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Case report

P4, the index case, presented with dizziness of a few days duration, followed by an epileptic seizure at the age of 13 years. She died five days after hospitalization and her CT scan showed intracranial calcification. She was never genotyped, but due to the clinical picture similar to her siblings, her genotype was inferred. Her two sisters, P5 and P6, also presented with basal ganglia calcifications, but without frequent seizures or cerebral atrophy, at the ages of six and eight years (they are now aged 11 and 13 years). CT scan showed deposits in the deep nuclei in the depths of the gyri, with unaffected white matter. The pattern was distinctive, but not specific and thus not pathognomonic for any condition other than putative IBGC. These children have no psychomotor disabilities and normal educational attainment. Routine blood tests, liver and kidney function, electrolyte levels, thyroid hormone and parathyroid hormone levels were normal. None of these children was vaccinated with BCG at birth (all were born at home, as reported by their mother). We performed chest X rays on P5, P6, the healthy brother and healthy mother and found no evidence of scarring. P1, P2 and P3 remain in good health. They also have no psychomotor disabilities and their educational attainments are normal despite the presence of intracranial calcifications. We had sequenced the ISG15 gene from 1,056 controls from 52 ethnic groups in the HGDP-CEPH human genome diversity cell line panel. None of these individuals carried the Chinese mutant *ISG15* allele. This allele was also absent from public and our own databases (Extended Table S1). Only one known variant of *ISG15* is nonsense, with a heterozygous frequency of 1 in 6502. This allele thus occurs with a homozygous or compound heterozygous frequency of less than one in one million individuals. All patients' information and ex vivo experiments were performed in accordance to an approved IRB protocol and patients' consents.