Relation between migraine and stroke

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A complex bidirectional relation between migraine, mostly migraine with aura (MA), and ischaemic stroke is known. A cerebral infarction can occur during a MA, and MA is a risk factor for ischaemic stroke, particularly in young women. Conversely, cerebral ischaemia can induce MA. Both ischaemic stroke and MA might be consequences of many underlying vascular disorders. Despite the relation between migraine and stroke, migraine as a primary headache disorder is mostly benign.

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Introduction

Migraine and stroke are two commonly occurring disorders that seem to have little in common. Migraine is a benign disorder that persists throughout life; it typically starts before age 40 years and affects 12% of the population with a 3 to 1 female preponderance. Recurrent attacks of headache, sometimes preceded by transient neurological disturbances, characterise migraine. Whether migraine is a single entity, a group of related disorders, or a syndrome due to other disorders is still unclear. The diagnosis of migraine is purely clinical and strict criteria have been proposed by the International Headache Society (IHS).[1]

By contrast, stroke is an acute event that occurs in 2 per 1000 people per year at a mean age of 70 years with a 2 to 1 male preponderance. Characterised by a focal deficit of sudden onset, stroke is readily diagnosed by use of neuroimaging techniques. Cerebral infarction occurs in 80% of strokes and intracerebral haemorrhage in 20%. The cause of both types of stroke is diverse; in individual patients, particularly those who are young, the cause is commonly unknown even after extensive investigation.

Despite these differences, many studies have suggested a complex bidirectional relation between migraine and stroke,[2–4] including migraine as a cause of stroke, migraine as a risk factor for or as a consequence of cerebral ischaemia, and migraine and cerebral ischaemia sharing a common cause.

Migrainous infarction

Charcot was probably the first to recognise that migraine could cause a stroke when he wrote that "any of the symptoms occurring during 'migraine ophthalmique' can . . . become permanent".[5] His resident, Féré, reported a case of "ophthalmic migraine with repeated attacks followed by death" in a man aged 53 years who had had migraine attacks with ophthalmic and dysphasic aura since childhood and who died after 2 months of left-sided headache, visual disturbances, and right or left hemiplegia. This case is typically referred to as the first case of lethal migrainous stroke, but in the absence of autopsy, the precise cause of death is unknown.[6]

After the first report and before the first IHS classification,[7] many cases of "migrainous infarcts" were reported, including disorders as varied as "strokes occurring in migraineurs", "strokes with migrainous features", "strokes with headache", and even "long-lasting deficits without stroke".

Standard description

In the dozen cases of "fatal migraine" reported,[8–15] there is no consistent pattern of infarction; infarcts are large or small, single or multiple, cortical or subcortical, and involve the carotid and/or the basilar territories. There is no consistent pattern of arterial changes: thrombosis, embolism, spasm, dissection, and normal arteries have all been reported. Whereas in most of these cases the imputability of migraine is doubtful, repeated attacks of severe migraine could lead to focal arterial injury, comparable to spasm induced by subarachnoid haemorrhage.[8,10,12]

There are no good data on the incidence of migrainous infarctions. The single largest study[16] before the IHS classification found 7 (3%) migrainous infarcts among 244 first cerebral infarctions, corresponding to an incidence of 3 per 100 000 per year in the UK. However, the causal relation between these strokes and migraine is highly debatable because only one patient had cerebral angiography, one had echocardiography, three were hypertensive, and one had widespread atheroma.

The most common clinical sign is a homonymous field defect, such as hemianopia or hemiopic scotoma, due to a posterior cerebral artery infarct, but other territorial infarcts affecting any large artery as well as single or multiple lacunar infarcts have also been reported. Similarly, all varieties of retinal infarcts and ischaemic optic neuropathies have been described as complications of retinal migraine.[2–4]

Much diversity in the location and type of infarcts is reflected in the neuroimaging findings: most patients have occipital infarcts, but single and multiple infarcts of any size and location have been reported.[17–20] Angiography is typically normal, but spasm and occlusion of large or small arteries have been reported,[21–23] as have dissections and aneurysms,[24,25] which could be consistent with symptomatic migraine.

