CHAPTER 7

THE WOMAN WITH THE NUMB HAND AND FACE

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Case History

A 22-year-old woman arrived at the emergency department with numbness of the right hand and face, and difficulty expressing herself. Her symptoms had begun while at work. She had first noted tingling in her right thumb. Over about 5 minutes, the tingling and associated numbness had spread to all the fingers of the hand and up the right arm to the midforearm. The sensation then began to affect her face, with progressive involvement of the right cheek, mouth, and the right half of her tongue. Her symptoms reached their maximum anatomic involvement about 10 minutes after onset in the right thumb. She then developed some difficulty expressing herself as well, but this was short lived, lasting only 10 to 20 minutes. The numbness persisted for almost 3 hours. About 90 minutes after the numbness began, she developed a mild constant left-sided headache. This became more severe later in the evening, with moderate pain intensity and some nausea. The headache lasted 5 or 6 hours.

In the emergency department, the only positive neurologic finding was some evidence of patchy sensory loss to pinprick over the right hand and face. When seen in follow-up several days later, her examination was normal.

When questioned about her past history, she indicated that she had begun to experience episodes of numbness and tingling in the right hand 2 years previously. Since that time, she had had several of these episodes. One year ago, she had a more intense attack in which the numbness had gradually progressed to involve the right forearm. This episode had also lasted somewhat longer, perhaps a total of 30 minutes. She could not recall any significant headache with these attacks, and denied any past history of significant headache.

She had been taking oral contraceptives for 4 years, and was currently on a preparation of 30 μg of ethinyl estradiol.

Questions about This Case

- What is the most likely diagnosis, and what would be an appropriate differential diagnosis?
- If her symptoms are the result of migraine, how would you specifically classify her migraine type?
- What investigations should be done?
- Is the fact that she is taking oral contraceptives important, and if it is, why?
- What would be your advice to her with regard to the treatment and prevention of her attacks?

Case Discussion

Diagnosis

The most likely diagnosis for this patient for most of her attacks would be migraine aura without headache (category 1.2.5, using the classification of the International Headache Society [IHS]). Her most recent attack might qualify for migraine with aura (IHS 1.2), in that she did have a unilateral headache of moderate intensity with associated nausea afterwards. However, to make this diagnosis, two attacks are necessary, and she had had only one. Finally, her aura was prolonged with one symptom (numbness and tingling) lasting 3 hours, well beyond the 60-minute time limit imposed by the IHS. Therefore, if classified as migraine with aura, she would be classified as having migraine with prolonged aura (IHS 1.2.2).

At the time when she came to the emergency department, with symptoms at that point of over 2 hours' duration, one could consider whether she was developing a migrainous infarction (IHS 1.6.2). Consistent with this diagnosis, she had persistent symptoms of the kind that occurred with her usual migraine aura but to make a

clinical diagnosis of migrainous infarction, the neurologic deficit must still be present to some extent 7 days later. Alternatively, the diagnosis can be made if neuroimaging demonstrates infarction in the relevant area.

The differential diagnosis would include a transient ischemic attack of the usual type secondary to an artery-to-artery embolus or an embolus of cardiac source. A third consideration would be a partial (focal) seizure, perhaps arising from a structural lesion in the left cerebral hemisphere.

For several reasons, migraine would be by far the most likely diagnosis in this patient. Her symptoms showed many features typical of the migraine aura.

- Her symptoms showed a slow progression through the anatomically involved areas, taking 10 minutes to progress from their onset in her right thumb to the time of maximal anatomic involvement of the right hand, forearm, face, and tongue.
- Her symptoms had pronounced positive components. Very considerable associated tingling was present in addition to the numbness.
- Involvement of the hand and lower face is a common form of somatosensory migraine aura. In recognition of this, auras of the type described by our patient have been called the "cheiro-oral" (hand-mouth) syndrome.

In addition, our patient had no significant cardiovascular risk factors, apart from the use of oral contraceptives (OCs), and had no signs on examination to suggest a source of embolus or a structural lesion which might cause focal seizures.

Investigation

In patients with a typical clinical presentation of migraine with aura which meets IHS diagnostic criteria, including a normal neurologic examination, laboratory and neuroimaging investigations are very likely to be fruitless and usually are not needed.

