

Before Cerebral Microbleeds can be attributed to Fabry Disease, All Other Causes Must Be Carefully Excluded

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LETTER TO THE EDITOR

The interesting study by Hsieh *et al.* [Hsieh, P. F. *et al.*, 2025] needs to be discussed on several points.

The first point is that causes of CMB other than FD were not adequately excluded [Hsieh, P. F. *et al.*, 2025]. The causes of CMB can be broadly categorized into small vessel disease (SVD) due to inflammatory, immunologic, and hematologic diseases, sporadic SVD, inherited or genetic SVD, and other types of SVD. The first category includes diseases such as systemic lupus erythematosus, sickle cell disease, systemic intravascular coagulation, immune thrombocytopenia and Sneddon syndrome [Agarwal, A. *et al.*, 2024]. The second category includes diseases such as sporadic cerebral amyloid angiopathy (CAA) and hypertensive arteriopathy. The third category includes diseases such as CADASIL, CARASIL, CARASIL, PADMAL, HTAR1-associated SVD, FD, hereditary CAA and SVD due to COL4A1 mutations [Mancuso, M. *et al.*, 2020]. The fourth category includes conditions such as radiotherapy, traumatic brain injury, PRES, Moya-Moya disease, chronic kidney disease and CMB associated with critical illness [Agarwal, A. *et al.*, 2024]. The two most common causes of CMB are CAA and arterial hypertension [Agarwal, A. *et al.*, 2024]. Were all these causes of CMB adequately excluded in the 26 patients included? Since 8 of 15 patients with lobar CMB had arterial hypertension, it cannot be ruled out that in these patients it was simply due to arterial hypertension and was independent of FS. Was arterial hypertension adequately controlled in the 8 FD patients with CMB?

The second issue is that it was not reported how differential diagnoses of CMB were adequately excluded [Hsieh, P. F. *et al.*, 2025]. Differential diagnoses of CMB include fat emboli, hemorrhagic metastases, familial cavernous

malformations, and radiation-induced cavernomas [Agarwal, A. *et al.*, 2024].

The third issue is the retrospective design of the study, which has several drawbacks [Talari, K. *et al.*, 2020]. A retrospective design allows only limited control over population sampling and only limited control over the type and quality of predictor variables. In addition, the relevant predictors may not have been recorded in the medical record, and it may be difficult or impossible to establish confounding variables and causality. Furthermore, it may be inevitable that some information is missing, as the data are based on the review of medical records that were not originally intended for the collection of data for research purposes [Talari, K. *et al.*, 2020].

The fourth issue is that it was not reported how long the 26 included patients were followed up. The length of follow-up is of critical importance because the longer the follow-up, the more likely patients are to develop CMB.

Before CMB can be attributed to FD, all other primary and secondary causes of SVD must be thoroughly ruled out.

REFERENCES

1. Hsieh, P. F., Lin, P. Y., Lee, N. C., Chen, C. H., Sung, P. S., Juang, J. M., Chen, Y. F., Jeng, J. S., Chien, Y. H. & Tang, S. C. "Unveiling the characteristics of lobar-predominant cerebral microbleeds in Fabry disease." *Journal of the Formosan Medical Association*, (2025): S0929-6646(25)00189-5.
2. Agarwal, A., Ajmera, P., Sharma, P. & Kanekar, S. "Cerebral microbleeds: Causes, clinical relevance, and imaging approach – A narrative review." *Journal of Neurosciences in Rural Practice*, 15.2 (2024): 169–181.
3. Mancuso, M., Arnold, M., Bersano, A., Burlina, A., Chabriat, H., Debette, S., Enzinger, C., Federico, A., Filla, A., Finsterer,

J., Hunt, D., Lesnik Oberstein, S., Tournier-Lasserre, E. & Markus, H. S. "Monogenic cerebral small-vessel diseases: Diagnosis and therapy. Consensus recommendations of the European Academy of Neurology." *European Journal of Neurology*, 27.6 (2020): 909–927.

4. Talari, K. & Goyal, M. "Retrospective studies – Utility and caveats." *Journal of the Royal College of Physicians of Edinburgh*, 50.4 (2020): 398–402.

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