Vasoconstrictor medications such as ergotamine or triptans might contribute, but in some reported cases, migrainous infarction was a misdiagnosis.[26] Beta-blockers known to occasionally increase the frequency and duration of auras have also been associated with migrainous infarcts.[27] Cerebral angiography, which is known to induce migraine attacks, carries a 1% risk of

stroke. However, cerebral angiography is not more common in people with migraine than in those who do not have migraine,[28] except for patients with familial hemiplegic migraine in whom it can precipitate severe migraine attacks leading to stroke.[29]

No single mechanism could account for every type of infarct or arterial change that has been reported. Spasm,[21,22] vessel-wall hyperplasia,[12] embolism,[24] and local arterial dissection[9] might be the immediate cause of the infarct. Whereas migraine itself might cause spasm or even hyperplasia, it is unlikely to be the cause of embolism or dissection.

Formal classification

According to the IHS classification,[1,7] migrainous infarcts are a direct consequence of an unusually severe hypoperfusion during aura—ie, they occur only in patients with MA during aura, and the symptoms of the infarct are partly those of the aura. A major criterion of this cause of infarction is that other possible causes of infarction are excluded by appropriate investigations.[7] However, which investigations should be done and when is not clear. In an extensive review of over 200 cases of migrainous infarcts reported before 1988, we found only 40 cases when we applied IHS criteria, including at least a transthoracic echocardiography and a cerebral angiography of any variety.[30]

The absence of causes other than migraine does not necessarily imply that migraine is the cause. Half the ischaemic strokes in the young have no detectable cause. Sometimes during follow-up possible causes are detected, as illustrated by two cases that we reported of intracranial aneurysm and cardiac myxoma discovered years after cerebral infarcts that had initially satisfied all IHS criteria for migrainous infarcts.[31–33]

All recent studies[34–37] refer to IHS criteria and assert that they have ruled out other disorders. Nevertheless, in some large hospital series,[34,35] important investigations such as echocardiography were done in only half the cases. In case reports,[36,37] the work-up was more extensive but typically catheter angiography was not done when magnetic resonance angiography was normal. The next case is an example of the cause of stroke being identified only at angiography. A man aged 35 years with a long history of typical migraine with visual aura after jogging had such an attack and then a permanent right hemianopia due to infarction of a posterior cerebral artery. Magnetic resonance angiography showed posterior-cerebral-artery occlusion for which no cause was found on non-invasive investigations. Intra-arterial angiography, however, showed a small dissecting aneurysm of the left V3 segment with an intra-luminal thrombus (figure 1).[38]

Over-diagnosis of migrainous infarcts is probably less common than before the introduction of IHS criteria and the development of non-invasive arterial and cardiac investigations. However, according to large series, migrainous infarcts account for 0·5–1·5% of all ischaemic strokes and 10–14% of ischaemic stroke in young patients.[34,39–41] Many of these cases occur during attacks of migraine without aura,[34,35,41–45] and in two large series, they were more common than infarcts during attacks of MA.[36,45] IHS criteria might therefore be too strict, particularly because the spreading depression could occur in migraine without aura.[46] Whether these criteria are too strict is difficult to answer because migraine-like headaches might occur in cerebral infarction, particularly in the posterior-cerebral-artery territory, and in some aetiologic varieties such as dissections which are not always ruled out in such circumstances.[4] Furthermore, a detailed description of headache characteristics is not always possible in patients with acute stroke, and whether attacks of MA and migraine without aura have the same pathogenesis is unknown.[46]

The mechanism by which a migraine induces cerebral infarction is unknown. The neuronal spreading

