Multidisciplinary Management of an Unusual Case of Vascular Dementia

Farhaanah Kadri[1,*] and Ejaz Nazir[2]

[1]The Redwoods Centre, Shrewsbury, Shropshire, UK

[2]South Staffordshire and Shropshire NHS Foundation Trust, University of Chester, UK

Abstract: Cerebral Autosomal Dominant Arteriopathy with Subcortical Infarcts and Leucoencephalopathy, also known as CADASIL is a non-amyloid form of small vessel disease [1]. CADASIL is an autosomal dominant condition mainly affecting the vasculature of the deep matter within the brain, and is caused by a mutation in the NOTCH3 gene on chromosome 19 [2]. The NOTCH3 gene encodes a receptor that is important for the structure and functioning of vascular smooth muscle cells [3]. There are a wide variety of mutations that can take place within the NOTCH3 gene and cysteine is the amino acid involved in the majority of mutations. The addition or deletion of a cysteine molecule affects the NOTCH3 receptor function in the cells of the vascular smooth muscle, and can lead to apoptosis of the cells [4]. This degeneration along with mural fibrosis can result in stenosis of the arteries [3]. Consequently the blood supply is reduced to the areas supplied by those vessels which in turn causes the symptoms experienced in CADASIL [5].

Keywords: CADASIL, Cerebral Autosomal Dominant Arteriopathy with Subcortical Infarcts and Leucoencephalopathy, NOTCH3 Gene, familial dementia.

CASE REPORT

- A 45 year old male and retired teacher presented with typical features of CADASIL to the Younger People with Dementia Services, Shropshire, UK.
- CADASIL is an autosomal dominant condition caused by a mutation in the NOTCH3 gene, affecting male family members and is diagnosed by a genetic blood test.
- This gentlemans blood test was tested positive for the NOTCH3 gene mutation.
- He presented with progressive cognitive decline, functional impairment, a significant change in personality and episodic display of a range of behavioural and psychological symptoms.
- His clinical presentation was also manifested by neurological problems such as recurrent seizures, spastic paraparesis, recurrent strokes leading to a stepwise decline and eventually presenting with a form of dementia, which is very much in keeping with the characteristic features of CADASIL.
- This condition was also diagnosed in his older brother.

MANAGEMENT ISSUES

- Of the various challenges encountered in the management of this case, the first issue of genetic counselling was addressed by referring the patient's siblings to a specialist CADASIL clinic to investigate whether they were at risk.
- His caring and supportive family members underwent immense psychological and financial strain owing to demand on their time and care costs.
- A multi-disciplinary team management plan was required to meet this young man's changing care needs and challenging behaviour.
- There is a lack of appropriate placement in the Shropshire County for such individuals, however with close cooperation from the family members and the team, a place was found for this gentleman in a local nursing home where he is reasonably settled with continued specialist input from the multidisciplinary team.

DISCUSSION

CADASIL commonly begins to present between the ages of 30-50 years [4]. It can present as migraine headaches and multiple strokes, which can eventually progress to dementia. CADASIL patients may also suffer with seizures, visual impairment, depression and anxiety [5,6].

*Address correspondence to this author at the The Redwoods Centre, Bicton Heath, Shrewsbury, Shropshire, UK; Tel: 01743 210000;
E-mail: farhaanah.kadri@nhs.net

E-ISSN: 2310-8231/14

There are 3 main ways of testing patients for CADASIL. After ruling out other possible causes of the symptoms a patient is experiencing, patients can undergo an MRI scan. In CADASIL, the blood vessels are affected mainly in the deep white matter of the brain where changes can be seen on MRI [6,7]. These MRI changes appear at a mean age of 30 years, increase with age, and are present in all individuals carrying the mutation after the age of 35 years [3].

