Clinical Problems

Migraine Variants

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My interest in the mechanism of migraine and its variants was initiated by Sir Charles Symonds. His classical paper in 1952 has fortunately been reprinted in his *Studies in Neurology*.¹ I am glad to acknowledge a debt.

The diagnosis of classical migraine is usually straightforward and can be made largely on the history. The recognition of its variants, however, especially when the headache element is not prominent, can present many difficulties.

Mechanism of Attack

Though migraine has been known and clearly described for some 2,000 years its cause is still not recognized. The diagnosis therefore rests on the clinical history and findings. In contrast to this lack of aetiology, a good deal is established about the pathophysiology or mechanism of the attack. An abnormality of blood-vessel behaviour is the background. During the earliest aura phase vasoconstriction, mainly intracranial, produces ischaemia of localized areas of the brain with consequent dysfunction. At the same time, or shortly after, the extracranial blood vessels show an increase in pulsation and external calibre and are often tender. It is blood coursing through these abnormal vessels that causes the headache. This, with modifications, is still the accepted theory.

BIOCHEMICAL CHANGES

Accompanying these changes is also evidence of biochemical upset. This may be local, in relation to the affected blood vessels, but also more generalized, in electrolytes and fluid balance particularly. It is still disputed whether these are primary or secondary to the attack.

Amines. Alterations in the level of certain biologically active amines may play an important part. Since much current research on migraine is occupied with this possibility it requires some mention. The amines concerned are those which have particularly vasomotor and pain-producing effects. **Serotonin** (5-hydroxytryptamine) is currently receiving most attention. This substance has vasoconstrictor properties. There is evidence that plasma levels are increased at the onset of a migraine attack and that as the headache develops they are lowered.² In addition, it may produce oliguria, reduced motility of gut, and nausea. At first sight this might suggest a chemogenic mechanism for many of the features of

migraine. Initially raised serotonin levels would cause vasoconstrictor, gastrointestinal, and renal changes, and as the level falls vasodilatation could result.³ Indeed this view led to the early therapeutic trials of methysergide, shown in vitro to be a serotonin antagonist.

The detailed timing of signs and symptoms in the attack, however, still presents difficulties for this theory, and we are also left with the problem of what causes the initial change in serotonin level. Noradrenaline and aldosterone have also been postulated as possible agents, but studies of the former have given conflicting results. With serotonin there are technical difficulties in obtaining reliable estimations and in interpreting results. Its role in migraine is therefore still sub judice.

Plasma Kinins. A number of pain-producing substances of the group of plasma kinins, known to be active in causing pain from local tissue trauma, have also been found to be present during the attack at the site of blood vessels affected by migraine; but here again whether they are cause or effect remains in question.

Vagaries of Migraine

Since some variants of migraine present in a very alarming way it is important to recognize their true nature. Apart from this the content of these variants may have interesting implications for the pathophysiology of migraine, and their study may finally lead to a clearer understanding of the aetiology.

Before describing the clinical picture of some of these conditions, which may depart very considerably from classical migraine, I must give the reasons for accepting them as migrainous. If a patient who is known to be subject to classical migraine develops episodes which differ in detail from his usual attacks but still have clear resemblances the diagnosis is suggested. When the attacks differ considerably but remain paroxysmal, episodic, and benign this also is suggestive. Family history can help. When variant attacks occur de novo in a patient the family history may contain examples of classical migraine or, still more helpful, examples of the variant which, in the family also, merged with the classical type. The situation when an unusual variant presents as the initial attack is more difficult. Here a knowledge of migraine and its vagaries and the repetition of stereotyped attacks which prove to be benign is of some help. This is one of the areas for clinical judgment, and particularly for careful consideration about how far ancillary tests should be pursued in excluding other diseases.

ROUTINE TESTS

When the condition presents as a cerebral episode—and most do—a number of routine tests need to be considered. Skull x-ray films and a lumbar puncture may provide broad

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screening tests. If localized cerebral disease is implied electroencephalograms (E.E.G.s), brain scans, and arteriograms usually come under consideration. The E.E.G. may show abnormalities simply as a result of migraine, but since these are usually diffuse and slight it can be of some value in excluding an organic focal lesion, where pronounced and persistent local abnormality may occur. Brain scans are now increasingly used, partly because they incommode the patient so little. They are useful in excluding local abnormality in the hemispheres but are of little value in posterior fossa lesions. The angiogram is here a two-edged weapon: it may show a local vascular abnormality unequivocally; but unfortunately in certain forms of migraine it may precipitate an attack, and at times a severe one. For this reason it must be used with some caution. Skull x-ray films and a lumbar puncture will often suffice to exclude serious organic disease. The need for all these tests probably decreases with clinical experience, but they remain essential in the occasional case.