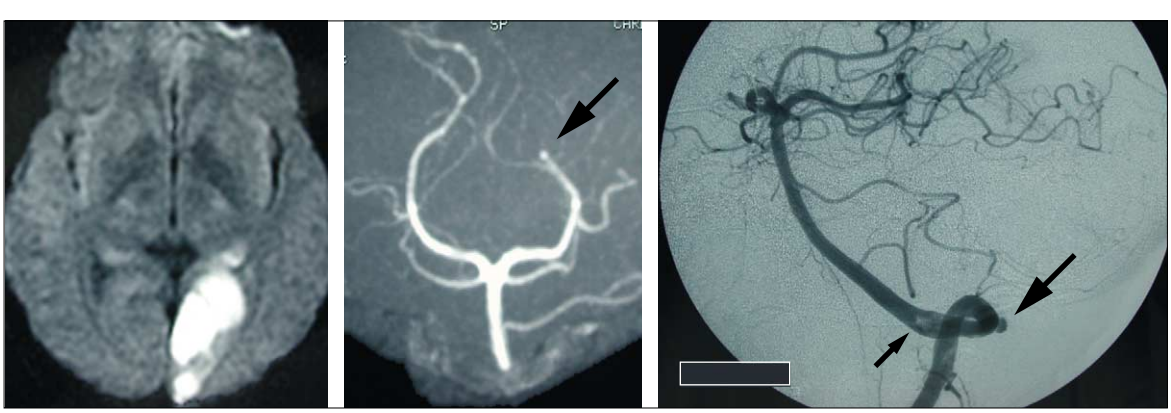

Figure 1: **Vertebral artery dissection looking similar to a migrainous infarct**
Left: Diffusion-weighted MRI of infarct of the left posterior cerebral artery. Middle: magnetic-resonance angiography showing occlusion of the posterior cerebral artery. Right: conventional angiography showing a small vertebral artery dissecting aneurysm (large arrow) with a small intraluminal thrombus (small arrow). Reproduced with permission from Doin.[38]

depression that underlies the aura is associated with oligaemia but the decrease in cerebral blood flow (CBF)—as assessed with methods including Xenon imaging, PET, and MRI—is more than 50% greater than the threshold for ischaemic injury (figure 2).[46–52] Furthermore, the decrease in CBF during aura is not accompanied by a change in diffusion-weighted imaging[51,53] and might even be associated with hyperoxia.[50]

One third of migrainous infarcts involve the occipital lobe.[34,35,45] The spreading depression originates in the occipital lobe[54,55] which is supplied by the posterior cerebral artery, the most densily innervated of the major vessels arising from the circle of Willis.[45] Thus the occipital cortex may be the most vulnerable to infarcts because of both its neuronal and arterial characteristics. An illustrative case is that of the pathologist Frank Mallory who, at age 47, had one of his typical attacks of migraine with a left scintillating scotoma but instead of completely recovering was left with an upper left quadrantic defect. He died 30 years later, and at autopsy there was an old small calcarine infarct that could not be attributed to arterial disease or any other cause.[56]

Migrainous infarcts, due to severe hypoperfusion during an attack, are rare and probably over-diagnosed.[3,30,57–61] They mostly involve the posterior-cerebral-artery territory and are more common during attacks of MA than of migraine without aura. The precise mechanism of this severe hypoperfusion is unknown.

