generalised slowing without periodic discharges. CSF analysis was negative for 14-3-3 protein. MRI showed hyperintense signals involving the dorsofrontal and parieto-occipital cortices and both medial thalamus which were particularly evident on DWI sequence. The motor and sensory primary cortices remained unaffected. Genotyping of the prion protein gen identified heterozygosis methionine-valine at codon 129 and no mutations. The patient developed progressive worsening in the behavioural, cognitive and motor domains that left him in a state of akinetic mutism for a few months before death, which occurred four years after the clinical onset. A pathological study demonstrated spongiform changes, gliosis, neuronal loss and Kuru-type plaques. Immunohistochemistry exhibited a synaptic pattern with focal plaques. A western Blot analysis was not possible, but an atypical long-duration MV2 sporadic Creutzfeldt-Jakob was the most probable diagnosis.

Keywords

Sporadic Creutzfeldt-Jakob disease; Magnetic resonance imaging; Long- duration, Kuru-type plaques; Heterozygosis methionine-valine

Introduction

Sporadic Creutzfeldt-Jakob disease (sCJD) is characterised by rapidly progressing dementia, myoclonus and extrapyramidal and pyramidal involvement. Patients worsen weekly until reaching a state of akinetic mutism before death. The median survival is around 6 months and 90% of patients die within a year [1,2].

A small percentage of cases of sCJD have a longer survival [1-3]. This difference might be explained by the polymorphism at codon 129 of the prion protein gene and the type of prion strain [1-3].

We herein report the clinical, neuroimaging and pathological findings of a particularly long-duration case of sCJD.

Case Study

A 55-year-old man with cognitive complaints was referred to our department.

Ten months before he had left his job due to anxiety, depression and conflicts at work, but his family had noticed he was also experiencing cognitive problems. He did not remember what he had just done or where he had left things. He repeated the same questions and became lost even at home. His speech became less fluent. He did not know how to handle his mobile phone. He was not able to find the knob in the shower. He made mistakes when counting and dressing. His gait was awkward with frequent tripping and some falls.

Neurological examination showed frontal release signs (palmomental and grasp). The muscle tone was spastic, and the tendon reflexes were brisk with clonus. His gait was spastic without ataxia. Myoclonus was not noted. The MMSE score was 23/30 and a detailed neuropsychological examination detected failures in multiple cognitive domains (memory, executive function, praxis and visuospatial tasks). The patient showed anosognosia and difficulties in visual tracking. He scored positively on various items of NPI (anxiety, apathy, indifference, irritability and lability).

Laboratory findings were within normal ranges, including tests for syphilis, thyroid function, vitamins (A and E), ceruloplasmin, urine copper and immunological study. CSF revealed normal biochemistry and was negative for 14-3-3 protein. An initial electroencephalogram (EEG) showed little beta activity in the frontal areas without periodic discharges.

MRI (1.5 TESLA) showed hyperintense signals involving the dorsofrontal and parieto-occipital cortices and both medial thalamus which were particularly evident on DWI sequence. The motor and sensory primary cortices remained unaffected (**Figure 1**).

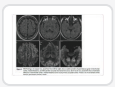

Figure 1: MRI findings: (A) Upper row, axial Flair from left to right, shows subtle symetric hyperintense signal in the frontal cortex, medial thalamus, and the parieto-occipital and calcarine sulcus. (B) In lower row, axial DWI shows restricted diffusion in the frontal cortex, medial thalamus and visual primary occipital cortex. There is no involvement of the sensory and motor primary cortex.

Genotyping of the prion protein gene did not reveal mutations. Codon 129 was heterozygous for methionine-valine (MV).

Seven months later the patient's condition had worsened. He was suffering from agitation, visual hallucinations and false recognition delusions and was started on quetiapine up to 200 mg every day.

One year after the first evaluation the patient had double incontinence and his gait had worsened. On neurological examination, new signs had appeared such as supranuclear downgaze palsy, optic ataxia, facial hypomimia and rigidity. A new EEG showed generalised slowing without epileptiform discharges or periodic complexes.

Two years after the initial assessment the patient was no longer able to speak or move by himself. He had occasional irregular jerking in his limbs.

He died due to a respiratory infection in a state of akinetic mutism three years after the initial assessment and at least four years after the clinical onset.

Postmortem samples were taken from the cortical regions to confirm the diagnosis. Microscopic examination revealed typical diffuse spongiform changes with small vacuoles uniformly distributed all over the cortical layers, marked astrocytosis and severe neuronal loss. Characteristic Kuru-type plaques with dense PAS-positive centres were frequently identified (**Figure 2A**). An immunohistochemistry study showed an extensive accumulation of prion protein in a synaptic pattern with focal plaques (**Figure 2B**). Frozen tissue was not available