Clinical Variants

Variants may present as extensions or modifications of the basic classical picture involving essentially the cranium and nervous system or, more rarely, as a picture that is entirely extracranial. I will not attempt to cover all possibilities but will mention those examples that I myself have seen fairly commonly and those which may be especially alarming if the diagnosis is not recognized. Their incidence is difficult to assess. In some 2,000 cases of migraine seen during the past 25 years over 80% have been of classical type or close to it. Of the other 20%, which may be regarded as variants, most have been basically cranial and neurological in their presentation. A smaller proportion—the rarities—have been extracranial. I will discuss them roughly in their order of frequency, but would emphasize that the cases I see are inevitably selected.

BASILAR MIGRAINE

In 1961 Bickerstaff defined a group of cases which he referred to as basilar migraine because most of the signs and symptoms accompanying the attack could be related to abnormalities of vertebrobasilar circulation.⁴ The aura in these cases may be of vertigo, ataxia, and dysarthria. When vision is involved it tends to be bilateral, and fortification spectra and scotomata may be replaced by total loss of vision. Tinnitus sometimes occurs. Somatic sensory symptoms are also bilateral—numbness and tingling of both hands, sometimes of the feet, and of the face, lips, and tongue. Vomiting is a prominent feature and may occur early. During the attack pronounced nystagmus may be found. A feeling of faintness and actual loss of consciousness are not uncommon. A throbbing, bilateral, mainly occipital headache usually occurs. The rapid, complete loss of vision may be alarming, as may be the brainstem signs. Distribution of headaches may add to the diagnostic difficulty. Fortunately in most attacks the aura is brief, but vision is occasionally lost for half an hour or more. The fully-developed picture is uncommon, but minor forms with bilateral sensory symptoms are not infrequent: more often in women than in men and in the young than in the old.

HEMIPLEGIA

Hemiplegic migraine varies from the classical type in several respects. The aura is of a motor and sensory hemiplegia, which may be dense. Headache may accompany or even precede the aura. Dysphasia occurs when the hemiplegia is right-sided, but some general confusion is often present even without dysphasia. Sometimes drowsiness is pronounced and

the picture almost one of coma. The signs and symptoms may last for days rather than hours, and the whole picture becomes very alarming. Some of these cases seem to be precipitated by mild head trauma, which adds to the diagnostic confusion. A family history of very similar pattern is not uncommon and if it can be obtained is helpful. These cases, however, especially in their first attack, are likely to run the gamut of neurological investigation, particularly as the C.S.F. during the attack may show a rise in cells and protein.⁵ These cases also are especially liable to have an attack precipitated or worsened by angiograms.

As with basilar migraine, this type is rare in its full form, but minor degrees involving hemiplegia are not uncommon. Some people distinguish between a syndrome of familial hemiplegic migraine—the clearly-defined picture I have described—and milder forms in which migraine with a hemiplegic aura occurs.

CLUSTER HEADACHES

A variety of migraine now known as cluster headaches was described by B. T. Horton and his colleagues.⁶ The nomenclature and the clinical picture were rather confused for a time because in his earlier descriptions he claimed that histamine desensitization cured the condition and therefore referred to it as histamine cephalgia. This name was generally but not completely abandoned some years later when the claim for a specific treatment was fading out, and the descriptive term of cluster headaches, suggested by E. C. Kunkle and his colleagues, was adopted.⁷ The situation, however, was further confused, and still is somewhat, because the clinical syndrome so clearly described resembled closely that mentioned by Harris as early as 1926 under the name "migrainous neuralgia."⁸ To this has now been added the further term "facial migraine." Thus four names, still occasionally used, refer to the same condition.

The clinical picture is characteristic. Headaches occur in bursts or clusters, with long free intervals—weeks, months, or even years. They are severe and usually periorbital or retro-orbital. Their severity is notable, and people who are otherwise stoical may be terrified of their recurrence. They do not have the usual vascular throbbing character but are described rather as sharp and stabbing. During a bout they often occur at the same time in each 24 hours, and the 2–4 a.m. period is common.

A point of diagnostic importance is the common occurrence of local autonomic signs, tearing of the eye, nasal congestion, local redness of the skin, sometimes with sweating, and less often a partial Horner's syndrome on the side of the pain. The severity of the pain, its abrupt onset, and its character all make differential diagnosis from tic douloureux important. The age incidence, however—much younger than in tic—the association with other forms of migraine, and the characteristic autonomic signs distinguish it. Response to treatment can also help. The condition does not respond to carbamazepine, but often shows a clear-cut response to ergotamine. On the whole the earlier claims for histamine desensitization have not been fulfilled. This variant is infrequent on its own—though my impression is that its frequency is increasing—but it not uncommonly occurs interpolated with attacks of a more classical form. It is commoner in men than in women, and in the young rather than in the old.

