CEREBRAL ARTERIOSCLEROSIS

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The problem of cerebral arteriosclerosis demands first a consideration of recent views on the mechanism of experimental hypertension in animals and on the applicability of the proposed mechanism to the clinical pictures of hypertension and arteriosclerosis in man.

Experimental hypertension in animals

The results of his work on the pathogenesis of hypertensive encephalopathy in rats have recently been summarised in an outstanding paper by Byrom (1954). Hypertension was induced, after excision of one kidney, by applying a simplified Goldblatt clamp to the renal artery of the remaining kidney. This procedure regularly leads to the development of hypertension, and has the great advantage that the hypertension can be reversed by removing the clamp. Cerebral symptoms occur when the blood pressure reaches a height of about 200 mm. Hg., the most frequent manifestations being epileptic convulsions, myoclonic contractions, focal neurological signs, and the development of coma. The symptoms are rapidly relieved with the fall of blood pressure resulting from removal of the clamp.

Organic brain lesions were found in only a little more than half the rats at post-mortem, and consisted of focal arterial necrosis, areas of cerebral infarction, or haemorrhages arising from arteries or capillaries. The frequency of organic lesions was, therefore, not great enough to account for the symptoms encountered, and a functional change was sought to account for this finding and for the rapid return to normality following relief of the hypertension. When the dye trypan-blue is injected intravenously shortly before a normal animal is killed, the brain is unstained since the dye does not pass the blood-brain barrier. However, in 87 per cent. of rats with encephalopathy, conspicuous areas of staining of the cerebral grey matter were found, these areas occurring not only in relation to organic changes, but also where the brain appeared histologically normal or showed only evidence of focal oedema. Byrom therefore suggested that increased capillary permeability with focal oedema antedated structural damage.

The clamped kidney is free from the arterial necrosis found in many other organs of the hypertensive rat, suggesting that this lesion is dependent on the physical strain of increased intra-arterial tension and follows on the spasm which is the response of an artery to this form of strain. This hypothesis was tested by direct observation of the blood-vessels of the rat's brain through a transparent cranial window. The vessels appeared normal in animals before the appearance of cerebral symptoms and after their disappearance following removal of the clamp. With the onset of encephalopathy there was a consistent change in the smaller cerebral arteries, a widespread sustained contraction of many of the vessels of this calibre with occasional localized areas of dilatation.

Byrom concluded that a state of focal but widespread vascular spasm is the basis of severe experimental renal hypertension, and that the effects of the spasm, depending on its intensity, duration, location and extent, 'comprise in increasing order of severity: (1) transient disturbance of function, (2) increased capillary permeability with attendant focal oedema, and (3) local necrosis of the arterial wall and/or the tissue supplied.'

Pathology of Hypertension and Cerebral Arteriosclerosis in Man

Man, unlike the rat, is subject to atheroma, and the possible presence of this factor in addition to hypertension is responsible for much of the difficulty in ascribing cerebral symptoms to their underlying pathological bases, particularly since atheroma is found more frequently in the presence of hypertension. Haemorrhage from an artery is a common complication of cerebral arteriosclerosis, the patient usually being found to have an accompanying hypertension. Arterial thrombosis with resultant infarction of the corresponding part of the brain may occur in arteriosclerotic patients without hypertension. Cerebral embolism may give rise to permanent neurological signs, or to symptoms and signs which are transitory and leave no deficit. From their occasional fleeting nature it has been argued, notably by Pickering (1951) that

a structural change such as thrombosis may well underlie also the similar clinical picture found in severe hypertension. The above-mentioned work of Byrom makes it likely that hypertension alone may eventually cause structural changes leading to arterial necrosis, thrombosis and haemorrhage. The co-existence of atheroma may well render an artery more sensitive in its response to raised intra-arterial pressure by spasm, and a more extreme degree of atheroma may lead to focal cerebral infarction, with or without arterial thrombosis, in the absence of hypertension or of arterial spasm.

