Subacute sclerosing panencephalitis: rapidly progressive cognitive decline in a young patient

Introduction

This article presents a rare case of rapidly progressive cognitive decline in a young patient as a result of subacute sclerosing panencephalitis. The patient presented with a rapidly progressive cognitive decline over the preceding year with psychiatric and behavioural disturbances. She had also developed a movement disorder.

Magnetic resonance imaging of the brain showed non-specific foci of increased signal throughout both hemispheres and an electroencephalogram demonstrated high amplitude intermittent complexes. Measles antibodies were found in both the serum and CSF with evidence of intrathecal synthesis. The diagnosis was subacute sclerosing panencephalitis, a rare sequelae of prior measles infection.

Subacute sclerosing panencephalitis could become more common with the increasing incidence of measles infection in the UK and Europe. Clinicians need to consider this diagnosis in young patients presenting with rapidly progressive cognitive decline alongside other differential diagnoses, notably Creutzfeldt–Jakob disease.

Discussion

This patient presented with rapidly progressive cognitive decline. The differential diagnosis is wide and includes infectious (e.g. human immunodeficiency virus, prion), autoimmune encephalopathies (e.g. N-methyl D-aspartate receptor encephalitis), mitochondrial (e.g. myoclonic epilepsy with ragged red fibre), inflammatory CNS vasculopathies, space-occupying CNS lesions or Wernicke's encephalopathy (Kelley, 2008; Kelley et al, 2009).

Often the main differential is between prion disease and subacute sclerosing panencephalitis, although there are distinguishing factors. Subacute sclerosing panencephalitis has a younger age of onset than variant Creutzfeldt–Jakob disease (21 *vs* 28 years), and myoclonus, oligoclonal bands in the CSF and periodic complexes on electroencephalogram are common in subacute sclerosing panencephalitis, whereas psychiatric features and pulvinar hyperintensity on magnetic resonance imaging of the brain are more in keeping with variant Creutzfeldt–Jakob disease (Heath et al, 2008).

Subacute sclerosing panencephalitis is a chronic encephalitis secondary to measles virus infection. From 4 to 11 cases of subacute sclerosing panencephalitis are

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Case Report

A 26-year-old woman was referred to the neurology outpatient clinic from the psychiatry department. She had presented to her local GP because she had become forgetful, repeating phrases, withdrawn and neglecting personal hygiene.

The rapidly progressive cognitive decline had started and progressed over the preceding year. She had previously worked as a crowd steward and lived independently with her daughter. In retrospect her family could recall that initially she became more aggressive, had altercations with the police and started abusing alcohol. She had then become disinterested in her appearance, becoming emotionally labile and forgetful. She had paranoid delusions, for example thinking her cigarettes were poisoned, and she became phobic about driving. Subsequently she gave up her job. By the time she was seen in the neurology clinic, she was living with her parents, unable to dress herself, needing help with eating and personal hygiene and was no longer able to care for her daughter.

Her past medical history included a right convergent squint, appendicectomy, dental caries (with dental extraction) and cervical intraepithelial neoplasia, which had been treated. She was on no regular medication and her only family history was that her mother had had congenital cataracts and her grandfather had suffered from an unspecified 'paranoid disorder'.

On examination she was cognitively impaired with a mini-mental state examination of 11/30. Cardiovascular, respiratory and gastrointestinal examinations were unremarkable. On neurological examination she had evidence of left facial and left arm myoclonus. This had a characteristically 'hung-up' appearance with slow relaxation following sudden contraction. There were no pyramidal signs, ataxia or neuropathy. She had left-sided neglect and left-sided dyspraxia. She demonstrated good understanding, but expressive language, executive function and memory were impaired. A retinal examination demonstrated a normal fundus. The investigations listed in *Table 1* were performed.