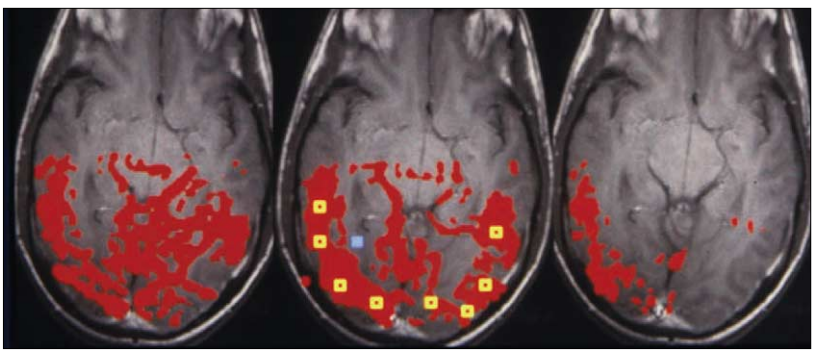

Figure 2: **Serial T2-weighted MRI of a patient with migraine during a visual aura of expanding and contracting left homonomous quadrantanopia**
Increased T2-weighted contrast intensity (an indirect measure of hyperoxia) of bilateral regions in the occipital cortex grey matter and the red nucleus and substantia nigra bilaterally is shown (red); the opposite would occur during ischaemia. Yellow squares show signals from grey matter and the blue square shows the absence of a signal from white matter—spreading depression is a grey-matter event. Reproduced with permission from the American Academy of Neurology.[50]

Migraine: a risk factor for ischaemic stroke

Epidemiology

Whether migraine is a risk factor for ischaemic stroke has been addressed in two cohort studies, nine case-control studies, several neuroimaging studies, and a meta-analysis. In the two cohort studies,[62,63] the risk of ischaemic stroke was slightly more than doubled in patients with migraine. Among the nine case-control studies,[64–72] three found no increased risk, taking into account all age groups. By contrast, all case-control studies found an increased risk in young women (table). The risk among young women is higher during MA (RR 6·2, 2·1–18·0)[67] and increased by smoking (RR 10·2, 3·5–29·9),[67] oral contraceptives (RR 13·9, 5·5–35·1),[67] and both smoking and taking oral contraceptives (RR 34·4, 32·7–36·1).[70] However the absolute risk of stroke in young women with migraine is low: 18 per 100 000 per year.[67,73] A recent meta-analysis confirmed an increased risk of ischaemic stroke in patients with migraine, with relative risks of 2·16 (1·89–2·48) for migraine in general, 2·88 (1·89–4·39) for MA, 1·56 (1·03–2·36) for migraine without aura, and 2·76 (2·17–3·52) for women younger than 45 years.[73] Despite several possible biases, such as selection, diagnosis, recall, or publication biases, this increased risk is probably real, particularly with regards to MA in young women. The reason the effect of migraine as a risk factor for stroke decreases with age is unknown. Improvement of migraine or an increased prevalence of other vascular risk factors could explain the decrease in risk.

Reference	Patients	Migraine diagnosis	Stroke risk in women with migraine
66	212 with IS aged 15–80 years 212 controls matched for sex, age, hypertension	Direct interview by neurologist IHS criteria	OR 4·3 (1·2–6·3) in women <45 years
67	72 women hospitalised for IS aged 15–44 years 173 controls matched for age	Direct interview by neurologist IHS criteria	OR 3·0 (1·5–5·8) OR 6·2 (2·1–18·0) for MA
68	692 with IS 591 controls matched for age and sex	Questionnaire	OR 2·8 (p<0·001)
69	308 with TIA or IS aged 15–44 years 591 controls matched for age and sex	Direct interview by neurologist IHS criteria	OR 3·7 (1·5– 9·0) in women <35 years OR 8·6 (1·0–75·0) for MA
70	291 with IS aged 20–44 years 736 controls matched for age	Direct interview by neurologist IHS criteria	OR 3·5 (1·3–9·6) OR 2·9 (0·6–13·5) for migraine without aura OR 3·8 (1·2–11·5) for MA
72	160 with first IS or TIA aged <46 years 160 controls matched for age and sex	Direct interview by neurologist IHS criteria	OR 2·11 (1·16–3·82) OR 2·68(1·25–5·75) in women

IS=ischaemic stroke; TIA=transient ischaemic attack.

Table: **Case-control studies of migraine and stroke in young women**

Two recent population-based studies found a relation between MA and ischaemic stroke: the Atherosclerosis Risk in Communities study[74] on 12 750 patients (OR 2·81, 1·60–4·92) and the Women's Health study[75] on 39 754 US health professionals older than 45 years (OR 1·71, 1·11–2·66). Women with MA younger than age 55 years had a greater increase in risk (OR 2·25, 1·30–3·91).[75] Neither study found an association between migraine without aura and ischaemic stroke.