Hypertensive Encephalopathy in Man

That the cerebral symptoms which may accompany renal disease are not related to nitrogen retention but to hypertension was shown originally by Volhard, whose term 'pseudo-uraemia' has been replaced by 'hypertensive encephalopathy' (see Fishberg 1954) and by 'hypertensive cerebral attack' (McAlpine 1933). McAlpine differentiated two forms of attack, the first, commoner in patients below the age of 40, with headache, vomiting, drowsiness, convulsions and papilloedema, the second found in middle-aged patients and characterized by epileptiform attacks and focal neurological signs in the absence of papilloedema. Fishberg and McAlpine agree that the mechanism of the second type of attack is focal arterial spasm, and of the first type cerebral oedema secondary to the rise of blood pressure from generalized vasoconstriction, not necessarily accompanied by cerebral vasoconstriction. From the experimental findings of Byrom it now seems that cerebral arterial spasm, generalized or localized, is the basis of each type of attack.

Symptoms of Benign Hypertension and of Cerebral Arteriosclerosis in Man

Benign hypertension in man may lead to no symptoms whatsoever, the condition being found on routine examination of the blood pressure. The greater frequency of symptoms such as headache, unsteadiness, and mild hypochondriasis, which are to be found in those subjects who are aware that their blood pressure is raised, has led to the view that many of the symptoms of uncomplicated hypertension are due to a secondary anxiety state. It is certain that symptoms in many hypertensive patients are aggravated or even induced by the anxieties following on their awareness of the raised level of their blood pressure, and for such patients the most profitable line of treatment is one of mild sedation and superficial psychotherapy, with an explanation of the role of emotion in causing various somatic symptoms. However, the occurrence of such symptoms in patients without knowledge of their hypertension, and the presence

of mental and physical fatigue and a mild organic personality change, suggest that this clinical picture can arise in benign hypertension without the necessity of an interpretation along psychopathological lines.

The clinical picture of cerebral arteriosclerosis with or without accompanying hypertension, is more definite. The symptoms and signs depend on a progressive cerebral anoxia, with the general and focal signs appropriate to the arteries involved. In essence there is a fluctuating development of an organic intellectual and personality change. Memory for recent events is impaired whilst happenings in the distant past are well recollected. There follows a more general intellectual impairment with failure of judgment and an inability to grasp new problems, with narrowing of the outlook and diminution in initiative. Insight is often preserved to an extent that is not seen in senile dementia, and with the realisation of his failing powers the patient becomes easily depressed. Emotional lability may develop, and the patient will then more readily than his wont be amused or depressed, and will, furthermore, give excessive expression to these often transitory emotions, a picture of emotional incontinence ultimately developing. In spite of these changes, the basic personality is often surprisingly well preserved, although previously latent personality traits may emerge, such as irritability or suspiciousness.

Neurological symptoms and signs appear irregularly during the course of the illness. There may be focal disturbances resulting from the underlying impairment of cerebral function; these disturbances may be transitory or permanent and may take the form of minor paralyses, or disturbances of sensation, vision or speech. Major disturbances such as a hemiparesis or a series of epileptic attacks may follow. There are two clinical pictures which may result from a generalized affection of the cerebral arteries; an arteriosclerotic Parkinsonism with marked rigidity, and a pseudo-bulbar palsy with bilateral pyramidal involvement and pronounced emotional incontinence. The most extreme change seen in advanced cerebral arteriosclerosis is of a profound organic dementia, with double incontinence and complete mental inaccessibility.

Differential Diagnosis of Cerebral Arteriosclerosis

The differential diagnosis of cerebral arteriosclerosis resolves itself into the separation from it of other diseases causing or mimicking organic intellectual and personality change in later life.

Space-occupying lesions within the skull tend to give rise to headache and vomiting with papilloedema, all of which are infrequent in

cerebral arteriosclerosis unless this is complicated by hypertensive encephalopathy. The most characteristic psychological symptom is a blunting of the mental faculties and a lack of alertness, a contrast with the impairment of recent memory of cerebral arteriosclerosis. An exception is the pronounced memory impairment seen in lesions of the base of the brain (Williams and Smith 1954), which is as a rule more extreme than that seen in cerebral arteriosclerosis and is often unaccompanied by other features of organic intellectual impairment. Finally, the neurological signs in an expanding lesion usually point to a single rather than multiple lesions, and the mode of evolution is more steadily progressive.