An ultrasound of the abdomen was performed to rule out an ovarian teratoma, which can be associated with N-methyl D-aspartate receptor encephalitis (Dalmau et al, 2007), and was normal. Genetic testing of codon 129 of the PRNP gene demonstrated methionine-valine rather than methionine homozygosity, which has been found in all patients with definite variant Creutzfeldt–Jakob disease (Ironside, 2012). This made variant Creutzfeldt–Jakob disease unlikely. Magnetic resonance imaging of the brain only demonstrated a few non-specific scattered foci of increased signal throughout both cerebral hemispheres (*Figure 1*). An electroencephalogram was performed (*Figure 2*).

Subsequently, measles antibodies were found to be present in both the serum and CSF at titres of 1:128 and 1:16 respectively. Oligoclonal bands against measles were seen in the CSF but not the serum. Reverse transcription polymerase chain reaction was not performed on the CSF.

On retrospective questioning of the patient's parents and her GP, it was reported that she had had a rash aged 1 and 7, but the nature of this was unclear. No formal diagnosis of measles infection had previously been made. There was no record of previous measles, mumps and rubella vaccination.

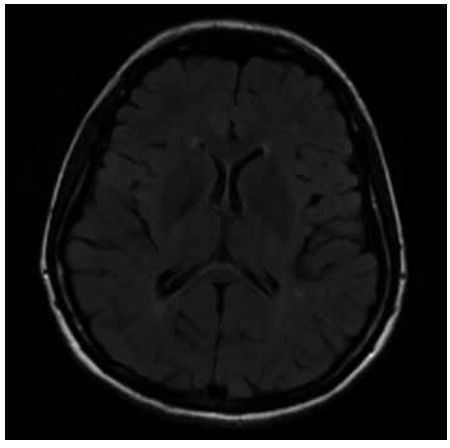

Figure 1. Magnetic resonance imaging T2 fluid-attenuated inversion recovery demonstrating non-specific foci of increased high signal.

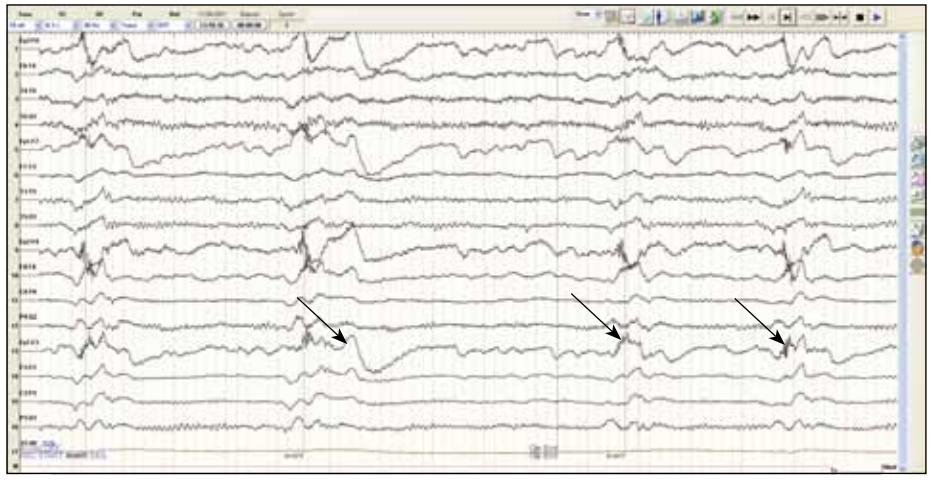

Figure 2. Electroencephalogram demonstrating long amplitude periodic complexes every 4–5 seconds (arrows). The complexes coincided with myoclonus.

expected for every 100 000 cases of measles and the prevalence is related to poor vaccine uptake (Campbell et al, 2007). The usual age of presentation is 8–11 years with a 6-year latency. There are four stages of the disease, starting with personality change and ending with akinetic mutism and death (Gutierrez et al, 2010). Diagnosis is made by clinical features, periventricular white matter changes on magnetic resonance imaging, periodic complexes on electroencephalogram and measles virus and IgG enzyme-linked immunosorbent assay detection (Gutierrez et al, 2010). There are many ocular manifestations of subacute sclerosing panencephalitis but the most common are fundus changes, especially macular retinitis and macular pigment disturbances (Colpak et al, 2012). Immunization does not guarantee immunity but subacute sclerosing panencephalitis incidence is inversely proportional to vaccine use (Anlar et al, 2001).

