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Letter to the Editor

Secondary alzheimer started by cryptococcal meningitis

In the manner of the tuberculous or cysticercous meningitis, cryptococcal meningitis (CM) has a predominant basal location, i.e., in the chiasmatic cistern and anterior perforated space (APS). Here, all blood vessels originated from the supraclinoid carotid arteries (C4 portions) and circle of Willis can be affected by mild to severe basal exudate, especially the perforating arteries are the much more damaged. Thus these collateral branches present endarterial proliferation that produces obliteration, hypertrophic sclerosis of the media of the artery and lymphocytic adventitial infiltration. Therefore, CM can develop ischemic and/or infarct lesions in basal ganglia and surrounding areas [2,7].

The study in a group of 51 patients with CM they presented the following symptoms (9): 1) headache (74.5%); 2) mental changes (51%); 3) visual changes (37.2%), 4) nausea or vomiting (37.2%), and 5) fever or chills or both (31.3%) among the main symptoms. In contrast, in approximately 10% of this series of patients there were no symptoms referable to the central nervous system, and the diagnosis of CM was made only after a routine lumbar puncture and microscopic examination or by culture of cryptococcus neformans.

So therefore, I found the article by Ala et al. [1] to be of great interest in relation to a secondary Alzheimer case started by CM. Because the early clinical features of this patient (short-term memory impairment and occasional inappropriate behavior) responded to the early stage of Alzheimer's disease (AD) [4,6], but provoked by CM. Thereby, this clinical case suggest that there are two types of Alzheimer: Primary Alzheimer or AD, caused essentially by atherosclerosis in the supraclinoid portions of the internal carotid arteries, circle of Willis and its collateral branches [5,6,8,10], and Secondary Alzheimer to previous atherosclerosis in the large and small vessels of the chiasmatic cistern associated with hemorrhage due to traumatic brain injury or basal meningitis among another causes [1,3,9]. Moreover, besides this suggestion, in AD there are three clinical varieties [6]: 1) sporadic cases (81.2%); 2) uncertain cases (15.3%); and 3) familial cases (3.5%).

However, in both types of Alzheimer (primary and secondary), the early stage (mild degree) of this disease is *initiated* in the medial temporal lobes and subcommissural regions (constituted by cholinergic and neuropeptidic nuclei as well as their fiber bundles, especially medial forebrain bundles), and caused by progressive hypoperfusion and hypometabolism into the intraparenchymal territory of the anterior choroidal and anterior perforating arteries [5,6]. Because, in contrast to this, its revascularization of these brain areas with omental tissue placed on the optic chiasma, the carotid bifurcation and the APS [5,6], or by means of the medical treatment for basal meningitis [1,9], we can revert the symptoms in the mild AD patients. In my opinion, gradual and partial improvement of the symptoms in the patient reported by Ala et al. [1] was due to incomplete recovery of the blood flow in the intraparenchymal territory of the anterior choroidal and/or anterior perforating arteries following the treatment with amphotericin B, 5-flucytosine and finally, fluconazole.

In summary, the head trauma, the basal meningitis and another medical conditions are risk factors for developing Alzheimer that may accelerate neuronal loss in the intraparenchymal territory of the anterior choroidal and anterior perforating arteries. For these reasons, I postulate that in the pathogenesis of secondary Alzheimer there are risk factors associated to

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previous atherosclerotic changes in the supraclinoid carotids, circle of Willis and its perforating branches. Morevoer, this clinical case support our hypothesis that AD is of microvascular origin and it is not a neurodegenerative disorder.

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References

[1] T.A. Ala, R.C. Doss and Ch.J. Sullivan, Reversible dementia: A case of cryptococcal meningitis masquerading as Alzheimer's disease, *J Alzheimer Dis* **6** (2004), 503–508.
[2] S.A. Luse, Pathology of chronic inflammation in the nervous system, *Clin Neurosurg* **14** (1967), 227–238.
[3] R.D.S. Nandoe, P. Scheltens and P. Eikelenboom, Head trauma and Alzheimer's disease: A case report and review of the literature, *J Alzheimer Dis* **4** (2002), 303–308.
[4] R.C. Petersen, Mild cognitive impairment: Transition between aging and Alzheimer's disease, *Neurología* (*Esp*) **15** (2000), 93–101.
[5] H. Rafael and R. Mego, Omental transposition, *Surg Neurol* **52** (1999), 539–541.
[6] H. Rafael, R. Cortés and M.T. Valadez, Early clinical features of Alzheimer's disease, *J Neurol Sci* (*Turk*) **20** (2003), 222–227, www. med.ege.edu.tr/norolbil, Dec., 2003.
[7] R. Selby, Neurological disorders in Malaysia, in: *Tropical Neurology*, J.D. Spillane, ed., l973, pp. 299–320.
[8] D.A. Snowdon, L.H. Greiner, J.A. Mortimor, K.P. Riley, P.A. Greiner and W.R. Markesberg, Brain infarction and the clinical expression of Alzheimer's disease: The nun study, *JAMA* **277** (1997), 813–817.
[9] J.P. Utz, Fungal infections of the central nervous system, *Clin Neurosurg* **14** (1967), 86–100.
[10] S.E. Vermeer, N.D. Prins, T. den Heijer, A. Hofman, P.J. Koudstaal and M.M.B. Breteler, Silent brain infarcts and the risk of dementia and cognitive decline, *N Engl J Med* **348** (2003), 1215–1222.