Response
The term “Tumoral” has been substituted with “neoplastic” or “tumor related”.

Comment
The introduction should complement and enlarge upon the abstract, not repeat it.
Response
The introduction was enlarged with topics concerning the link between dementia and brain tumors, and the more frequent aetiologies of secondary parkinsonism.

Comment
Needs some language corrections
Response
Language corrections have been made by a native English speaker.
Referee # 2 (Eric Molho)

Thank you for your constructive comments and suggestions. Each of your comments is addressed and is followed by a description of the modifications.

Comment
My major concern with the paper is that the Case Report, upon which it is based, contains no detail regarding the specific aspects of the neurological exam that would support a diagnosis of parkinsonism. Without video tape documentation of the exam additional details in the written Case Report are necessary. Facial expression, speech, dexterity and specifics of gait should be included. The reader needs to be able to distinguish between true parkinsonism and pseudo-parkinsonism.
Response
The neurological exam was reported more precisely (facial expression, speech, gait, symmetrical signs).

Comment
I would also like the authors to consider defining the medication Candesartan in the text for the reader.
Response
The medication Candesartan has been defined.

Comment
The authors should consider showing the original CT scan as a Figure.
Response
The original CT scan was added as a figure (Figure 1).

Comment
Any treatment that was prescribed for the patient for parkinsonism or dementia should be described and the implications of the patient’s response or lack there of should be discussed.
Response
We mentioned that we introduced an L dopa treatment as well as an anti cholinesterase treatment (Galantamine) without any efficiency which was consistent with the final diagnosis.

Comment
In the Discussion the first line should use the term parkinsonism with a small “p” rather than a “Parkinson’s disease”. On Page 4, on the eighth line of the Discussion, explained should be changed to “corresponded” too. In the first line of the next paragraph “Parkinson’s disease” should be changed to “parkinsonism of tumoral origin”. The next line should read “Ironically, they are usually due to “.
Response
All these modifications were made.

Comment
More importantly, the Discussion should include limitations of this Case Report, i.e. the lack of pathological confirmation of the diagnosis and if there is no information regarding treatment, that this would also represent a significant limitation since a positive response to
definitive antiparkinsonian treatment would not be expected in Parkinsonism of tumoral origin.

Response
We mentioned the lack of pathological confirmation and we added information about response to L dopa.

Comment
One final minor suggestion would be to change “Parkinsonism” throughout the manuscript to “parkinsonism”.

Response
This change was made.
Referee # 3 (Gilles Fenelon)
Thank you for your constructive comments and suggestions. Each of your comments is addressed and is followed by a description of the modifications.

Comment 1
Introduction. ... "a very rare tumor affecting the elderly". Gliomatosis cerebri (GC) does not predominantly affect the elderly.
Response 1
We corrected the phrase: GC seldom affects the elderly.

Comment 2
A more precise description of memory impairment and of parkinsonism (asymmetry ? gait ? speech ? severity of bradykinesia and rigidity ? ...) should be provided.
Response 2
The neurological exam was reported more precisely as well as the neuropsychological assessment.

Comment 3"Parkinson disease" is used instead of "parkinsonism"
Response 3
The term Parkinson disease was removed from the text.

Comment 4
The authors mention the diagnosis of dementia with Lewy bodies. Did the patient report hallucinations?
Response 4
Hallucinations were not obvious (questioning was very difficult) but the patient developed dementia and atypical parkinsonism which have led us to raise the diagnosis of dementia with Lewy Bodies.

Comment 5
Where lesions enhanced following gadolinium administration? Fig 1 should include a MR image at the level of lenticular nuclei.
Response 5
Some little nodes were enhanced with gadolinium injection. We added a figure 2 corresponding to the level of lenticular nuclei.

Comment 6 Tell the fact that the diagnosis of GC is probable and not certain (no histological confirmation) should be acknowledged.
Response 6
We mentioned this limitation of our case report.

Comment 7
Another case of parkinsonism + cognitive impairment secondary to GC as been published and should be quoted : Slee et al. J neuroNeurosurg psychiatry 2006;77:283-4.
Response 7
This case report was taken into account and the reference was added.