Article *NIMHANS Journal*

Multiple Sclerosis with an Associated Diffuse Oligodendroglioma

Volume: 04 Issue: 02 July 1986 Page: 105-110

T Vasudev Rao ,

Reprints request

,

- *Department of Neuropathology, National Institute of Mental Health & Neuro Sciences, Bangalore 560 029, India*

S Mushtaq, - *Department of Neurosurgery, National Institute of Mental Health & Neuro Sciences, Bangalore 560 029, India*

Sarala Das, - *Department of Neuropathology, National Institute of Mental Health & Neuro Sciences, Bangalore 560 029, India*

B S Das &, - *Department of Neurosurgery, National Institute of Mental Health & Neuro Sciences, Bangalore 560 029, India*

S K Shankar, - *Department of Neuropathology, National Institute of Mental Health & Neuro Sciences, Bangalore 560 029, India*

Abstract

A case of multiple sclerosis in association with an oligodendroglioma is presented. The aetiopathogenesis is briefly discussed. The unusual features were the clinically silent multiple sclerosis lesion and the associated diffuse oligodendroglioma, a combination hitherto not reported. The etiopathogenesis of such collisions is ill understood. Separate factors may initiate the lesion or a common agent can be oncogenic as well as cause demyelination. Tumour specific antibody can cross-react with myelin or reactive glia bordering plaques may show neoplastic transformation. Availability of computed tomography should reduce the number of undiagnosed or silent cases of multiple sclerosis and cerebral tumours.

Key words -

Neuro-ectodermal tumour,
Oligodendroglioma,
Multiple Sclerosis
Neuro-ectodermal tumour,
Oligodendroglioma,
Multiple sclerosis

The association of multiple sclerosis (MS) and a primary intracranial neuro-ectodermal tumour is relatively rare [1], [2], [3], [4], [5], [6], [7], [8], [9], [10], [11], [12], [13], [14]. Scherer reported the first case and subsequently 20 more case reports have appeared in the literature. A concurrence of these two lesions, whether casual or otherwise, has been a matter of discussion and opinions differ. Majority of the associated tumours were astrocytomas and very few case reports of oligodendrogliomas associated with sclerotic plaques have been reported [10], [14]. Occasionally, the astrocytomas have been of a diffusely infiltrating type [5], [7]. We report in this communication, a diffuse oligodendroglioma in combination

with MS. The tumour and the demyelinating plaques had remained silent till autopsy. Such atypical and clinically silent MS is extremely rare with only 18 cases reported in the literature [15].

Case Report

M, a 65 year old male patient was reported to have been knocked down by a speeding motor car on 15.4.1983. He had no attendants at the time of the accident. He was admitted to K. R. Hospital, Mysore, by a passerby. At the time of admission he was said to have been in a semi-conscious state. Over the next 24 hours his level of sensorium deteriorated and was therefore referred to the neurosurgical unit of the National Institute of Mental Health & Neuro Sciences, Bangalore on 17.4.1983. On arrival at the Casualty department the patient was deeply unconscious and not responding to painful stimuli. Both pupils were dilated and fixed. He was gasping for breath. There was no ENT or scalp bleeding. His pulse and blood pressure were not recordable. In spite of resuscitative measures, he succumbed within 15 minutes of admission. Time did not permit any investigation.

Retrospective history taken after confirming the pathology was non-contributory. The patient was said to have been a security-watchman, having enjoyed good health all through, with no previous history of head injury, fever, headache, vomiting or exanthemata. There was no history of occular pain or visual disturbance.

There were no features to suggest vertigo, gait disturbance or motor weakness. His higher mental functions were normal and he was not vaccinated in the recent past. He was not a known epileptic, hypertensive, or diabetic and had no tremors.

A routine autopsy was performed 4 hours after death. At autopsy, both the lungs showed contusions with significant haemothorax. The other viscera were unremarkable. The brain showed a thin film of extradural and subdural blood over both cerebral hemispheres. There was also diffuse subarachnoid haemorrhage. A 3" inch long linear fracture was seen in the right squamous temporal bone. The right cerebral hemisphere was larger than the left. The vessels and cranial nerves were normal. Serial coronal slices showed prominence of central white matter with islands of puckering suggesting gliotic scarring. There was diffuse spotty calcification, confirmed by soft tissue x-ray. The deep ganglionic masses showed mild distortion with a granular surface. The corticle mantle was relatively well preserved. Multiple small 'ring-like' lesions (2 × 5 mm) were seen in the right frontal white matter. Smaller cystic spaces were also encountered in the right frontal, parietal and temporal white matter. The frontal horn of the right lateral ventricle was compressed. However, there was suggestion of mild ventricular dilation elsewhere.

