‘Hot-Cross-Bun’ Sign: Could It Be Spinocerebellar Ataxia?

Carlo Canepa-Raggio*

Neurologist and Stroke Consultant, James Paget University Hospital, Great Yarmouth, UK

*Corresponding Author: Carlo Canepa-Raggio, Neurologist and Stroke Consultant, James Paget University Hospital, Great Yarmouth, UK, E-mail: neurocanepa@gmail.com


Copyright: © 2016 Carlo Canepa-Raggio. This is an open-access article distributed under the terms of the Creative Commons Attribution License, which permits unrestricted Access, usage, distribution, and reproduction in any medium, provided the original author and source are credited.

Summary

43-year-old man with a 12-year history of progressive ataxia, incoordination, hypokinetic-flaccid dysarthria, supranuclear palsy and dysphonia. The hot-cross-bun sign and cerebellar atrophy is noted on his MRI. Genetic testing revealed an expanded allele (38 CAG repeats) in the SCA2 gene.

Case Presentation

43-year-old man of Indian descent presented to our neurology clinic with a 12-year history of ataxia and incoordination. From the onset, he developed broad-based ataxic gait and apraxia of both upper limbs. During the course of the following 8 years he developed hypokinetic-flaccid dysarthria, bradykinesia and generalized rigidity; no tremor or dyskinesia was present. Approximately 2 years later, he also presented hypometric saccades and restricted upward eye movement (supranuclear palsy). Approximately 8 months before his evaluation in our clinic, he began to have difficulty swallowing solids and dysphonia. By the time of his evaluation in clinic, he was profoundly ataxic, apraxic and bradykinetic and was practically wheelchair-bound. Cognitively, he was also impaired, with deterioration of his short-term memory and in his capacity to plan ahead and to read.

On examination, he had severe ataxia, upper and lower limb dysmetria, dysdiadochokinesia, hypertonia, hyporeflexia in all four limbs, and restriction for upward eye gaze and flexor plantar response. He was incapable of walking unassisted and fatigued with minimal exertion (he used a wheelchair most part of the day). There was extensive muscle wasting in all four limbs. This led him to require a wheelchair for the most part of the day.

There was an important family history of ataxia. His father died at the age of 40 after a 14-year history of progressive ataxia and 2 of his 4 siblings suffered also from incoordination and ataxia; one of them had died at an early age (no genetic confirmation was available) and the other was bedbound by the age of 19.
All blood investigations (including autoimmune and oncologic antibodies) were normal. Nerve conduction study revealed a moderate-to-severe sensory-motor axonal polyneuropathy and his brain MRI showed the important hot-cross-bun sign (Figure 1) in the pons and significant cerebellar atrophy (Figure 2). DAT-scan was normal, no signs of abnormal uptake suggestive of Parkinson disease. Lumbar puncture results were normal, no abnormal protein, cell count, glucose or lactate. Finally, genetic testing revealed an expanded allele (38 CAG repeats) in the SCA2 gene, confirming the diagnosis of spino-cerebellar ataxia type 2.

Figure 1 [T2-FLAIR]: Hot-cross-bun sign in the pons

Figure 2 [T1WI]: Cerebellar atrophy
Investigations

- Blood investigations (normal)
- Normal vitamin B1 (thiamine), B2, B6 and B12, no thrombocytopenia or anaemia
- Electrolytes (sodium, potassium, magnesium, phosphate), calcium, thyroid and CRP normal
- All antibodies requested (ANCA p/c, ANA, Anti-Ro/La, MPO/PR3) were normal
- ELISA for HIV, hepatitis B and C were negative
- Protein electrophoresis in serum and urine was normal
- Lumbar puncture was normal (no oligoclonal bands, viral PCR, culture and cancerous cells)
- Albumin levels were mildly decreased; creatinine, urea and GFR were normal.
- MRI head: hot-cross-bun sign in the pons
- NCS: moderate-to-severe sensory-motor axonal polyneuropathy

