coronary disease. We also suggest that stroke location depends on the route of catheterisation, with left hemispheric strokes being more common when the femoral artery is used for access. This finding calls for special care to be taken to avoid excessive catheter manipulation near the origin of the left common carotid artery.

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Cavernomas in the central nervous system and the relevance of multiple intracranial lesions in the familial form of this disease

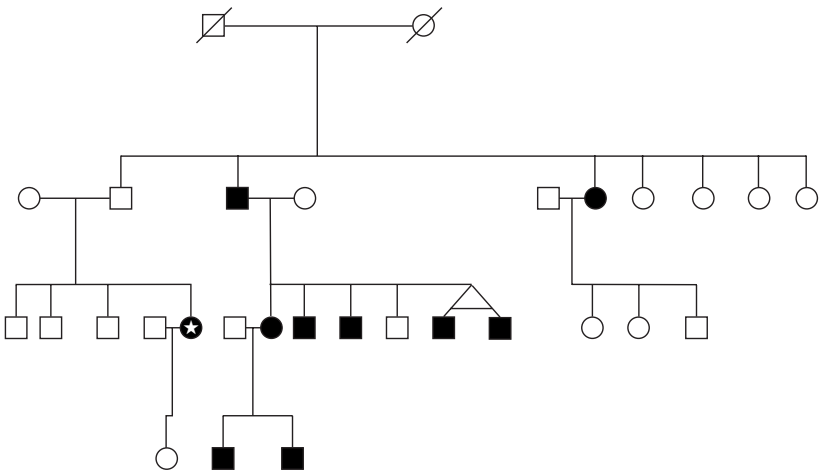
The availability of MRI has greatly increased the detection of cavernous malformations of the CNS in both symptomatic and asymptomatic patients. These lesions may be responsible for previously unexplained neurological events or may even have been incorrectly diagnosed. Cavernomas have a characteristic MRI appearance consisting of an area of mixed signal intensity, thought to be due to extracellular methaemoglobin, surrounded by an area of reduced signal intensity reflecting a zone of haemosiderin. Missing an angiographically occult vascular malformation on MRI seems likely only if the lesion contains no haemoglobin breakdown products or is microscopically so small as to be unidentifiable. This may explain the sudden appearance or "growth" of cavernomas occasionally described.

We report on a family, spanning three generations, in which at least 10 members are affected. The original reference patient was a woman aged 34. She developed a sudden weakness of the left leg subsequently found on MRI to be due to a rare intramedullary cavernoma at C3. Two intracranial cavernomas were also found during the same study. All three were subsequently removed. It has been suggested that in patients in whom multiple lesions are found a familial link is more likely. We therefore took a detailed family history. The patient told us of an aunt who has epilepsy. She had recently been diagnosed by CT as having a low grade glioma. Subsequent MRI studies have shown the lesion to have the characteristics of a cavernoma. As the family tree (figure) was constructed it became apparent that five first cousins—four males (two of whom are monozygotic twins) and one female, all siblings—had presented independently to different consultants at our institution with either seizures or unexplained intracerebral haemorrhages. Brain MRI studies in the males had shown multiple intracerebral cavernomas. Their sister has two epileptic children, both shown to have cerebral cavernomas. She was symptom free and declined investigation, until the development of persistent headaches. Brain MRI has now shown intracranial cavernomas. When the medical history of the siblings' parents was reviewed, their father admitted to a sudden spontaneously resolving hemiparesis when aged 20. He was noted to have the cutaneous angiomas sometimes associated with this condition. He was anxious to undergo investigation. Brain MRI has disclosed multiple cavernomas in the brain.

The familial occurrence of cavernomas has been reported previously, notably in Mexican-American families.[1] As in the family we report, it takes the form of multiple intracranial lesions. The inheritance would seem to be autosomal dominant with strong penetrance. Recently the gene implicated has been mapped to the 7q locus.[2] The finding of more than one cavernoma in one person should alert investigators to the possibility that other family members may be affected.