In patients with migraine aura without headache, or if the aura is atypical because it is prolonged, the situation is less clear-cut. Our patient had the typical slow march of symptoms consistent with migraine, and had a normal cardiovascular examination. Because of this, we did not do an electroencephalogram, an investigation which may be helpful if partial epilepsy is considered a significant possibility. Investigations directed at potential embolic sources, such as carotid ultrasound examinations and echocardiograms, likewise were not done. Because her focal neurologic symptoms had consistently involved the same central nervous system anatomic site, and appeared to be progressing in severity, an elective (nonurgent) brain magnetic resonance imaging (MRI) was done to exclude a focal lesion, such as an arteriovenous malformation. The MRI scan could also have shown a migrainous infarction had one occurred despite the resolution of the patient's clinical symptoms. Admittedly, the chances of an MRI scan showing a significant lesion in her case were small, and in areas of the world where medical resources are limited, it could not be justified.

Hemoglobin, white blood cell count and differential, sedimentation rate, and antinuclear antibody tests were also done, and were normal.

Management Strategies

This patient's attacks of right-sided numbness were infrequent and for the most part short lived. Like most patients with a migraine aura, she required no symptomatic treatment directed at the aura symptoms themselves.

The main management questions to be considered in her case are:

- Can the frequency of her attacks be reduced through avoidance of migraine trigger factors?
- Do her attacks place her at risk of any serious complications such as a stroke, and can this risk be reduced? In her case, this relates most specifically to her use of oral contraceptives.

In a patient such as this, her history might reveal that the attacks tend to occur when she has missed a meal, has been exposed to bright sunlight or glare, or is under unusual stress. The patient should be made aware of migraine trigger factors so that these can be avoided if possible.

In my opinion, the main issue in her case relates to the use of OCs. Her attacks of focal neurologic symptoms began while she was on OCs, and she was experiencing progressively more severe attacks. As early as in 1975, Bickerstaff noted that some women experienced migraine attacks for the first time after starting the pill, and that others experienced a change in the pattern of their migraine headaches. For example, women who had a long history of migraine without aura, could suddenly begin to have attacks of migraine with aura after starting OCs. Admittedly, the onset of migraine is most common in young women and this is the very population that also uses OCs. The occurrence in our patient of migraine aura without headache while she was using OCs may have been purely coincidental.

Our patient was advised to stop her OCs. The main reason for doing this was because it is likely that her OCs put her at significantly increased risk of stroke, given her history of prolonged migraine aura. This area is still somewhat controversial, but evidence is accumulating from carefully done case-control studies that migraine, and in particular migraine with aura, puts patients at an increased risk of ischemic stroke. There are also many

studies in the literature which indicate that OCs increase the risk of ischemic stroke. There is reason to believe that the combination of the two risk factors may result in a quite significant and unacceptable risk of stroke in some patients with migraine with aura. Although the evidence is anecdotal, this may be especially true for patients with unusual, complex, or prolonged migraine auras. Although the newer low-estrogen-dose OCs may pose less of a risk of stroke than the older contraceptives, there is at present little reason to doubt that they do contribute some risk of stroke, at least in patients with other stroke risk factors.

The whole issue of migraine, OCs, and stroke will be addressed in more detail below.

Case Summary

The patient was a 22-year-old woman who had a history of migraine aura without headache, and in addition had suffered a recent attack which was probably migraine with prolonged aura. These symptoms developed while she was taking OCs. Her symptoms were quite characteristic of migraine aura, and investigations were limited to a brain MRI and blood tests. She was given enteric-coated acetylsalicylic acid for a few weeks until investigations were completed, and was advised to stop taking her OCs. The reasons for stopping her OCs were twofold. It was likely that her focal neurologic episodes would become less frequent and/or less severe. Secondly, given her history of migraine with prolonged aura, her OCs would put her at an increased risk of ischemic stroke.

Overview of Migraine, Oral Contraceptives, and Risk of Ischemic Stroke

Migraine and Risk of Ischemic Stroke

Several case-control studies have examined the effect of migraine on the risk of ischemic stroke in women under the age of 45 years. One of the best known is that of Tzourio et al. (1995), which found a relative risk of ischemic stroke of 3.0 for patients with migraine without aura, and of 6.2 for patients with migraine with aura, compared to controls without migraine.

Similarly, Carolei et al. (1996) also found a strong association between migraine with aura and ischemic stroke. For patients with migraine with aura (their population included both men and women), they found a relative risk of ischemic stroke of 8.6 as compared to non-migraine controls. In their study, although patients with migraine without aura had an increased risk of transient ischemic attack, they could not confirm an increased risk of stroke in this patient subgroup.

In conclusion, to date, evidence suggests a much higher risk of stroke in young adults who have migraine with aura. It must be kept in mind, however, that given the very low incidence of ischemic stroke in young adults, the risk even in patients who have migraine with aura is not very high in absolute terms. For women with migraine with aura the risk has been estimated to be approximately eight ischemic strokes per year per 100,000 women for those under the age of 35, and 22 per year per 100,000 women ages 35 to 44.