Differential Diagnosis

Hereditary – autosomal recessive or dominant – forms of cerebellar ataxia

Differential diagnosis of hot-cross-bun sign:

- Olivo-ponto-cerebellar degeneration
- Creutzfeldt-Jakob Disease
- Spino-cerebellar ataxia (type 2)
Vasculitis-related PD

Treatment

There is no curative treatment. However, there are supportive measures that can potentially delay the progression of SCA2. One of the fundamental parts of management is speech and language therapy for dysarthria, swallowing assessment (and PEG insertion if needed) for dysphagia, L-Dopa for parkinsonian features (which tend to improve), physiotherapy for balance control and mobility and occupational therapy for cognitive assessments. Psychological support is also encouraged and appropriate genetic counselling for all affected family members.

Discussion

The exact prevalence of SCA worldwide is unknown. However, we do know that SCA type 2 is the most common subtype, particularly in Cuba (Holguin province). It is caused by a mutation in the AXTN2 gene, leading to an abnormal CAG-trinucleotide repeat. The CAG segment is normally repeated approximately 22 times within the gene. It can be repeated up to 31 times without causing clinical problems. However, people with 32 or more repeats develop SCA2. Usually repeat length between 35 and 45 produce a clinical onset of symptoms between 20 and 60 years of age, while patients with more than 45 repeats have an onset before 20 years of age [1]. The inheritance pattern obeys an ‘anticipation’ pattern (increase in the phenotypic severity and earlier age of onset in later generation).

Clinically, SCA is characterized by progressive truncal ataxia, speech and swallowing difficulties (dysarthria), REM-sleep disorder, muscle wasting, pyramidal signs (increased tone, hyperreflexia and Babinski sign), peripheral neuropathy and occasionally dyskinesia (chorea [2]). All patients display truncal and gait ataxia. Some patients, like ours, can display parkinsonian features such as late onset of symptoms, slow progression, bradykinesia and rigidity and good response to levodopa [3]. Essentially, SCA should be suspected in individuals with:

(a) progressive ataxia (and dysarthria),
(b) nystagmus and
(c) family history (consistent with AD inheritance).

Hot-cross-bun sign (HCBS) represents a cruciform hyper-intensity typically within the pons, visualized on T2-MRI. It represents the selective deterioration of the myelinated ponto-cerebellar fibres (sparing the corticospinal tracts) [4]. It is classically associated with multisystem atrophy [5] (olivo-ponto-cerebellar degeneration). However, it can also be seen in Creutzfeldt-Jakob disease, Parkinsonism secondary to vasculitis and SCA type 2 and 3. Lee YC et al. [6] described an overall prevalence of the HCBS with SCA of 8.7% [6] (but the frequency varies depending on the subtype. Lee YC et al. (6) described 25.7% cases associated with SCA2). Multisystem atrophy type C (olivopontocerebellar degeneration) is difficult to distinguish from SCA and many times, symptoms can overlap. Like MSA, SCA tends to progress quickly. The presence of hot-cross-bun sign on the MRI can make the differential diagnosis more difficult, as it can present in both conditions (it is not pathognomonic of MSA [7]). When a young patient has similar radiological findings to MSA-C, SCA must be considered [8]. One of the main distinguishing factors is that SCA is a genetically inherited condition, while MSA is not.
Learning Points

- SCA can be associated with hot-cross-bun sign on the MRI
- SCA must be considered in a patient with:
  a) Strong family history of ataxia and incoordination (consistent with autosomal dominant pattern)
  b) Slowly progressive ataxia and dysarthria
  c) Abnormal eye movements (hypometric saccades/supranuclear palsy)
- Hot cross bun sign is a radiological sign representing the selective loss of myelinated ponto-cerebellar fibres, sparing the cortico-spinal tracts. It can be seen in CJD, SCA, MSA and vasculitis.
- When a young patient has similar radiological findings to MSA-C, SCA must be considered

References