Neuromyelitis optica versus subacute necrotic myelitis:

Part II. Anatomical study of two cases

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In 1959 we published in a local journal the anatomical findings of a case of neuromyelitis optica which suggested the possibility of a vascular mechanism in the lesions of that disease (Matera, Tamaroff, Ortiz de Zárateg, and Gruzman, 1959). In addition, connections between it and myelomalacia and subacute necrotic myelitis of Foix and Alajouanine (1926) were assumed. Recently we had the opportunity of studying another similar case.

CASE I

The personal and family history of I.G., a man aged 49, was noncontributory. His illness began abruptly with blurred vision of both eyes and in five days he turned completely blind. The neurological examination was then entirely normal. His blood pressure was normal, as well as the CSF, urine, and blood examination with the exception of the erythrocyte sedimentation rate which was 47-68 mm/hr. After two and a half months a paresis of the right lower limb appeared. A week later he was paraplegic. At that time the cutaneous sensibility was normal, but a month later it was impaired from the costal border down and in a few days it was abolished from the second rib down. He died of sepsis in the fifth month of his disease. The CSF was examined three times, the last being seven days before death, and it was always found to be normal.

**NECROPSY FINDINGS** On naked eye examination the right optic nerve was thinner than the left. Arteriosclerotic lesions of the circle of Willis were evident. On sectioning the brain some small miliary foci of disintegration in the subcortical white matter, caudate nucleus, and anterior part of the lenticular nucleus were observed.

In the spinal cord a lesion was seen which extended from T2 to L1; its core was necrotic between T6 and T12. In the middle of the lesion the whole cord was involved; in the upper part the lesion flattened, involving the horizontal bar of the gray matter with a right and posterior extension to the pyramidal tracts and the posterior gray horns reaching the spinal cord surface.

Caudally the lesion ended in a tip located in the posterior part of the gray commissure and the base of the posterior columns.

In the viscera there was fibrosis of lungs with gray hepatization, atheromatous lesions of the aortic walls, atrophic gastritis, congestive liver, and normal heart.

Sections of the central nervous system were stained with haematoxylin-eosin, Heidenhain-Woelke for myelin, Nissl, Mallory's trichrome, and PAS. In the centre of the cord there was a distinctive myelomalacia (Fig. 1). Connective septa separated lakes devoid of nervous tissue and filled by scavenger cells. In the periphery of the section the nervous tissue was dissociated by interstitial oedema which in certain places resembled status spongiosus. All the stages of neuronal degeneration and of astrocyte hyperplasia could be seen to 'gemästete gliazellen' and then fibrosis.

The nerve roots were normal throughout the spinal cord.

The anterior and posterior spinal arteries and veins were normal, but the medium sized vessels, specially

**FIG. 1. Case 1. Softening of spinal cord. (a) Holzer staining (b) Heidenhain-Woelke. × 7.**

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those belonging to the roots, showed clear pathological changes. Their walls were thicker and hyalinized; they often seemed to be like a rubber tube (Fig. 2). With PAS staining the hyaline mass went a homogeneous light pink colour with subendothelial reddening. In some sections nuclei were observed but they were almost always lacking, while in some of the vessels remains of the elastic layer could be seen. The adventitial layer was very thin and seemed to be involved in the hyalinization process. The endothelium was normal and the lumen narrow, but nowhere was there occlusion. All these changes were clearly seen in the vessels of the roots and in those of the cord septa.

The pathological structure of the vessels just described was observed only in the diseased segments and not in the other parts of the cord or in the brain, with the exception of the surroundings of the malacic foci. The lesion involved the vessels of small diameter.

In the optic chiasm the lesion was just the same as that of the spinal cord—total central malacia with plenty of scavenger cells and some remains of nervous tissue and scar reaction in the periphery (Fig. 3). Vascular lesions were not observed here, but it must be remembered that in the chiasm there are no vessels of a size similar to those grossly affected in the spinal cord.

In numerous sections of the brain only the loci of disintegration were found, and near one of them a vessel could be seen with the changes of its wall already described in relation to the spinal cord.

The vessels were normal in all the other slides in which there were no signs of alterations of the parenchyma. In

The rest of the encephalon only sporadic clusters of lymphocytes could be seen in the hypothalamus and at the pes pedunculi, which may be interpreted as a pre-mortem finding.

**CASE 2**

A. G. de A., a woman aged 36, married at 29 years old. One year later she had eclampsia gravidarum (convulsions, loss of consciousness, blood pressure 220 mm Hg) and a therapeutic abortion was carried out. She had two more abortions and one livebirth with death four days after. At 31 years old she had four convulsive seizures in one day. Thereafter she took anticonvulsants for three years and had no more seizures. Her blood pressure remained high throughout.