There is no cure for subacute sclerosing panencephalitis with treatment aimed at slowing disease progression. Recommended treatment is weekly intrathecal interferon-α and daily oral inosine pranobex (Gutierrez et al, 2010). This patient was started on inosine pranobex and ribavirin but this was discontinued as a result of intolerance. Intrathecal interferon was offered but the family declined further treatment.

The patient remains under neurology review 4 years after disease onset, but has declined further with more frequent intrusive myoclonus, and is wheelchair bound with a few words only. This case is currently relevant because of the increasing measles prevalence seen across Europe in recent years (Health Protection Agency, 2013). With an increasing number of people being infected with measles the incidence of subacute sclerosing panencephalitis may increase. This is therefore a diagnosis that both neurologists and general physicians should consider when faced with a young patient with progressive cognitive decline. BJHM

Table 1. CSF analysis and blood results for this patient

CSF analysis	
White cell count	0
Protein	0.51 g/litre
Glucose	3.9 (paired plasma sample 4.1)
Microscopy	Negative
Oligoclonal bands	Positive
Protein 14-3-3	Negative

Normal or negative blood results were found for full blood count, urea and electrolytes, liver function tests, coagulation, creatine kinase, vitamin B_{12}, folate, thyroid function tests, copper/caerulopasmin, ammonia, venereal disease research laboratory, human immunodeficiency virus, very long chain fatty acids, lactate, anti-N-methyl D-aspartate receptor antibodies, anti-voltage-gated potassium channel antibodies, anti-thyroid peroxidase antibodies

Anlar B, Köse G, Gürer Y, Altunbaşak Ş, Haspolat S, Okan M (2001) Changing epidemiological features of subacute sclerosing panencephalitis. *Infection* **29**(4): 192–5

Campbell H, Andrews N, Brown KE, Miller E (2007) Review of the effect of measles vaccination on the epidemiology of SSPE. *Int J Epidemiol* **36**(6): 1334–48

Colpak AI, Erdener SE, Ozgen B, Anlar B, Kansu T (2012) Neuro-ophthalmology of subacute sclerosing panencephalitis: two cases and a review of the literature. *Curr Opin Ophthalmol* **23**(6): 466–71

Dalmau J, Tüzün E, Wu HY et al (2007) Paraneoplastic anti-N-methyl-D-aspartate receptor encephalitis associated with ovarian teratoma. *Ann Neurol* **61**(1): 25–36

Gutierrez J, Issacson RS, Koppel BS (2010) Subacute sclerosing panencephalitis: an update. *Develop Med Child Neurol* **52**(10): 901–7

Health Protection Agency (2013) Health Protection Report. Weekly report. Measles cases in England and Wales: update to end-December 2012. www.hpa.org.uk/hpr/archives/2013/hpr0613.pdf (accessed 13 February 2013)

Heath C, Smith C, Davenport R, Donnan GA (2008) Progressive cognitive decline and myoclonus in a young woman: clinicopathological conference at the Edinburgh Advanced Neurology Course, 2007. *Pract Neurol* **8**(5): 296–302

Ironside JW (2012) Variant Creutzfeldt-Jakob disease: an update. *Folia Neuropathol* **50**(1): 50–6

Kelley BJ (2008) Young-onset dementia. *Arch Neurol* **65**(11): 1502–8

Kelley BJ, Boeve BF, Josephs KA (2009) Rapidly progressive young-onset dementia. *Cogn Behav Neurol* **22**(1): 22–7

LEARNING POINTS

- Young patients with progressive cognitive decline have a wide differential diagnosis.
- Subacute sclerosing panencephalitis is a rare manifestation of measles infection and should be considered in young patients with progressive cognitive decline.
- CSF and electroencephalography are important investigations for rapidly progressive dementias.
- This case is clinically pertinent because of the rising incidence of measles infection in the UK and Europe with a subsequent potential increase in cases of subacute sclerosing panencephalitis.