CADASIL can affect many parts of the body and so an invasive skin biopsy can be taken and viewed with electron microscopy [8]. The changes that are consistent with CADASIL can be seen within the vascular walls. Immunohistochemical examination of the biopsy sample can display the presence of NOTCH3 within the vessel walls and electron microscopy specific granular deposits between the vascular smooth muscle cell membrane and lamina externa [9]. This is only seen in the skin specimen if it contains affected vasculature and therefore this investigation is not completely reliable.

A blood sample can be taken from patients and genetically tested for the NOTCH3 mutation. There are many different potential mutations that can occur in the NOTCH3 gene, which can cause CADASIL, however, within a family, all those affected with CADASIL will have the same mutation [8].

Currently the management for CADASIL is supportive risk reduction in a multi-disciplinary setting with on-going research to try to understand the pathophysiology better as a prelude to future research on treatment modalities. The mainstay goal is to target and manage any risk factors for stroke and the psychiatric management is dependent upon the presentation [10]. SSRIs are mainly the medication to use post-stroke in patients with other comorbidities. The SSRI treatment should be commenced at a low dose and gradually titrated up [10].

The European and NICE guidelines suggest that non-pharmacological methods such as psychosocial and behavioural therapies to managing behavioural symptoms should be tried first. Antipsychotic medications should only be used in severe situations [10].

Symptoms usually progress slowly and by the age 65, cognitive impairment and dementia are common in CADASIL patients. Furthermore, by this age they are likely to have had multiple strokes [5].

In conclusion, this unusual case of familial dementia highlights the importance of working in close partnership within the multidisciplinary team members and also the family for achieving the best possible outcome in managing such cases within a biopsychosocial framework.

REFERENCES

[1] Christian O, Nils P, Jürgen H, Rainer L, Martin D. Long-term prognosis and causes of death in CADASIL: a retrospective study in 411 patients. Brain A Jr Neurol 2004; 127(11): 2533-9. http://dx.doi.org/10.1093/brain/awh282

[2] Hayley Willacy. Cerebral Autosomal Dominant Arteriopathy. http://www.patient.co.uk/doctor/Cerebral-Autosomal-Dominant-Arteriopathy.htm (accessed 2014).

[3] Saskia AJLO, Elles MJB, Gisela MT. CADASIL. University of Washington, Seattle: GeneReviews® [Internet] 2000.

[4] Professor Hugh Markus, Glen Brice. CADASIL. http://www.cadasil.sgul.ac.uk (accessed 2014).

[5] NINDS. NINDS CADASIL. http://www.ninds.nih.gov/disorders/cadasil/CADASIL.htm (accessed 2014).

[6] Genetics home reference. Cerebral autosomal dominant arteriopathy with subcortical infarcts and leukoencephalopathy (often shortened to CADASIL). http://ghr.nlm.nih.gov/condition/cerebral-autosomal-dominant-arteriopathy-with-subcortical-infarcts-and-leukoencephalopathy (accessed 2014).

[7] Tomas P, Libor M, Martin H, Hana V, Ilona C, Ales B. Clinical spectrum in CADASIL family with a new mutation. Biomed Papers 2013; 157(XX).

[8] Butler Hospital Memory and Aging Program. CADASIL, Cerebral Autosomal Dominant Arteriopathy with Subcortical Infarcts and Leucoencephalopathy. http://www.butler.org/cadasilsite/ourprogram.htm (accessed 2014).

[9] Mark HT, Gillian AD. CADASIL: a guide to a comparatively unrecognised condition in psychiatry. Adv in psych treat 2008; 14: 350-7. http://dx.doi.org/10.1192/apt.bp.107.004655

[10] Chabriat H, Joutel A, Dichgans M, Tournier-Lasserve E, Bousser MG. Cadasil. Lancet Neurol 2009; 8(7): 643-53. http://dx.doi.org/10.1016/S1474-4422(09)70127-9

Received on 31-03-2014 Accepted on 10-11-2014 Published on 18-12-2014

DOI: http://dx.doi.org/10.12970/2310-8231.2014.02.03.2