The only relevant fact in the family history was that her mother had been in hospital since she was 51 years old for treatment of a demential syndrome.

The present disease of the propositus began at the age of 35 with tingling in her legs. Eight days later the sensory disablement involved the upper limbs, plus neck pain and blurring of vision in the right eye, which in a few days turned blind. With phenothiazines and vitamin treatment her paraesthesiae disappeared but reappeared five months later associated with ataxia of all four limbs. In a few days she developed paralysis of both lower limbs and paresis of both upper limbs. The sensory examination showed syringomyelic dissociation in both upper limbs and abolition of deep sensibility in the trunk and both lower limbs.

From then on during the six months until her death, she had three remissions with subsequent relapses. Her systolic blood pressure was always over 200 mm Hg. There was albuminuria and she had severe anaemia which required several blood transfusions. The cerebrospinal
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Fluid, which was examined several times, was always normal. She died the day after a laparotomy for obstructive jaundice, in the 16th month of her neurological disease.

Necropsy findings necropsy was confined to the nervous system. There were no macroscopically visible changes.

In the spinal cord there was a long necrotic focus which extended from C5 to T1 segments. In its central part there was a malacic lesion which affected the whole section apart from a left posterior shell (Fig. 4). The lesion sharpened upwards and flattened downwards. Microscopically it was a malacia, its core full of scavenger cells traversed by dense connective septa which indicate scar transformation. In one place there was a well delimited cystic formation (Fig. 5). Different degrees of necrosis were seen from the malacic focus outwards with an intense proliferation of glia and connective tissue and formation of new blood vessels. The borders between the diseased and healthy portions were well defined but there was no capsule.

The vessels had changes which topographically and in structure were similar to Case 1, so its description will not be repeated. Those inside the area of softening had masses of scavenger cells forming a cuff around them (Fig. 7). The optic chiasm showed changes identical with those of Case 1 but in an advanced state of cicatrization with cellular and fibrous glial hyperplasia and connective tissue scarring which completely altered the structure of the organ (Fig. 6). There were no abnormalities in the encephalon.

Discussion

The diagnosis of neuromyelitis optica seemed acceptable for both cases, even in the restrictive sense of Michaux (1930) and others who stated that in true neuromyelitis optica there is always necrosis of


FIG. 6. Case 2. Optic nerve. (a) normal. (b) Case 2 with the same staining (H. and E.) and magnification (× 40). Thick collagenous scarring.

FIG. 7. Case 2. Spinal cord. The histiocytes, full of debris, follow their way through the adventitial spaces. Compare with Fig. 3. H. and E. × 70.
the cord. In both cases the spinal cord and the optic lesions were characterized by total destruction of all components of the nervous tissue with glial and connective tissue reaction.

In some 65 anatomical cases published hitherto (Michaux, 1930; Stansbury, 1949; Szobor and Szegedy, 1962) the lesions were always in the spinal cord and optic nerves or chiasm, but frequently isolated or multiple lesions existed also in the brain. The lesions were sometimes necrotic, sometimes pure demyelination, sometimes inflammatory.

It is hard to accept that all these forms are only different degrees or stages of the same disease. It is more reasonable to propose that the syndrome may have several physiopathological mechanisms and undoubtedly several aetiologies as well, and they would be named as multiple malacia, multiple sclerosis, or encephalomyelitis.

In our cases vascular changes occurred which made us consider the disease described by Foix and Alajouanine (1926) as subacute necrotic myelitis and also other forms of myelomalacia. The cases of Foix and Alajouanine had a softening of the spinal cord associated with gross changes in the vessels especially the anterior spinal artery. It would seem that at least only minimal relations between neuromyelites optica and subacute necrotic myelitis should exist, owing to the vascular changes present in the second but absent in the first of our cases and the optic changes present in the first and absent in the second. However, a review of the literature shows that subacute necrotic myelitis does not always show exactly the picture described by Foix and Alajouanine. Several papers quote the clinical or pathological involvement of the optic nerve—for instance, those of Bassoe and Hassin, Case 2 (1921), Van Bogaert, Ley, and Brandes (1930), Minea (1932), Moersch and Kernohan, Case 2 (1934), Zhitomirskaya and Ovcharenko (1937), Hoffman, Case 3 (1955), Nunes-Vicente (1961) and, last but not least, one of the two main cases of Foix and Alajouanine (1926). The latter showed bilateral papilis with severe diminution of vision, though at necropsy a meticulous histological examination of the chiasm and optic nerves showed no abnormalities. The damage had obviously been regressive.

The vascular changes were reported in detail by Foix and Alajouanine (1926) who reasonably emphasized the most outstanding abnormalities—namely the extreme hyperplasia of the middle layer of the extramedullary vessels—but hyalinization of the wall and disappearance of the whole structure was also mentioned and illustrated.