Oral Contraceptives and Risk of Ischemic Stroke

The risk of ischemic stroke posed by oral contraceptives is controversial, partly because the estrogen content of OCs has been declining gradually during the time that the various case-control studies have been carried out.

Since 1968, no fewer than 13 case-control studies have been carried out which examine the relationship between ischemic stroke and OCs. With one exception, all have shown an increased risk of stroke, with odds ratios varying from 25 and 19, in some of the older studies, to 2.1 and 3.0 in more recent studies. There is indirect evidence from a variety of sources that the risk of thromboembolism including cerebral thromboembolism is reduced as the estrogen content of OCs is reduced.

One recent study, that of Petitti et al. (1996) raises an interesting question. This was the one case-control study which did not show an increased risk of ischemic stroke from the use of OCs. While this may have been because most women in the study used low-estrogen preparations (use of OCs with more than 50 μg of estrogen was rare), other recent studies have also included large numbers of such patients. The Petitti study, however, which came from a health maintenance organization, appears to have examined a population of young women for whom the OCs were prescribed very selectively, and were probably not often given to patients with significant stroke risk factors. Only 12% of females under the age of 45 in their control population were on OCs. This contrasts many other studies, for example the study by Tzourio et al. from France in which 36% of women in the control population were current users of OCs. The Petitti study, therefore, raises the issue of whether OCs increase the risk of stroke very little in patients without risk factors, but increase it more in patients with risk factors. The Tzourio study suggests that this might be so. They found the relative risk of ischemic stroke to be 13.9 for patients who had migraine and used OCs, compared to women without migraine who did not use OCs. These results require

confirmation, as they are based on a relatively small number of cases.

It must be clearly understood that the great majority of ischemic strokes which occur in patients with migraine are not due to migrainous infarction but appear due to the usual causes of stroke, including thrombosis, embolism, and arterial dissection. The same is true of patients with migraine on OCs. Why patients with migraine, and especially those with migraine with aura, should have an increased risk of stroke is not clear. What role, for example, any migraine-related vasoconstriction might play is purely speculative. The majority of strokes occurring in migraine sufferers in the various case-control studies have occurred outside of the time period of an actual migraine headache. Documented alterations in platelet activity in migraine sufferers may be significant.

With regard to OCs, changes in blood coagulation and blood coagulation factor levels have been demonstrated. Fortunately, at least for low-dose preparations containing 20 μg and 30 μg of estrogen, the changes in the levels of the various procoagulant and anticoagulant factors appear to be balanced, with stimulation of both procoagulant and fibrinolytic activity. It is of interest that changes in the levels of some coagulation factors begin within 4 days of starting OCs, and these may progressively increase over 6 months of use. Surprisingly, once OCs are stopped, the levels of the various coagulation factors may return to baseline very quickly, i.e., within 14 days. The concern is that in some women, particularly those who may have some undetected abnormality in their coagulation or fibrinolytic systems, OCs may shift the balance significantly in favour of procoagulant effects. This has already been shown in some women with genetic mutations leading to clotting abnormalities.

Recommendations

In general, when women with migraine request OCs, the risks, as much as are known, should be discussed with them. If it is decided that OCs are the best option for the patient, she should be carefully monitored for a significant change in migraine frequency, severity, and pattern. This applies particularly if patients already have migraine with aura, or if they develop migraine with aura while on OCs.

Recommendations for specific situations are as follows:

- Women with migraine without aura can probably use OCs safely, unless other major risk factors for stroke (e.g., hypertension) are present.
- Women who have migraine with aura are often advised not to use OCs. However, if OC use is important to the patient, it would seem reasonable to consider OCs in patients with typical, relatively simple auras (i.e., typical visual auras lasting less than 60 minutes), who are young (under the age of 35), and who have no significant cardiovascular risk factors. Such patients should be carefully monitored, however, and OCs should be stopped if the aura or headache pattern changes significantly. It would seem prudent not to prescribe OCs for women with more complex or prolonged migraine auras (i.e., complete hemianopsia, hemiparesis, etc.). In other words, OCs should be avoided in women with moderate to severe neurologic events in migraine.
- Oral contraceptives should be discontinued in patients with migraine without aura who develop a migraine aura for the first time on the pill, and in patients who develop transient ischemic attacks, stroke, or ischemic vascular disease elsewhere.

Selected Readings

Becker WJ. Migraine and oral contraceptives. Can J Neurol Sci 1997;24:16–21.

Bickerstaff ER. Neurological complications of oral contraceptives. Oxford(UK): Clarendon Press; 1975.

Carolei A, Marini C, de Matteis G, et al. History of migraine and risk of cerebral ischemia in young adults. Lancet 1996;347:1503–6.