The surgical treatment of CNS cavernomas remains controversial. It seems that most cavernomas show evidence of previous haemorrhage to varying degrees. Most surgeons would agree on surgery in a symptomatic patient with a readily accessible lesion. An argument for surgery can also be made with lesions producing repetitive or progressive symptoms where there is significant neurological disability.[3] Unfortunately, to date predictors of timing and size of haemorrhage are unclear. However in a recent study involving 145 patients the authors suggest that risk factors for "aggressive behaviour" include pregnancy, familial or multiple form, previous whole brain or stereotactic radiotherapy, incomplete removal, associated venous malformation, and female sex.[4] A conservative approach is best adopted when a clinically silent lesion in an eloquent area is discovered incidentally or in the case of multiple clinically silent lesions. In cases of epilepsy, well controlled on drugs, many would adopt a conservative approach. Further controversy surrounds management strategies after a single bleed in a vital area such as the brain stem. Options here include MR directed stereotactic radiosurgery or direct surgery, which has been achieved with acceptable morbidity.[5]

Review of the literature has shown this to be the largest number of affected members in a single family



The family tree. Males appear as squares and females as circles. Affected people are shaded and those who are dead appear with an oblique slash. The original reference case is marked with an asterisk.

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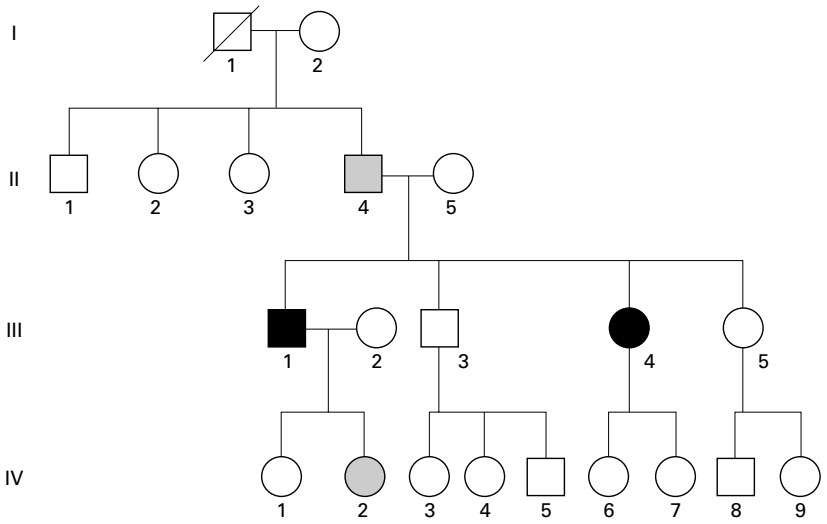
Molecular genetic diagnosis of Friedreich's ataxia in a pedigree with apparent autosomal dominant spinocerebellar degeneration

Friedreich's ataxia is a progressive neurodegenerative disorder of autosomal recessive inheritance, in which gait ataxia followed by upper limb ataxia, dysarthria, nystagmus, areflexia, loss of joint position sense, and spastic paraparesis develop from the second decade of life.[1] It is the commonest hereditary ataxia, with a prevalence of 1 in 50 000 and a deduced carrier frequency in European populations of 1 in 120. Recently, Friedreich's ataxia has been associated with mutations of the frataxin gene on chromosome 9



Family tree.

(X25 at 9q13).[2] Most patients are homozygous for expansions of a GAA triplet repeat within intron 1 of this gene. Normal alleles have between 7 and 22 repeats, whereas the range in affected patients is 200 to 900 copies. Around 5% of patients carry heterozygous mutations, a GAA expansion on one allele being accompanied by a point mutation on the other. In this report, the clinical features of a family being investigated for presumed autosomal dominant spinocerebellar degeneration, and in which GAA expansions were identified, are reported. The finding raises the possibility that heterozygous carriers of this mutation may manifest clinical symptoms and signs.

The proband (figure; III.1) is currently 28 years of age, and has a 10 year history of insidious onset and progressive unsteadiness when walking. Upper limb ataxia and dysarthria had supervened around 7 years previously. He needs the support of a single person or a rollator Zimmer for walking, and uses a wheelchair for longer distances. A week long course of synthetic gonadotrophin had been received in childhood for delayed puberty. Examination disclosed pes cavus and kyphoscoliosis. He was dysarthric. There was no optic atrophy, but horizontal gaze evoked nystagmus and bidirectional hypermetropic saccades were noted. He had intention tremor and dysmetria, worse on the left. Reflexes were retained and plantars were flexor. Gait was ataxic, with no clinical evidence of lower limb weakness or impairment of joint position sense. The following investigations gave normal or negative results: serum biochemistry, thyroid function, lipids, urinary amino acids, blood film and full blood count, serum vitamin B_{12}, red cell folate, vitamin E, phytanic acid, syphilis serology, autoantibody profile, chest radiography, EEG, MRI of head and cervical spine, CSF cytology, biochemistry, and immunology, antiPurkinje cell antibody assay, and gene tests for spinocerebellar ataxia types 1 and 3. Nerve conduction studies showed an axonal neuropathy affecting sensory fibres. Lower limb somatosensory evoked potentials were unobtainable, and those in the upper limbs were of low amplitude but normal latency. Echocardiography disclosed mildly impaired left ventricular contractility.