Neuroimaging studies

Some neuroimaging (CT and MRI) studies in patients with migraine have shown an increase in white-matter abnormalities compared with controls,[76–82] with an odds ratio of 3·9 (2·3–6·7) in a meta-analysis of seven case-control studies.[83] A study of 161 patients with MA, 134 with migraine without aura, and 140 controls found no difference in the overall prevalence of silent infarcts except in the cerebellum (5·4% in patients with MA *vs* 0·7% in controls, OR 7·1, 0·9–55·0) and when the frequency of attacks was more than once a month (OR 9·3, 1·1–76·0).[84] The load of periventricular white-matter abnormalities were not different for patients with MA and controls, but deep white-matter abnormalities were high in women with migraine (OR 2·1, 1·0–4·1). Risk for white-matter abnormalities was similar in patients with MA and migraine without aura, and ergotamine increased the risk. The authors hypothesised that white-matter abnormalities were due to ischaemic insults,[85] which has led to the suggestion that migraine could be a progressive brain disorder.[86]

The mechanism of the increased risk of ischaemic stroke in migraine is unknown. A first hypothesis is that it is due to migrainous infarcts, but the incidence of these infarcts, at least as defined by the IHS, is too low to explain the increased risk. Further, in case-controlled studies, ischaemic strokes mostly occur between migraine attacks.[66,67]

A second hypothesis is that migraine is a risk factor for some aetiopathogenic subtypes of ischaemic strokes. This hypothesis seems plausible for cervical-artery dissections. Migraine was twice as common in patients with cervical-artery dissections than in controls in two case-control studies; the odds ratio of 3·6 (1·5–8·6) increased to 6·7 (1·9–24·1) in patients with multiple dissections.[87,88] In some patients, the arterial wall could play a role in migraine, as also suggested by the increased serum-elastase activity in patients with migraine.[89] Again, the number of dissections in patients with migraine is too low to explain the increased risk of stroke.

Patent foramen ovale, a risk factor for ischaemic stroke (OR 1·83, 1·25–2·66),[90] might have a bidirectionnal relation with MA. In three small retrospective case-control studies, patent foramen ovale was two to three times more common in patients with MA than in controls.[91–93] Similarly, in patients with ischaemic stroke[94,95] or decompression illness,[96] MA was twice as common in patients with patent foramen ovale than in those without. No association was found between patent foramen ovale and migraine without aura. In several studies,[93,97,98] patent-foramen-ovale closure was associated with a decrease in attacks of migraine. However, these data must be interpreted with caution because of several methodological shortcomings and potential biases, including recall bias, use of antiplatelet drugs, and also the placebo effect of any treatment for migraine, particularly those that are invasive. A large double-blind randomised trial of patent-foramen-ovale closure in MA prophylaxis is underway in the UK. Patent foramen ovale is probably associated with MA. Is any such association a mere comorbidity or is it causal? Is spreading depression triggered by focal cerebral ischaemia or by substances or by hypoxic blood bypassing the lung filter and reaching the brain in large amounts? Is patent foramen ovale related to MA an example of symptomatic migraine having little to do with migraine as a primary headache disorder (ie, migraine without aura)?

A third hypothesis is that there is a general increase in the risk of ischaemic stroke in migraine, particularly in young women. A relation between this risk and female hormones seems unlikely because the effect of oestrogens is crucial in migraine without aura, whereas the risk of ischaemic stroke is mostly high in MA.[99] Conventional vascular risk factors are conflicting: an inverse relation has been found between migraine and blood pressure,[100,101] and there is no increase in the risk of major coronary heart disease[102,103] or in other vascular risk factors such as homocysteine, vitamin B12, and apo-LpA[103] in migraine in general. However, in a recent population-based study in the Netherlands[104] patients with MA were more likely to have an unfavourable cholesterol profile and high blood pressure, with about doubled odds of a high Framingham risk score for coronary heart disease. Inconsistent results have been found for the various biological or clinical markers of thrombotic risk[105,106] studied, such as platelet activation, factor V Leiden mutation,[107] von Willebrand factor,[108] prothrombin factor 1.2,[109] platelet leucocyte aggregation,[110] antiphospholipid antibodies,[111–113] and livedo reticularis.[114,115]