OPHTHALMOPLEGIC MIGRAINE

This type of migraine is distinguished by a motor aura of usually unilateral ophthalmoplegia, the sixth and third nerves being commonly involved. Headache is often insignificant, so that it may present as episodic ophthalmoplegia. The condition seems to have been more common before angiograms

were used in investigation. It is suggested, therefore, that a number of these cases were really "symptomatic" migraine due to expansion or leakage from an intracranial aneurysm or other vascular malformation in the region of the oculomotor nerves. Nevertheless, not all cases can be thus explained, and it is still seen without angiographic or other evidence of fixed vascular abnormality. The ophthalmoplegia may, like hemiplegia, last some days. A family history of similar type may be elicited. Onset may occasionally be early, in the first decade of life. The syndrome is often unaccompanied by other migrainous attacks. Here, as in the hemiplegic type, a range of neurological investigations are probably required for diagnosis.

AURA WITHOUT HEADACHE

A difficult problem can sometimes be presented by the occurrence of the aura without any headache. Thus the patient arrives with an isolated neurological episode without any clue to its cause. When classical migraine has occurred in the personal or family history the problem is easier. This is usually the case. A common form to present thus is the attack with visual aura. This is then replaced by the emergence of sudden homonymous scintillating scotomata with no headache. Rarely, individuals may complain only of this symptom throughout their life, and the clue to diagnosis then lies in a positive family history. When the symptoms are visual and brief they do not cause much anxiety; but when hemiplegia or dysphasia or some of the more emphatic accompaniments of basilar migraine occur without headache, both patient and doctor may be more concerned. In the basilar condition the cerebral symptom may sometimes be vertigo or vertigo and tinnitus. The diagnostic distinction from Ménière's syndrome then becomes important.

In one patient of mine, whose case must be regarded as extremely rare, recurrent bouts of dense hemiplegia, quite unaccompanied by headache, occurred every few months for some 20 years. He was seen by a number of neurologists in Britain and abroad. Investigations were profuse, but no clear diagnosis was ever suggested. I have labelled his case as migraine on the tenuous basis of a family history of classical attacks.

Extracranial Variants

Before I discuss the extracranial variants I should perhaps mention a type of migraine which, though not strictly a variant, may be unusual in its setting and is topical. There is no doubt that attacks of migraine are occasionally precipitated by the contraceptive pill. Classical migraine arising *de novo* has been described. More often headaches of vascular type without aura occur. They seem to be related to the relatively high oestrogenic preparations, and so, we may suppose, will become less common with the new less oestrogenic pills. In view, however, of the possible vascular catastrophes that very rarely occur in this situation, if a patient does develop migraine, particularly with an aura, the type of contraceptive and the particular preparation used should be reviewed.

With the exception of abdominal pictures, the extracranial variants of migraine are rare. In childhood cyclical vomiting or the bilious attack is now generally regarded as an early

form of migraine. It is certainly true that if one investigates the past history of those who have migraine a history of cyclical vomiting is found to be far commoner than in a control population with other forms of headache, as J. W. Lance has recently confirmed.² The condition is common and well recognized. Occasionally, however, attacks occur in which vomiting is severe and prolonged, constipation absolute, and abdominal pain pronounced. Bowel sounds may be absent. In these circumstances the occurrence of previous less severe attacks which have ended spontaneously is reassuring. In an initial attack, however, surgical opinion may favour laparotomy. Since attacks usually last 48 hours or so, time will sometimes decide the issue. One recent case was that of a child whose parents were abroad and who had changed school frequently. When I saw him after some years of attacks the history included two negative laparotomies—a reminder of the value of record linkage.

Very rarely, a true abdominal migraine occurs in adult life. Here the presentation may be a sudden severe abdominal pain with vomiting and prostration. Electrolyte and fluid balance upsets follow the vomiting, and abdominal rigidity may be pronounced. Here again the brevity of the attack, a history of similar episodes proved benign, or of other evidence of migraine may help the diagnosis. In an initial attack these cases require very careful assessment to avoid a laparotomy.

Though not strictly a variant loss of consciousness in association with migraine should be mentioned. This is an occasional part of basilar migraine. It also occurs at the height of a severe headache or when vomiting has been prolonged in some patients; and, again rarely, patients with typical migraine may, often in their middle years, start having attacks of loss of consciousness of vasomotor syncope type unassociated with their migraine attack. These are not the same as frank epilepsy occurring in association with migraine and should not be labelled epileptic. The two may be linked, however, via a genetic factor, since those migraineurs who lose consciousness in this way may also be those in whom there is a family or personal history of epilepsy.

Conclusion

I have not discussed treatment, a large and important subject, and would only say that ergotamine tartrate remains the mainstay in classical and other forms of migraine. It is important to use an effective dosage, which may be larger than the traditional one, and to get the drug into the circulation as rapidly as possible.

In conclusion, all variants of migraine are far less common than the classical form, and many merge into mere fluctuations of the classical picture.

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