The proband's sister (III.4) is currently 24 years of age, and has had poor balance and ataxia since 15 years. Dysarthria has been present for four years. She is wheelchair bound. She has taken valproate for presumed complex partial seizures since the age of 8. Examination disclosed limb incoordination, worse on the left. Lower limb reflexes were hyperactive, especially on the left, and both plantars were upgoing.

The proband's father (II.4) is currently 47 years of age. He sought help 4 years ago for partial and generalised seizures, and is currently taking lamotrigine. He admitted to heavy alcohol intake. Examination disclosed hepatomegaly and some memory impairment. There was sustained horizontal gaze evoked nystagmus, limb incoordination worse on the left, diminished knee jerks, absent ankle jerks, and flexor plantar responses. He has marked truncal ataxia. Brain MRI was normal.

The proband's daughter (IV.2) was seen at the age of 8 months after becoming floppy, unable to sit, or control her head acutely. She was intermittently irritable and sleepy, and had vomited repeatedly. She was admitted to hospital, where she was afebrile and well perfused. She could not sit unsupported, was unable to reach out for toys, and was hypotonic. She had gaze dependent very fast vertical nystagmus with no failure of upgaze. Ultrasound examination of the head, blood gases, blood and urinary amino acids, liver function tests, and blood ammonia were normal. At review 6 months later, a further episode of acute ataxia in the context of a febrile infection was reported. This had settled within a few hours, and she had not been admitted to hospital. Since then she has been well (currently 3.5 years) with normal development.

Polymerase chain reaction for the GAA triplet repeat in Friedreich's ataxia was carried out using the primers and method described by Campuzano *et al.*[2] III.1 showed two expanded alleles carrying 320 and 840 GAA repeats. III.4 was homozygous for two expansions of 660 repeats. II.4 and IV.2 were heterozygous for the GAA expansion, the expanded allele bearing a repeat of 840 triplets consistent with their carrier status. II.5 was also heterozygous for the expansion, and III.2 had no expanded alleles.

The presentation of this family with ataxic features in three generations had suggested a form of autosomal dominant cerebellar ataxia. However, the proband and his sister have clinical phenotypes consistent with Friedreich's ataxia, and this diagnosis has been established by genome analysis. The carrier status of the two other members of this pedigree manifesting ataxic features has been confirmed. This finding raises the possibility that Friedreich's ataxia carriers are at risk of developing ataxia, especially in the context of environmental insults (such as alcohol in II.4 and and viral infections in IV.2). In a recent series of 56 pedigrees, at least two heterozygous parents (both fathers) manifesting ataxic features were identified.[3] No data are available on possible environmental insults in these members. The current finding lends support to the conclusion of Lamont *et al*,[3] that a history of ataxia in preceding (or successive) generations should not preclude a diagnosis of Freidreich's ataxia. Finally, it may be fruitful to investigate those who develop spinocerebellar ataxia secondary to recognised environmental insults for their carrier status of Friedreich's ataxia.

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Intracerebral haemorrhage due to possible venous obstruction in the neck

Multiple concurrent cerebral haemorrhages in the absence of trauma or a bleeding diathesis suggest venous sinus thrombosis, multiple haemorrhagic infarcts, and haemorrhagic metastases. Iatrogenic venous obstruction is another possible cause. Patient 1 was a 55 year old obese woman who underwent a left posterior fossa craniotomy (Jannetta procedure) for trigeminal neuralgia. Examination and a CT of the head were normal. At surgery she was positioned on her right side with her head held in slight lateral flexion to place the left occipital area uppermost. During the operation the anaesthetist reported that on two occasions the pulse rate slowed only to return to normal when the retractor was immediately removed. The patient's head was repositioned to provide increased lateral flexion and because of her short neck and broad shoulders, slight Trendelenberg tilt was applied. A large artery was found indenting