Collaborative Group for the Study of Stroke in Young Women. Oral contraceptives and stroke in young women. JAMA 1975;231:718–22.

Committee of the International Headache Society. Classification and diagnostic criteria for headache disorders, cranial neuralgias and facial pain. Cephalalgia 1988;8 Suppl 7:1–96.

Lidegaard O. Decline in cerebral thromboembolism in young women after introduction of low dose oral contraceptives: an incidence study for the period 1980–93. Contraception 1995;52:85–92.

Petitti DB, Sidney S, Bernstein A, et al. Stroke in users of low dose oral contraceptives. N Engl J Med 1996;335:8–15.

Tzourio C, Tehindrazanarivelo A, Iglesis S, et al. Case-control study of migraine and risk of ischemic stroke in young women. BMJ 1995;310:830–3.

Winkler UH, Schindler AE, Endrikat J, et al. A comparative study of the effects of the hemostatic system of two monophasic gestodene oral contraceptives containing 20 μgm and 30 μgm ethinylestradiol. Contraception 1996;53:75–84.

Editorial Comments

The area of migraine and stroke and their inter-relationships with the use of oral contraceptive agents is controversial, and demands working knowledge of the issues in order to best treat and advise migraine patients. Dr.

Becker presents a most interesting case and discusses and overviews these issues in a comprehensive fashion with very reasonable recommendations. This balanced approach has great utility.

Appendix 7–1: Diagnostic Criteria of The International Headache Society for Selected Migraine Syndromes with Aura

The following material has been taken from the classification and diagnostic criteria for headache disorders, cranial neuralgias, and facial pain of the Headache Classification Committee of the International Headache Society, published in Cephalalgia, Volume 8, Supplement 7, 1998 by Norwegian University Press.

1.2 Migraine with Aura

DESCRIPTION

Idiopathic, recurring disorder manifesting with attacks of neurologic symptoms unequivocally localizable to cerebral cortex or brain stem, usually gradually developed over 5 to 20 minutes and usually lasting less than 60 minutes. Headache, nausea, and/or photophobia usually follow neurologic aura symptoms directly or after a free interval of less than an hour. The headache usually lasts 4 to 72 hours but may be completely absent (1.2.5).

DIAGNOSTIC CRITERIA

A. At least two attacks fulfilling B
B. At least three of the following four characteristics:
   1. One or more fully reversible aura symptoms indicating focal cerebral cortical and/or brain stem dysfunction
   2. At least one aura symptom develops gradually over more than 4 minutes, or two or more symptoms occur in succession.
   3. No aura symptom lasts more than 60 minutes. If more than one aura symptom is present, accepted duration is proportionally increased.
   4. Headache follows aura with a free interval of less than 60 minutes. (It may also begin before or simultaneously with the aura).
C. At least one of the following:
   1. History, physical, and neurologic examinations do not suggest another cause for the headache.
   2. History and/or physical, and/or neurologic examinations do suggest such disorder but it is ruled out by appropriate investigations.
   3. Such disorder is present but migraine attacks do not occur for the first time in close temporal relation to the disorder.

1.2.1. Migraine with Typical Aura

DESCRIPTION

Migraine with an aura consisting of homonymous visual disturbances, hemisensory symptoms, hemiparesis or dysphasia, or combinations thereof. Gradual development, duration under 1 hour, and complete reversibility characterize the aura which is associated with headache.

DIAGNOSTIC CRITERIA

A. Fulfils criteria for 1.2 including all four criteria under B.
B. One or more aura symptoms of the following types:
   1. Homonymous visual disturbance
   2. Unilateral paresthesia and/or numbness
   3. Unilateral weakness
   4. Aphasia or unclassifiable speech difficulty

1.2.2 Migraine with Prolonged Aura

DESCRIPTION

Migraine with one or more aura symptoms lasting more than 60 minutes and less than a week. Neuroimaging is normal.

DIAGNOSTIC CRITERIA

A. Fulfils criteria for 1.2 but at least one symptom lasts more than 60 minutes and ≤ 7 days. If neuroimaging reveals relevant ischemic lesion, then it is classified as code 1.6.2 migrainous infarction regardless of symptom duration.

1.2.5 Migraine Aura without Headache

DESCRIPTION

Migrainous aura unaccompanied by headache

DIAGNOSTIC CRITERIA

A. Fulfils criteria for 1.2
B. No headache

COMMENT

It is common for migraine with aura that headache occasionally is absent. As patients get older, headache may disappear completely even if auras continue. It is less common to have always suffered exclusively from migraine aura without headache. When the onset occurs after the age of 40, and for other reasons, the distinction between this entity and thromboembolic transient ischemic attacks may be difficult and require extensive investigation. Acute onset aura without headache is not sufficiently validated.