A case of frontotemporal dementia due to *GRN* mutation with a giant right-hemispheric arachnoid cyst

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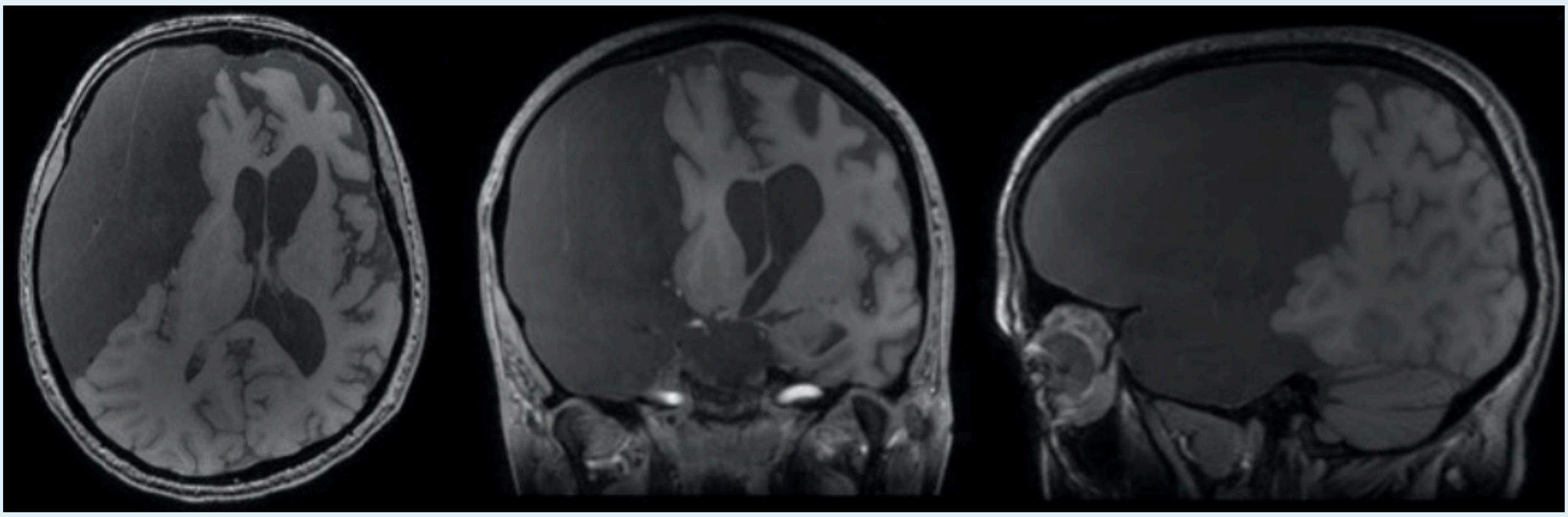
INTRODUCTION

Arachnoid cysts are relatively common and benign structures which can be found in the subarachnoid space adjacent to the brain. They constitute 1% of intracranial masses. They are congenital and usually asymptomatic. When very large, they can become symptomatic by displacing brain parenchyma or altering the flux of cerebrospinal fluid, thus causing hydrocephalus. Frontotemporal dementia (FTD) is the second most common dementia in the presenile age and presents most commonly with alterations in behaviour and/or language. In a high percentage of cases patients display a positive family history, often with autosomal dominant inheritance; one of the most common genes underlying familial forms of FTD is *GRN*, encoding the protein progranulin.

CASE REPORT

A 47-year-old woman insidiously developed poor work performance, fatuity, and dishinibition few months after a head trauma. Head CT demonstrated a giant arachnoid cyst compressing the right hemisphere. She underwent surgical fenestration of the cyst, but after surgery the size of the cyst was unchanged and mental deterioration progressed. The patient was therefore admitted to our department. Neurologic examination showed impairment of attention and abstract thinking, infantile behaviour, and difficulty with verbal expression; no motor signs were observed. Neuropsychological testing confirmed the presence of a severe frontal syndrome. Brain MRI showed the voluminous cyst (14.7 x 5.7 cm) but also atrophy of the left frontotemporal cortex (*see figure below*). It later emerged that that the patient's father had had dementia after age 80, and that his sister had had FTD in her sixties. We therefore suspected a familial FTD, which was confirmed by finding the Thr272fs mutation in our patient.



DISCUSSION

Arachnoid cysts are congenital and usually asymptomatic imaging findings. In this case, the cyst was initially considered to be responsible for the patient's mental deterioration for three reasons: its dimensions, its hemispheric location, and the recent head trauma which was hypothesized to have mechanically determined an enlargement of the cyst. However, in retrospect, some elements pointed towards a different diagnosis: absence of motor signs, language impairment (suggesting involvement of the left hemisphere), cortical atrophy, and, above all, relentless course and family history. The literature does not indicate an association of arachnoid cysts with *GRN* or FTD; on the other hand, only rarely have those cysts been reported to cause cognitive decline. It is nevertheless possible that in this patient the cyst facilitated the clinical manifestation of the genetic disease by reducing the patient's brain volume and "cognitive reserve": this could have contributed to the earlier onset of dementia in comparison to her two affected relatives. It is also possible that the head trauma had a role in precipitating the neurodegenerative process leading to dementia. From the clinical standpoint this case is noteworthy because it shows that in an issue of cognitive decline which at first evaluation seems to be caused by an obvious structural lesion, sometimes the cause must be sought in a radically different and less evident pathologic process. The case also indicates that an earlier and more detailed investigation of the family history would have helped direct correctly the diagnostic process from the beginning. Knowledge of this case could help in prognosis and management of similar patients in the future.

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