Vascular lesions of the same type and magnitude were rarely found in cases of subacute necrotic myelitis published subsequently. Two exceptions are the cases of van Bogaert and Brandes (1930), and of Greenfield and Turner (1939), which are also two of the very few cases where albuminocytological dissociation in the CSF appeared.

In most of the published cases hyalinization of the walls of the small vessels was the only pathological vascular finding. This change has been interpreted in different ways, usually as a congenital malformation because it is usually considered that the abundance of vessels is greater than normal. The disease would then be a "myelomalacia angiodisgenetica" (Scholz and Wechsler, 1959). The alteration of the wall of the vessels is of such magnitude that it is impossible to recognize the different layers, so it is always doubtful if the observed vessel is an artery or a vein. Taking into account the relation that exists between the lumen diameter and the wall thickness (a doubtful fact in a malformed vessel) it is often accepted that they are veins (Reinisch, 1963, 'angioma racemosum venosum') primarily maldeveloped or secondarily deformed because of the arteriovenous character (fistulae) of the disease.

It should be taken into account that, whatever the physiopathology of hyalinosis, it is confined to the CNS (Klissuwro, 1930; Arab, 1959). Jellinger (1967) includes the 'complete acellular and structureless transformation of the vessel wall into homogeneous, slightly eosinophilic tubes' in arteriosclerotic disease.

Some authors think that in subacute necrotic myelitis the parenchymatous lesions are produced by functional or organic ischaemia; in our two cases the picture of the cord in cross-section (Figs. 1 and 4) resembles very closely the classical topography of vascular softening. Other authors think that the parenchymal lesions could be produced independently by the same causal factor which determines the vascular lesion (Foix and Alajouanine (1926) insist that there is no obstruction to stenosis of the lumen of the vessels).

Our cases—which we classify as neuromyelitis optica—showed vascular alterations similar to the above and perhaps they should be named subacute necrotic myelitis. The optical nerve lesions, plus their exact coincidence with the anatomical picture of neuromyelitis optica sensu stricto, made us include them in the latter group, although the existence of vascular lesions would be an obstacle for that diagnosis.

From our review of the literature on neuromyelitis optica we are unable to draw conclusions about the frequency with which vascular changes appear in it. Some authors (Michaux, 1930) say that they never exist, others (Paarman, 1952; Moritz, 1962) mention the hyalinization but do not specify its intensity or abundance. Finally there are others (Szobor and Szegedy, 1962) who do not mention the state of the
Two considerations.

From these facts we conclude that the existence of vascular changes is not an obstacle to the diagnosis of neuromyelitis optica.

If we accept the evidence thoroughly analysed by Cestan, Riser, and Planques (1934) that neuromyelitis optica is a clinical syndrome and that their pathological findings do not allow a nosological unification, it would be possible to recognize different anatomical entities. There is no doubt that pure demyelinating cases, such as that of Cestan et al. (1934) show close resemblance to multiple sclerosis and, conversely, that they show clear differences with respect to pure necrotic or malacic forms, which in turn have a great resemblance to subacute necrotic myelitis. The latter perhaps should be also subdivided into different forms.

The hyalinosis may have several aetiologies (Lowenberg and Füstow, 1932; Arab, 1959; Jellinger, 1967) and it is described in some angiomas of the CNS, but it would be extremely rare for an angioma of the cord and of the optic chiasm to co-exist and become clinically evident at the same time.

It seems reasonable to collect cases of neuromyelitis optica and of subacute necrotic myelitis which resemble our cases in having spinal and optic softening associated with hyaline changes in the vessels—perhaps exclusively veins but possibly arteries too—that are generally limited to the malacic regions. As there is not the least sign of inflammation, the appropriate name would be 'Malacia opticomedularis'.

The coexistence of optic nerve and spinal cord symptoms make us think that it is an evolutive process which reaches decompensation simultaneously in all the affected regions, but we cannot imagine which type of a common pathosis affects the optic nerve and spinal cord. In this respect we remember tabes dorsalis and multiple sclerosis in which there would exist a similar pathosis.

Temporal arteritis with frequent involvement of the optic nerves on the one hand, and on the other hand the several published cases (cited by Arseni and Maretsis, 1967) of spinal cord tumours with papilloedema, in which this condition disappeared after the removal of the tumour, allow more theoretical considerations.

SUMMARY

Two patients had a clinical picture of blindness and transverse section of the thoracic spinal cord. In both, the necropsy revealed softening of the optic chiasm and cord.

The medium sized vessels of the malacic foci showed outstanding hyalinization of their wall.

These cases have features in common with both 'neuromyelitis optica' and 'subacute necrotic myelitis'.

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*J Neurol Neurosurg Psychiatry* 1968 31: 641-645
doi: 10.1136/jnnp.31.6.641

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