Increased risk due to treatments used in migraine, particularly vasoconstrictors, is supported by the increase in white-matter abnormalities[84] and in mortality[116] found in patients taking ergotamine, but two recent studies found no increase in severe vascular events with triptans.[116,117] Furthermore, drugs widely used in migraine, such as aspirin and non-steroidal anti-inflammatory drugs, decrease the risk of cerebral ischaemic events.

The increased risk of ischaemic stroke in patients with migraine, mostly for young women and patients with MA, might not be explained by a single factor.

Migrainous infarcts, dissection, infarcts related to patent foramen ovale, and infarcts induced by drugs might be involved. An association with known and as yet unknown vascular risk factors is most likely. Risk factors might be different for MA and migraine without aura; one study found that patients with MA and stroke had a greater prevalence of patent foramen ovale and more oral contraceptive use than patients with migraine without aura.[106] However, patients with migraine without aura who had stroke commonly had conventional risk factors or coagulopathies. A relation between an increased risk of stroke in migraine and chronic headache—which has been shown in men only, suggesting different mechanisms[118]—needs explanation.

Migraine caused by cerebral ischaemia

Ischaemia-induced symptomatic migraine attacks might be more common than migraine-induced ischaemic insults.[119] Among 15 patients thought to have a migrainous infarct, four had atherothrombotic or cardioembolic infarcts, three had daily attacks of MA with a tight carotid stenosis or occlusion, three were thought to have a migrainous infarct, and in five the relation between cerebral ischaemia and migraine was unclear. Cerebral infarction can thus present with migraine attacks at onset[120–122] and tight carotid stenosis, or occlusion with persistent focal low flow might induce several attacks of MA. Such ischaemia-induced migraine attacks are rare in atherothrombotic or cardioembolic occlusions and have been reported mostly in dissections.[123,124] The degree, location, and duration of ischaemia, the nature of the underlying arterial disease, and factors such as history of migraine, age, and genetic background are probably all involved in ischaemia induced attacks of MA, which should not be confused with migrainous infarctions.[2,60,124] For example, a woman with migraine who had an unusually severe attack followed by two cerebral infarcts was diagnosed with migrainous infarcts after an extensive work-up that included an angiogram and two transoesophageal echocardiograms. She died a few days later and autopsy revealed a carcinomatous endocarditis. Triggering of MA attacks by focal cerebral ischaemia is further suported by animal studies showing that cerebral ischaemia can induce cortical spreading depression.[125] Clinical and experimental evidence suggests that acute focal cerebral ischaemia can trigger one or several attacks of MA.

Common cause of migraine and cerebral infarction?

Several vascular disorders, local and general, can cause stroke and are also associated with a high risk of migraine, mostly MA. Arteriovenous malformations are the classical cause of symptomatic migraine[125] but well-documented cases of MA ceasing after removal of arteriovenous malformations[126] are balanced by cases being unchanged after surgery.[127] A causal relation is supported by the side of the aura being contralateral to the arteriovenous malformations and headache, and ipsilateral to the arteriovenous malformations.[127] Other examples of disorders with arteriovenous shunts that might be associated with MA include leptomeningeal angiomatosis (Sturge Weber syndrome)[128] and hereditary haemorrhagic telangiectasia.[129] Attacks of MA have also been anecdotally reported in patients with cerebral venous thrombosis,[130] saccular aneurysms,[31] and with the poorly understood syndrome of reversible cerebral segmental vasoconstriction,[131] which might occur in patients with migraine.[132]

