Clinical Problems

Chorea and the Oral Contraceptives

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Summary

The case histories are reported of six women who developed chorea while taking oral contraceptive drugs. The chorea that results from taking compounds containing oestrogen and progestogen has many features in common with chorea gravidarum, and the pathogenesis is probably similar. In some of the patients, however, the sudden onset of symptoms suggests a vascular aetiology.

Introduction

It is now recognized that women taking oral contraceptives run a risk of neurological complications. These range from major structural lesions such as intracranial vascular occlusion, through episodes of arterial insufficiency, to disorders of vascular function, as in migraine or other less well-defined headache syndromes. An effect on the frequency of fits in epileptics is possible but as yet unproved. In 1966 Fernando[1] reported the case of a 22-year-old woman who developed typical chorea while taking one of the contraceptive pills, and a further five similar cases seen at the National Hospital were recorded by Lewis and Harrison.[2] During the past five years we have seen six women who developed involuntary choreiform movements while on oral contraceptives, and as Sydenham's chorea has become so rare in young adults an association between this clinical picture and the taking of compounds containing oestrogen and progestogen seems undoubted. For this reason we report the following brief case histories.

Case 1

A 22-year-old married woman had been taking Serial 28 for six months. Having been perfectly well the previous evening she awoke one morning with involuntary movements affecting the left side of her body. Her past history included a miscarriage and a premature birth but not rheumatic fever or chorea. On admission to hospital she showed left hemichorea with involvement of the tongue and respiratory muscles. Investigations, including right carotid angiography, showed nothing abnormal. Oral contraception was stopped and her signs disappeared over the next four weeks, having dramatically decreased within 48 hours of discontinuing the pill. She was advised against using oral contraceptives again. Six months later there was a severe recurrence of chorea. It was discovered that she had not resumed the use of oral contraceptives but was then two months pregnant.

Case 2

The patient, a 21-year-old nulliparous woman, developed insidious twitching of the limbs in August 1966 which rapidly became severe. She had started taking Ortho-Novin the previous June and had stopped it of her own accord a month after the onset of her symptoms. Gradual recovery ensued, and when she was examined two months later there was only mild residual chorea of the left arm and right leg. The heart and joints were not affected. There was no past history of chorea or rheumatic fever. During the subsequent four years she had no recurrence.

Case 3

A nulliparous woman of 23 had been taking an oral contraceptive for three months before she suddenly developed typical generalized chorea. This disappeared within a week of stopping the drug. No follow-up details are available.

Case 4

Six months before her admission to hospital this 20-year-old woman's mother commented on her fidgetiness. Two months later the patient herself noticed involuntary twitching of the left hand, which gradually worsened and spread to involve the face and leg on the same side. Her past history was clear, but both chorea and rheumatic fever had occurred in the family. She had been taking Gynovlar 21 for the previous 12 months. Examination showed moderately severe chorea confined to the left half of the body but no other abnormality. Investigations carried out at the time showed nothing abnormal. The contraceptive pill was stopped and she was given diazepam with haloperidol, and later prednisone. The chorea gradually subsided and she was free from symptoms and signs seven weeks after admission. Over the two and a half years since that time she had taken an oral contraceptive (Lyndiol 2·5) for two separate periods of eight and six months without any ill effects.

Case 5

A 23-year-old nulliparous married woman had started taking Ovulen in January 1969. She changed to Norlestrin a year later when widespread publicity was given to a statement by the Committee on Safety of Drugs reporting a higher incidence of vascular complications in association with compounds containing a greater proportion of oestrogen.[3] After three months she suddenly developed weakness of the left hand associated with involuntary flexion spasms of the wrist. Though this episode lasted only a few minutes similar attacks occurred frequently over the next nine days and were then replaced by jerking of the left arm. She was admitted to hospital the next day.

Examination showed nothing abnormal apart from the left arm, which had frequent irregular jerking movements, more severe

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proximally than distally and increased by voluntary movement. They were thought to be intermediate between myoclonus and chorea. On investigation the only abnormality was a slightly raised antistreptolysin titre (500 Todd units). The contraceptive pill was stopped three days after admission and noticeable improvement in her involuntary movements was apparent within 24 hours.

