Great balls of fire! The basal ganglia on fire

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A 76-year-old man presented to the hospital with intermittent dizziness, memory impairment and jerky movements. Evaluation revealed them to be faciobrachial dystonic seizures and antibodies to voltage-gated potassium channel complexes were found. He was treated with intravenous methylprednisolone and rituximab, and made a remarkable recovery. Magnetic resonance imaging of the brain was normal, although positron emission tomography – computed tomography showed striking basal ganglia changes.

KEYWORDS: faciobrachial dystonic seizures, LGI1 antibodies, autoimmune encephalitis, PET-CT, FDG PET-CT

Diagnosis
With a normal MRI, the differential diagnosis included new late onset complex partial seizures (recently renamed as focal onset impaired awareness seizures), Ginkgo biloba toxicity, Creutzfeldt–Jakob disease (CJD), secondary paroxysmal non-kineticogenic choreoathetosis and faciobrachial dystonic seizures (FBDS). Other considerations included metabolic, neurodegenerative and paraneoplastic conditions.

We performed 24-hour video electroencephalography (EEG) that revealed multiple episodes of brief posturing of the right side of his face, and right arm and leg lasting a few seconds. These episodes were not accompanied by any EEG changes and were suggestive of FBDS. On day 3, his serum sample tested strongly positive for leucine-rich glioma-inactivated 1 (LGI1) antibodies by indirect immunofluorescence on transfected cells. His sample was negative for contactin-associated protein-2 antibodies. On day 3, 18 fluorodeoxyglucose positron emission tomography – computed tomography (FDG PET-CT) of the brain showed uniform diffuse hypermetabolism of bilateral basal ganglia with relative hypometabolism of the rest of the cerebral parenchyma (Fig 1). There were no other suspicious hypermetabolic foci suggestive of a neoplasm anywhere else. A final diagnosis of autoimmune encephalitis with FBDS was made.

Key points
> Treatable conditions should be considered in the differential diagnosis of progressive memory complaints in the elderly.
> Not all jerky movements are seizures. Basal ganglionic pathology can result in unilateral jerky movements.
> Faciobrachial dystonic seizures are associated with antibodies to voltage-gated potassium channel complexes.
patients had hypermetabolism in the basal ganglia region and 68% in the medial temporal lobe. Most of these patients had a normal MRI. These $^{18}$FDG PET-CT changes were reversible in most patients after treatment. In fact, $^{18}$FDG PET-CT is probably more sensitive than MRI in the diagnosis of this autoimmune encephalitis. Atypical facio-brachio-crusal movements and nonspecific EEG changes may occasionally be found in patients with CJD. CJD is, thus, an important differential diagnosis, which should be considered and ruled out by appropriate investigations. It is important to recognise this autoimmune encephalitis early. Antiepileptic monotherapy per se may not be effective to control the FBDS and adjuvant longterm immunotherapy may be needed to achieve disease remission. First-line treatment options include IV methylprednisolone and immunoglobulins. Second-line options include rituximab. Although many patients improve, some continue to show progressive cognitive impairment. Nearly 20% of patients suffer relapses and long-term follow-up and treatment are necessary.4,5

References
1 Irani SR, Michell AW, Lang B et al. Faciobrachial dystonic seizures precede Lgi1 antibody limbic encephalitis. Ann Neurol 2011;69:892–900.
2 Maramattom B, Jeevanagi S, George C. Facio-brachio-crural dystonic episodes and drop attacks due to leucine rich glioma inactivated 1 encephalitis in two elderly Indian women. Ann Indian Acad Neurol 2013;16:590–2.
3 Liu X, Shan W, Zhao X et al. The clinical value of 18F-FDG-PET in autoimmune encephalitis associated with LGI1 antibody. Front Neurol 2020;11:418.
4 Thompson J, Bi M, Murchison A et al. The importance of early immunotherapy in patients with faciobrachial dystonic seizures. Brain 2017;140:368–56.
5 van Sonderen A, Schreurs MW, Wirtz PW, Sillevis Smitt PA, Titulaer MJ. From VGKC to LGI1 and CASPR2 encephalitis: The evolution of a disease entity over time. Autoimmun Rev 2016;15:970–4.

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Initial management and prognosis
He was treated with intravenous (IV) steroids (methylprednisolone 1 g/day) for 5 days. He was then started on injection rituximab 1 g infusion, after which, the frequency of FBDS reduced.

Case progression and outcome
By day 7, his episodes had started diminishing. He was started on oral steroids (Wysolone 30 mg/day) and discharged with a plan for a second dose of rituximab 1 g after a month. Rituximab was preferred over IV immunoglobulins due to financial constraints.

Discussion
FBDS were first described in 2011, however, it was described in India only in 2013.1,2 A PubMed search with the keyword phrase ‘faciobrachial dystonic seizures’ showed only 125 related articles published to date, which shows the rarity of the diagnosis. Most patients display antibodies to the voltage-gated potassium channel complexes (VGKC). The specific antigenic target is the LGI-1 in 89% of patients and it is usually a non-paraneoplastic autoimmune condition. FBDS shows a 2:1 male predominance and is usually seen in the elderly (median age of onset is 60 years). The most common clinical presentations of FBDS are as newonset faciobrachial dystonic episodes, seizures, pilomotor seizures, memory deficits, personality changes, movement disorders (such as chorea) or as a rapidly progressive dementia. FBDS is characterised by a stereotypical brief (<3 seconds), intermittent unilateral dystonic contraction of the ipsilateral hemiface and arm more often than the leg.

It is commonly associated with hyponatraemia and it is postulated that LGI-1 antibodies bind to the antidiuretic hormone (ADH) producing paraventricular nucleus neurons in the hypothalamus. This binding increases ADH secretion causing water retention and hyponatraemia (syndrome of inappropriate antidiuretic hormone secretion).

Our patient had short duration non-epileptogenic dystonic episodes without any EEG correlates of seizures. MRI was normal but $^{18}$FDG PET-CT showed striking symmetrical basal ganglia hypermetabolism.3 The role of $^{18}$FDG PET-CT in LGI-1 encephalitis has been highlighted in a recent study, wherein 82% of the patients had hypermetabolism in the basal ganglia region and 68% in the medial temporal lobe. Most of these patients had a normal MRI. These $^{18}$FDG PET-CT changes were reversible in most patients after treatment. In fact, $^{18}$FDG PET-CT is probably more sensitive than MRI in the diagnosis of this autoimmune encephalitis. Atypical facio-brachio-crusal movements and nonspecific EEG changes may occasionally be found in patients with CJD. CJD is, thus, an important differential diagnosis, which should be considered and ruled out by appropriate investigations. It is important to recognise this autoimmune encephalitis early. Antiepileptic monotherapy per se may not be effective to control the FBDS and adjuvant longterm immunotherapy may be needed to achieve disease remission. First-line treatment options include IV methylprednisolone and immunoglobulins. Second-line options include rituximab. Although many patients improve, some continue to show progressive cognitive impairment. Nearly 20% of patients suffer relapses and long-term follow-up and treatment are necessary.4,5

Fig 1. $^{18}$ Fluorodeoxyglucose positron emission tomography – computed tomography of the brain showing uniform diffuse hypermetabolism of bilateral basal ganglia with relative hypometabolism of rest of bilateral cerebral cortex. a) Axial plane. b) Coronal plane.