Baló’s Encephalitis Periaxialis Concentrica

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Key Words
Baló · Concentric sclerosis · Demyelination · Multiple sclerosis · Heat shock protein

Abstract
In 1928, Baló described a law student with an unusual fatal illness marked by aphasia and a right hemiplegia, with later optic neuritis and normal cerebrospinal fluid. At autopsy, he found a disease of the white matter characterised by foci varying in size from a lentil to that of a pigeon’s egg and presenting gray softening and, in part, concentricity, where the medullary sheaths were destroyed and the axis cylinders were intact. He was uncertain whether this was a variant of acute multiple sclerosis or of Schilder’s disease. The basis of concentric sclerosis is still unclear though current opinion favours a variant of acute multiple sclerosis.

Schilder [1], in 1913, reported 3 cases in children that he referred to as ‘encephalitis periaxialis diffusa’, characterised by diffuse involvement of the cerebral hemispheres with severe myelin loss, which resembled multiple sclerosis because of the relative preservation of axons and the accumulation of lymphocytes; he also showed numerous fat-laden phagocytes and gliosis. Haberfield and Spieler [2] reported Schilder’s adrenoleucodystrophy in 1910 as did Siemerling and Creutzfeldt [3] in 1923. Patients reported with familial Schilder’s disease are probably instances of sudanophilic cerebral sclerosis, Krabbe disease or metachromatic leucoencephalopathy. Though phenotypic variations are common, the variant reported by Jozsef Baló [4] is remarkable and there is still uncertainty about whether his case represented a type of Marburg’s acute multiple sclerosis or a variant of Schilder’s disease [5]. Marburg, in a prescient paper described an acute illness, which terminated life within 1 year. He noted the close similarities to multiple sclerosis, with a perivascular distribution of lesions. He showed both demyelination and remyelination of the axons and, in line with present ideas, noted that the axons, too, were affected and atrophic in peripheral nerves as well as in the brain and cord. One of his 3 cases showed striking concentric sclerosis.

Baló’s Concentric Sclerosis

Jószef Baló (1895–1979) was a neuropathologist, born in Budapest, Hungary. Unfortunately, most of his biographical details [6] and publications [7] have not been translated into English or other European languages.

His first account was published in the Hungarian journal Ről Magy Orv Arch and was translated into English...
'Encephalitis periaxialis concentrica') in 1928. Baló [4] wrote:

'A law student aged 23 became ill with aphasia; then followed weakness of the inferior branch of the facial nerve and disappearance of the cremasteric reflex on both sides and of the abdominal reflexes on the right side. Later, a hemiplegia of the right side, incontinence of urine and feces and a total aphasia developed. Before death, tonic spasms occurred in the right arm and leg; trismus developed, and the patient lost consciousness. Simultaneously, the right knee reflex and the Achilles reflex became exaggerated, and the Babinski phenomena appeared on the right side. At the beginning, the fundi of the eyes were normal; later, optic neuritis developed (p. 254) ... one month before admission it became more difficult for him to write ... In certain words, he would stop and think how he should write the letter g for instance ...'

Examination showed the patient was afebrile, with normal blood pressure and normal general examination.

'... Right inferior facial nerve weaker than left ... speech was difficult and dysarthric. The patient could not write certain words or letters though he knew them. ... No pathological reflexes, ataxia and Romberg sign and hypotonia were absent ... Neither adiadookinesis nor astereognosis were present, sensation was normal. CSF was normal.' (p. 244)

A pathological description follows (fig. 1):

Baló summarised the findings:

'... an isolated disease of the white matter which is characterised by the occurrence of foci varying in size from a lentil to that of a pigeon’s egg and presenting gray softening and, in part, concentricity. In these foci, the medullary sheaths are destroyed, and the axis cylinders remain intact. Proliferation of the neuroglia follows the destruction of the medullary sheaths, and mast glia cells occur which partly undergo degeneration and become the subject of gliophagia. The concentric foci develop in such a manner that the degenerated layers alternate with normal layers of white matter (fig. 2). The changes about the vessels indicate the inflammatory character of the process (p. 263). Syphilis, apparently does not play a part in the etiology ... Intracerebral inoculation with material from the brain into rabbits did not transmit the disease ...'
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In order to classify my case according to the forms of diseases reported, acute multiple sclerosis and encephalitis periaxialis diffusa must be considered. The condition in my case differs from acute multiple sclerosis, since this disease affects both the brain and the spinal cord, involving the gray and white matter; nor does it correspond to encephalitis periaxialis diffusa, because of the presence of concentric foci instead of diffuse alterations. My case corresponds most closely with the third case of Marburg, and with that of Barré, Morin, Draganescu and Reys, and I would suggest the term leuko-encephalitis periaxialis concentrica for this group. Neubürgler criticized the term “periaxial.” I find that the destruction of axis cylinders is never so extensive as that of the medullary sheaths and hence feel that the term periaxialis is defensible. The term “leuko-encephalitis” is justified because the inflammatory process is restricted to the white matter, i.e., where the white matter occurs in the greatest quantity, in the centrum semiovale and the corpus callosum. The school of Spielmeyer uses the descriptive phrase “scleroticizing inflammation of the marrow of the hemisphere” for the same condition. Claude and Lhermitte reported that the term leuko-encephalitis was first applied by Rémond. He used this term in certain diseases of the brain associated with delirium. Rémond, however, merely hypothesized a leuko-encephalitis, but did not present anatomic evidence of it. Claude and Lhermitte recognized this disease in the living. Marie and Foix called it “sclérose intracérébrale centrolobaire et symétrique.”

Leuko-encephalitis periaxialis concentrica means a disease in the course of which the white matter of the brain is destroyed in concentric layers in a manner that leaves the axis cylinders practically intact. This disease seems to be more nearly related to encephalitis periaxialis diffusa than to acute multiple sclerosis.

‘Among the diseases of the brain known to date, the condition in the case reported resembles acute multiple sclerosis and the encephalitis periaxialis diffusa of Schilder. The disease differs from encephalitis periaxialis diffusa because of its focal character. It differs from multiple sclerosis because in that condition both brain and spinal cord and both the gray and the white matter are affected.’ (pp. 263–264)

Clinically, Baló’s concentric sclerosis commonly presents as an acute or subacute, sometimes monophasic, encephalopathy with a fulminating course. Diagnosis is ultimately proved by histopathology, but in life, MRI shows characteristic irregular, concentric zones of increased signal on $T_2$-weighted images. More recent publications show examples of a less malignant course and some response to corticosteroids.

The basis of concentric sclerosis is still unclear though current opinion favours a variant of acute multiple sclerosis [8]. A recent example reported was associated with primary human herpesvirus 6 infection [5]. The active concentric lesions follow a pattern of demyelination that resembles the tissue injury of hypoxia. Lesions show high expression of inducible nitric oxide synthase in macrophages and microglia, with oligodendrocytic dystrophy. At the edge of active lesions, proteins involved in tissue preconditioning, such as hypoxia-inducible factor 1 and heat shock protein 70, are expressed mainly in oligodendrocytes. Thus, this rim may be resistant to further damage in an expanding lesion and may therefore remain as a layer of preserved myelinated tissue [9].

Fig. 3. Baló’s [4] classification.

Baló provides an extensive discussion which repays study. He appraises the differential diagnosis and the possible relation of his findings to those in the earlier literature (fig. 3). He concludes:

References