A few days after leaving hospital she complained of heaviness and throbbing in the left arm and noticed a patch of numbness over the left side of the trunk. The former symptoms disappeared after two days but the numbness persisted as an area of contact dysaesthesia, which was still present nine months later. At the time of writing she was two months pregnant and had had no recurrence of her symptoms.

Case 6

This patient gave an indefinite history of St. Vitus's dance when aged 5. She was married at age 20 and started to take Norinyl-1. Four months later she developed involuntary movements of the left arm and leg of fairly sudden onset. After a month these lessened, only to be replaced by more severe symptoms down the right side of the body associated with slurring of speech. On examination four weeks later she showed typical severe chorea, the left side being less affected than the right, where there was a definite paralytic element. Investigations showed nothing abnormal. The Norinyl-1 was discontinued and she was treated with diazepam and thiopropazate. The chorea gradually improved and the drugs were slowly reduced. Two months later she was symptom-free, though occasional choreiform twitches were still visible.

Discussion

Obviously a cause-and-effect relationship between hormonal contraception and chorea cannot be proved on the basis of half a dozen cases. Thus a countrywide investigation was needed to establish the connexion between cerebral vascular disease and the use of oral contraceptives.[4] Nevertheless, the occurrence of these cases and those previously reported is by itself highly suggestive. Self-limiting chorea and rheumatic fever are believed to be allied conditions, and both have been declining in frequency for several years. Sydenham's chorea in adults has always been rare and is usually associated with pregnancy, in which it probably occurs in between 1 in 17,000 and 1 in 1,000 cases.[5] [6] During the past five years we have seen only seven adult patients with Sydenham's chorea. The cases of six of these are described above, and the seventh was a woman with systemic lupus erythematosus who had also been taking an oral contraceptive.

The mechanism whereby oral contraception might produce chorea is open to speculation. It is tempting to consider the similarities between the cases presented here and chorea of pregnancy, especially as the state of a woman taking hormonal contraceptives has been described as one of "pseudo-pregnancy."[7] Analogies are present in the similar age of the patients, the nulliparous state of five out of the six women, and the short period of time elapsing between starting the pill and the onset of symptoms (see Table).[8] A further link is provided by the recurrence of chorea in Case 1 when she became pregnant.

One difference lies in the absence of previous episodes of chorea or rheumatic fever in all but one of these cases. A past history of rheumatism can be elicited in most patients with chorea gravidarum and was present in four of the five cases of chorea in association with oral contraception reported by Lewis and Harrison.[2] The widely-held belief that chorea gravidarum arises as a result of activation of subclinical damage to the basal ganglia from past rheumatism is based on this evidence. Nevertheless, possibly such minimal brain damage could have other pathogenic causes—for example, perinatal brain injury or virus infection, either of which might pass unnoticed at the time of their occurrence, as could rheumatic fever. The changed hormonal state of pregnancy or oral contraception may highlight this damage, possibly through a direct biochemical effect on the neurones or their attendant glial cells.

Clinical Features of Patients with Involuntary Movements

Case No.:	1	2	3	4	5	6
Age	22	21	23	20	23	20
Marital status	M	M	M	S	M	M
Parous or nulliparous	P	N	N	N	N	N
Past history of chorea or rheumatism	No	No	No	No	No	? Yes
Length of time on pill in months	6	2	3	12	15	4
High (>0·05 mg) or low (≤0·05 mg) content of oestrogen	H	H	?	L	L	L
Onset (sudden or gradual)	S	G	S	G	S	G
Unilateral or generalized	U	G	G	U	U	G
Antistreptolysin titre (Todd units)	125	—	—	100	500	166
Time to recovery in weeks	4	8	1	4	3	8

Though the similarity of the cases reported here to chorea gravidarum stands out the pathogenetic mechanisms are not necessarily the same. Cerebral vascular episodes are now recognized as complications of hormonal therapy,[9] [10] and chorea might arise from ischaemic damage to the basal ganglia. The sudden onset of symptoms in Cases 1, 3, and 5 was compatible with a vascular cause. In two of these patients the chorea was unilateral, and in one accompanied by symptoms and signs suggestive of damage to central sensory pathways (Case 5). In this context it is of interest that three of our patients were taking contraceptives with a low oestrogen content.

Whatever the mechanism involved it seems difficult to escape the conclusion that oral contraception may play a part in the development of chorea.

References

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