Ischaemic stroke and MA are major features of three syndromes characterised by chronic alterations of the vessel wall of small arteries: mytochondrial myopathy, encephalopathy, lactacidosis, and stroke (MELAS),[133] cerebral autosomal dominant arteriopathy with subcortical infarcts and leucoencephalopathy (CADASIL),[134,135] and autosomal dominant vascular retinopathy, migraine, and Raynaud's phenomenon.[136] Migraine as a part of MELAS syndrome, which is associated with mitochondrial DNA mutations, raises the possibility that mitochondrial dysfunction could play a role in MA and in migrainous stroke but the main MELAS mutation (3243) could not be detected in two groups of patients with MA.[137] However, other yet undetected mutations could play a role. CADASIL is an autosomal dominant disease of vascular and smooth muscle cells due to Notch-3 mutations,[134,138] mostly characterised by leucoencephalopathy, small deep infarcts, and subcortical dementia. MA is present in one third of patients, and if present, is typically the first symptom of the disease, presenting about 15 years before the first ischaemic stroke.[139] Symptoms of migraine are those of MA as defined by IHS, but there is an unusually high rate of atypical attacks, with prolonged aura or with acute-onset aura without headache.[135,139] MRI of patients with CADASIL always shows striking white-matter abnormalities and, later in the disease, small subcortical infarcts. These abnormalities must not be interpreted as migraine related white-matter abnormalities. The mechanisms underlying MA in these chronic small-artery diseases affecting the brain are to be established. In patients with CADASIL, MA is not a consequence of subcortical infarcts that occur 10–20 years after migraine onset.[135,139] Chronic subcortical hypoperfusion is also unlikely to be involved because MA does not occur in other varieties of small artery diseases such as hypertensive lipohyalinosis, and in CADASIL there is no difference in the frequency and distribution of white-matter abnormalities between patients with and without MA.[135] Another hypothesis is that MA directly relates to dysfunction of smooth muscle cells of meningeal and cortical vessels, triggering spreading depression.[4,135] Another possibility is that if the cells

signalling abnormality (resulting from the mutation) extend and reach neurons, the resulting hyperexcitable membrane instability could predispose to spreading depression.

Ischaemic strokes and MA might also occur in many general vascular disorders: cardiac disorders such as patent foramen ovale and mitral valve prolapse,[140,141] and blood disorders such as essential thrombocythaemia,[142] thrombocytopenia,[143] leukaemia,[144] and systemic lupus erythematosus.[145] Some cases could be explained by comorbidity, others by ischaemia-induced attacks of MA, and others by biochemical factors such as serotonin changes in platelet disorders or to some immunological changes, particularly in antiphospholipid syndrome and systemic lupus erythematosus.

Migraine mimicking cerebral ischaemic events

Migraine auras or transient ischaemic attacks?

Transient ischaemic attacks and migraine auras are both characterised by temporary focal neurological deficits; differential diagnosis, which is made from the patient's description, is clear when symptoms are typical. In migraine auras, positive symptoms such as scintillations progress gradually over several minutes and last about 30 min, after which a severe headache commonly occurs. In transient ischaemic attacks, there is a focal deficit of sudden onset that typically lasts less than 15 min, without ensuing headache. MA typically starts in childhood whereas transient ischaemic attacks tend to occur in adulthood. Nevertheless, migraine can present with transient-ischaemic-attack-like symptoms—eg, haemianopia without headache—for the first time after 40 years. Also transient ischaemic attacks, particularly basilar transient ischaemic attacks, can sometimes be associated with headache.[4,146–148] The crucial distinctive clinical feature is the mode of onset. Thus, among 68 patients with migraine, 52 had a slow progression of symptoms, which was absent in 57 patients with posterior-cerebral-artery occlusion.[146]

Long migrainous deficit or cerebral infarction?