General paralysis of the insane is differentiated by its occurrence at a younger age, by the physical signs of this disorder, and by the positive Wassermann reaction. In this condition there is an early change in the patient's personality, with the frequent emergence of latent personality traits such as depression, grandiosity and suspiciousness. The presenile dementias comprising Pick's disease, Alzheimer's disease and a larger undifferentiated group may be distinguished by the earlier age of onset, the occasional positive family history, the absence of other signs of arteriosclerosis, and by the more steadily progressive course of the illness.

A relatively uncommon cause of an illness which may be taken for cerebral arteriosclerosis is myxoedema: the importance of considering this condition in the diagnosis of any psychiatric illness in later life lies, of course, in the frequency of a favourable response to thyroid medication. A single one of the following features, coarsening of the face, dryness of the skin, a slow pulse, mental and physical torpor, or excessive sensitivity to cold, may be the only outstanding evidence of hypothyroidism, and should prompt investigation of the serum cholesterol and basal metabolic rate.

The final conditions to be considered in the differential diagnosis of cerebral arteriosclerosis are the mental diseases of the aged. Kraepelin (1904) stated: 'We must, however, recognize that the interpretation of those cases of disease which occur at the beginning of old age is often very difficult.' He pointed out one criterion thus: 'The great prominence of this inability to retain impressions in the more severe forms of the insanity of old age seems to me to justify the view that those states of depression and excitement in which it is a leading feature . . . are also to be considered as varieties of senile insanity. If further experience shows that this view is correct, we may perhaps have found a criterion for the distinction of melancholia . . . from real senile imbecility.' In recent years considerable progress has been made in the distinction of the various psychoses which

occur in the aged, in particular by Roth (see Mayer-Gross, Slater, and Roth 1954) who has utilized amongst other approaches, that of Kraepelin himself in the emphasis he has placed on the importance of prognosis in distinguishing various categories of illness.

Roth classifies the mental diseases of old age into five main categories, with arteriosclerotic psychosis as one group. Senile psychosis is characterized by intellectual impairment (with memory affected early), emotional blunting, and reduction in initiative, with involvement of the personality as a whole, and a steady progression to death in a few years. The absence of epilepsy and of focal neurological signs, and the steady course of the disease, serve to distinguish it from cerebral arteriosclerosis. Delirious states in old age may depend on an intercurrent infection or on toxic or vitamin-deficiency states, the latter often without any of the more characteristic signs of vitamin deficiency. When delirious states are due to any of these causes, the primary state may be detectable, and the confusion will have appeared somewhat suddenly in a person who was previously well. Delirium, however, is not uncommon as a complicating factor in cerebral arteriosclerosis, and may be due to one of the above-mentioned causes or may be dependent directly on further arteriosclerotic lesions, the effect of which is more likely to be permanent than transient. The group of late paraphrenia is distinguished from cerebral arteriosclerosis by the consistency and systematization of the delusions, in contrast to their fleeting nature and poor hold on the personality when they occur in cerebral arteriosclerosis.

The final group in Roth's classification of the psychoses of the aged is the affective psychoses; their differentiation from cerebral arteriosclerosis is of outstanding importance in view of their excellent response to electro-convulsive treatment. The most important feature in the illness of a patient with endogenous depression is that the history will show that there was little or no impairment of intellect or personality before the fairly sudden onset of an illness with reduction of psychomotor activity and a predominantly depressive colouring. Often the classical features of an endogenous depression will be present, with retardation or agitation, insomnia with early waking, and a lifting of the depressive mood towards the evening. Such features, even in the presence of hypertension or cerebral arteriosclerosis, should call for the consideration of electro-convulsive treatment. (Partridge, 1954).

Future Treatment

The present treatment of cerebral arteriosclerosis is entirely non-specific, and consists

largely of general management of the everyday routine of life, and appropriate measures for the various complications that may ensue. The success of sympathectomy and of hexamethonium in the treatment of severe hypertension (see Rosenheim, 1954) indicates that similar measures may well be of help in the management of cerebral arteriosclerosis to the extent that this condition is accompanied by cerebral arterial spasm secondary to the stress of intra-arterial tension: the answer to this problem and to that of the value of anti-coagulants in treatment depends on a controlled comparison of treated and untreated patients.

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