Selected Summaries

Stroke and dementia with familial occurrence

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SUMMARY

Cerebral autosomal dominant arteriopathy with subcortical infarcts and leukoencephalopathy (CADASIL) is an inherited arterial disease of the brain mapped to chromosome 19. It was described between 1977 and 1994 as a new Mendelian condition which led to stroke and dementia in 9 European families. The authors studied 148 subjects belonging to 7 families. Forty-five family members (23 males and 22 females) were clinically affected. Frequent features were recurrent subcortical ischaemic events (84%), progressive or step-wise subcortical dementia with pseudobulbar palsy (31%), migraine with aura (22%), and mood disorders with severe depressive episodes (20%). All symptomatic subjects had prominent signal abnormalities on MRI with hyperintense lesions on T2-weighted images in the subcortical white matter and basal ganglia. These were also present in 19 asymptomatic subjects. The mean age at onset of symptoms was 45 years with attacks of migraine with aura occurring earlier in life [mean (SD) 38.1 (8.03) years] than ischaemic events [49.3 (10.7) years]. The mean age at death was [64.5 (10.6) years]. On the basis of MRI data, the penetrance of the disease appears complete between 30 and 40 years of age. Genetic analysis showed strong linkage to the CADASIL locus for all 7 families. The authors suggest that the disease is largely underdiagnosed.

COMMENT

CADASIL is a hereditary cause of stroke, migraine with aura, mood disorders and dementia. The diagnosis should be considered whenever MRI reveals prominent signal abnormalities in the subcortical white matter and basal ganglia. Clinical and MRI investigations of family members are then crucial for the diagnosis which can be confirmed by genetic linkage analysis.

CADASIL is a newly described entity. Post-mortem studies of affected patients show multiple, small, deep infarcts and a diffuse leukoencephalopathy much like Binzwanger's disease—a small artery disease of the brain. The underlying lesion is a vasculopathy distinct from arteriosclerosis or amyloid angiopathy and affects leptomeningeal and perforating vessels 100–400 μm in diameter. The media is thickened by an eosinophilic granular, electron-dense material of unknown origin. The disease is hereditary and is mapped to chromosome 19.

The three main characteristics for diagnosis are: (i) a history of recurrent subcortical infarcts; (ii) white matter abnormalities on MRI/CT; and (iii) one first-degree relative with strokes or dementia.

The authors point out that migraine with aura may be a presenting feature before the strokes, which may appear between 29 and 60 years of age. Mood changes and depression are not uncommon (20%). Dementia is seen in one-third of the cases initially and in 90% before death.

The condition differs from Binzwanger's disease in that the patients do not have hypertension. Migraine with aura is not seen in Binzwanger's disease and there is a positive family history. Another related condition is migraine with white matter abnormalities which has been described in cases of migraine with aura and it may well be that some of these are cases of CADASIL. It is also interesting that familial hemiplegic migraine also maps to chromosome 19. In this condition, migraine occurs in several members of a family and hemiplegia occurs as an aura or sequel.

The exact frequency of CADASIL is unknown but it is not a rare disease. The occurrence of dementia and trans-ischaemic attacks should always prompt a CT scan or MRI of the brain especially in young subjects without vascular risk factors (migraine and depression—the other characteristics—are not an indication for imaging as both are common and can easily be diagnosed on clinical grounds).

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Anticonvulsants in eclampsia: Is this the final answer?

The Eclampsia Trial Collaborative Group. (Perinatal Trials Service, NPEU, Radcliffe Infirmary, Oxford, United Kingdom.) Which anticonvulsant for women with eclampsia? Evidence from the collaborative eclampsia trial. *Lancet* 1995;**345:**1455–62.

SUMMARY

The 'eclampsia trial' which began in July 1991 was conducted at 23 centres in 8 countries. The centres in India were Vellore and Mumbai. There were two arms to the trial: (i) magnesium sulphate was compared against diazepam; and (ii) magnesium sulphate was compared against phenytoin. Each centre was given the option of joining either arm of the trial. All women with a clinical diagnosis of eclampsia entered the trial and were randomly allocated to an anticonvulsant regimen. Overall, 1687 women were randomized: 910 for the comparison of magnesium sulphate and diazepam and 777 for the comparison of magnesium sulphate and phenytoin.