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Neuroimaging Highlight

Progressive Neurological Decline Associated With Intracranial Calcification in Down Syndrome; Fahr Disease Mimic?

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Intracranial calcification (ICC) has been described commonly in association with congenital infections, head trauma, and endocrine or systemic metabolic derangements. However, it is also noted in patients with pathogenic genetic mutations and defects in inborn error of metabolism.[1–4] We report the clinical, imaging, and genetic findings in an adult with Down syndrome (DS) referred to the clinic for further investigation for Fahr disease.

A 43-year-old lady with DS, secondary to Robertsonian translocation of chromosomes 13 and 21 and a background history of hypothyroidism who remained highly functional till the age of 38 years, was noted to have progressive neurological decline affecting cognitive, motor, visual, adaptive, and linguistic abilities. At baseline, the patient had a grade 1 level in literacy and writing and was working in a nursing home with minimal supervision. However, over the span of 5 years, she progressively lost executive function, short-term recall, expressive communication, and ambulation capabilities. She also started experiencing epileptic seizures, which were controlled following the introduction of antiseizure medication, levetiracetam, and lacosamide. The patient was adopted at two years of life, details of the family history could not be elicited. A limited examination in the clinic demonstrated no eye contact; she would not interact with the examiner. She was sitting in her wheelchair, and bilateral spasticity was pronounced in the lower extremities with diffuse brisk deep tendon reflexes, however, ankle clonus was not elicited. The patient was rated by her sister for the Dementia Questionnaire for Persons with Mental Retardation[5] and found to score 30/66, within the range of moderate cognitive difficulties as well as moderately severe behavioral symptoms.

A CT scan requested by her neurologist as part of her investigative work up for neurological decline demonstrated calcifications within the basal ganglia, dentate nuclei, and parasagittal occipital sulci bilaterally (Figs. 1 and 2). The patient has since undergone biochemical testing, showing intact parathyroid and thyroid function; PTH:2.7 pmol/L (1.6–6.9), calcium:2.26 mmol/L (2.15–2.60), phosphorus:0.98 mmol/L (0.80–1.45), TSH:1.090mIU/L (0.465–4.680). Her karyotype was reported as 46, XX, der (13;21) (q10;q10),+21, consistent with Robertsonian translocation, between the long arms of one copy of each of

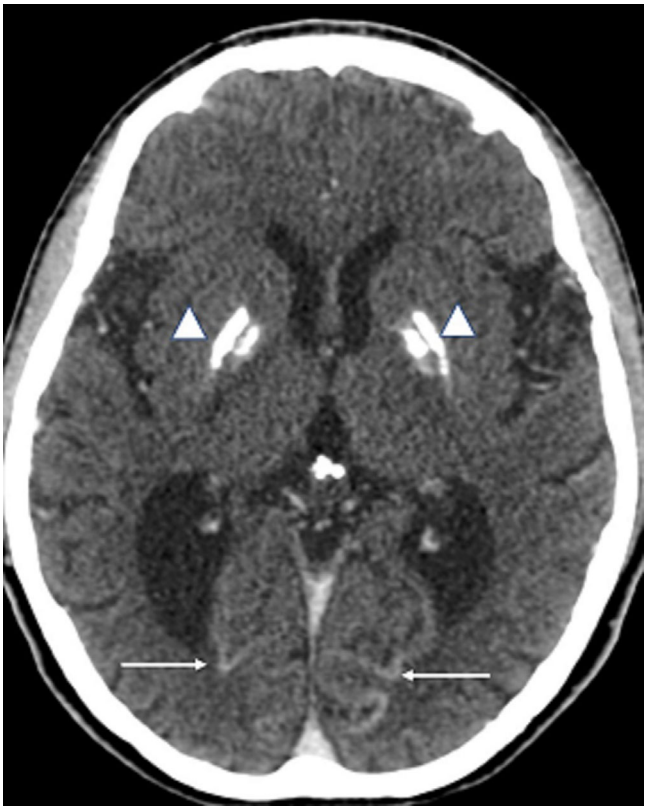

Figure 1: Axial CT illustrates dense calcification of the bilateral lentiform nuclei (white arrowheads) and bilateral parasagittal occipital cortices (thin white arrows).

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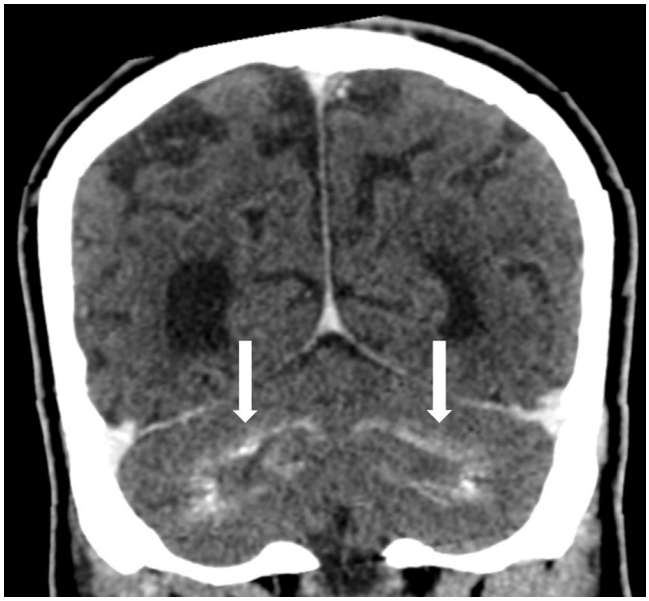

Figure 2: Coronal CT shows dense calcification of the bilateral cerebellar white matter including the dentate nuclei (thick white arrows).

chromosomes 13 and 21. Molecular genetic testing for Fahr disease was conducted with no pathogenic variant identified.

Patients with DS have a higher prevalence of basal ganglia calcifications with a frequency of 10%–26.2% compared to only 0.3%–0.6% in the general population.[4,6,7] On scans, globus pallidus and, less commonly, the head of the caudate are the most affected structures, while other areas like the choroid plexus and pineal body are found to be just as frequently calcified in healthy individuals.[6] Histopathology reveals that the calcification involves the media of small arteries in the perivascular regions and amyloid degeneration.[7] The exact underlying pathogenesis of calcium deposit in DS remains to be elucidated. Clinically, the identification of ICC has been linked to accelerated aging and premature onset of dementia in DS.[8]

Imaging studies (Figs. 1 and 2) in this individual confirm that the intracranial calcification extends beyond the basal ganglia to the cerebellum's dentate nuclei, providing additional justification for molecular testing for Fahr disease. Being aware of this phenomenon in DS could help with early diagnosis and prevent unneeded, costly, and time-consuming investigations.

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Statement of authorship. MA wrote the manuscript; KT reviewed the CT of the patient and provided labeled figures; and CP, ANP, and DD provided consultation and diagnosis for the patient and supervised the manuscript.

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