Migrainous infarcts should be differentiated from long lasting neurological symptoms that can occur after a migraine with no neuroimaging evidence of infarction and with complete recovery. This has been well documented in familial hemiplegic migraine, an autosomal dominant variety of MA in which hemiplegia, commonly associated with aphasia, haemianopia, drowsiness, and sometimes coma, can persist for several weeks before complete recovery.[149,150] During these severe attacks, PET and magnetic-resonance-diffusion studies have shown patterns of change that are not typical of an infarct: increased CBF with a moderate decrease in the cerebral metabolic rate of oxygen pointing to a severe neuronal dysfunction[149] and extensive restricted diffusion completely resolved in 9 days.[151] Magnetic resonance diffusion with apparent diffusion coefficient maps is now the crucial investigation for differentiating these long-lasting migrainous deficits from infarction.

Search strategy and selection criteria

References for this review were identified by searches of MEDLINE from 1966 to June 2005 for "migrainous infarcts". Several articles were also identified through searches of the authors' files. Several references were excluded; the final reference list was generated from original references relevant to the topics covered in the review.

Practical implications

The bidirectional relation between migraine and ischaemic stroke, though poorly understood, has important practical implications. Cerebral infarcts in patients with migraine should be investigated and treated as any cerebral infarct in the young and followed up with the usual approaches to secondary stroke prevention, such as cessation of oral contraceptive use and smoking, and daily intake of antiplatelet drugs. Ergot derivatives and triptans should be avoided.

The IHS has published recommendations on oral contraceptive use: young women with migraines should avoid smoking and have a regular check for conventional vascular risk factors.[99,152] Although no systematic contraindication for combined oral contraceptive use exists, a low oestrogen combination should be used. In MA or when vascular risk factors are present, progestagen only should be used. Regular physical activity should be encouraged. After menopause, migraine is not a contraindication for the use of hormone replacement therapy, but stroke risk with hormone replacement therapy needs to be weighed-up.[153]

At this time, data suggesting that migraine could be a progressive brain disease[85] is too limited to start systematic investigations with MRI, or to recommend lifetime migraine prophylaxis or use of antiplatelet drugs. Patent-foramen-ovale detection is not indicated in patients with migraine, unless they also have a history of ischaemic events and until it is shown that patent-foramen-ovale closure is effective, either for long-term migraine prophylaxis or for reduction of the risk of recurrent ischaemic stroke. No indication exists, even in patients with MA, for a systematic detection of all the general or cerebral disorders that can cause both migraine and stroke. A simple blood-cell count and blood-sugar and lipids measurements are recommended as part of the assessment of risk factors, particularly in young women who take oral contraceptives. There is also a case for recommending neuroimaging in patients with constantly unilateral aura and contralateral headache, symptoms suggesting unilateral brain dysfunction. In patients with migraine

and white-matter abnormalities, systematic genetic testing for syndromes such as CADASIL is not recommended, at least until an effective treatment is available. When migraine auras and transient ischaemic attacks cannot be differentiated, complete ophthalmological, neurological and vascular work-up should be done, and even if no vascular cause is found, long-term aspirin use could be recommended, particularly for those older than 50 years.

Conclusion

Research findings suggest a bidirectional relation between MA and cerebral ischaemia; however the evidence is very weak for migraine without aura. One should be extremely cautious about simplistic and eventually deleterious generalisations such as contra-indicating oral contraceptive use in all young women with migraine, presenting migraine as a progressive brain disease, or suggesting patent-foramen-ovale closure as a treatment for migraine. Migraine is too complex and poorly understood to allow such oversimplifications. Like epilepsy, migraine is both a disease and a symptom but whether, as a disease, it is a single entity or a constellation of related disorders is unknown. From the available evidence, migraine as a primary headache disorder, though painful and often detrimental to quality of life, is an essentially benign condition.

Authors' contributions

MGB wrote the first draft, which was reviewed and modified after extensive discussion with KMAW.

Conflicts of interest

MGB and KMAW have been investigators in several trials of stroke prevention and acute treatment, as well as migraine prophylaxis and acute treatment.

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