After sufficient fixation of the brain in neutral formalin, representative sections of the brain tissue were processed to be blocked in paraffin. Sections were cut at a microtome setting of 5 microns. HE, Luxol Fast Blue, PTAH and silver stains were done on all the sections.

Microscopy revealed multiple geographic areas of plaque-like demyelination, involving the central white matter of both the hemispheres, right more than left, (Fig. 1) deep ganglionic masses, subependyma and the corpus callosum. The lesions appeared pale and had astrocytes and thick PTAH positive glial fibres (Fig. 2). A few plaques had distinct margins while others merged gradually into the surrounding parenchyma. The plaques were seen to spare the cortical 'u' fibres - Schilder's type (Fig.

3). Surrounding the plaques, was a rim of intense oligodendroglial proliferation and numerous reactive astroglia. Presence of microcystic spaces separated by thin glial fibres was another interesting feature (Fig. 4).

- ***Right parietal lobe with sharply demarcated demyelinated areas. Whole mount LFB Eosin***
- ***Demyelinated areas with reactive astrocytes and glial fibrils. (PTAH × 40)***
- ***Right frontal lobe showing sparing of the subcortical 'U' fibres by the demyelinating lesion. Whole mount LFB-Eosin***
- ***Microcystic spaces separated by PTAH positive glial fibres. (PTAH × 63)***

The oligodendroglial proliferation was not limited to the periphery of the plaques but was diffuse, attaining tumourous proportions in many zones (Fig. 5). Groups of neoplastic oligodendroglia were seen separated by vascularised collagenous connective tissue. Spotty calcification within the tumour was also seen. At no place was the tumour well demarcated, but always merged with the cells around the plaque. The right hemisphere was considerably more involved than the left. The neoplasm was seen infiltrating the opposite hemisphere through the corpus callosum. The tumour was seen to breach the piaglial membrane in the temporal lobe. The ring lesions were represented by groups of neoplastic oligodendroglial cells with a central less dense zone.

- ***Oligodendroglioma showing groups of neoplastic oligodendroglia separated by vascularised connective tissues (HE × 16)***

Hypovolemic shock was the immediate cause of death. The demyelinating lesions and the diffuse oligodendroglioma were considered to be incidental findings.

Discussion

Multiple sclerosis (MS) and primary neuro-ectodermal tumours of the central nervous system (CNS) are well established entities. The incidence of MS [16], [17], [18], [19], [20], [21], [22], [23], [24] and oligodendroglioma [24] in the Indian-subcontinent is low and a combination of the two lesions has not so far been reported from India. The pathogenesis of a combination of these two diseases is poorly understood. Whether a concurrence of the two is coincidental and a result of casual relationship [3], [4], [5] or whether the tumour develops secondary to neoplastic transformation [1], [6], [7], [8] of reactive glial cells is controversial. Anderson et al. [2] calculated the expectation of such an association and statistically ruled out the likelihood of the two lesions being a chance finding.

The inter-relationship between MS and gliomas could be postulated as follows:

(1) There are separate factors responsible for initiating gliomas and demyelination;
(2) The same factor(s) could possibly be oncogenic as well as cytolytic resulting in demyelination;
(3) A common antigen shared between the glial tumour and myelin membrane could result in immune mediated demyelination, or
(4) The reactive glial plaques may develop neoplastic transformation as a result of some immune reaction.

So far, 21 cases of MS with an associated glial tumour have been reported [1], [2], [3], [14]. Of these, 14 were astrocytomas, 2 oligodendrogliomas, 2 mixed gliomas, 1 was doubtful ependymoma [5] and details of another case were not available [13]. Two of the astrocytomas described showed diffuse infiltration [5], [7]. There have been no case reports of diffuse infiltrating oligodendrogliomas with MS

similar to the one described by us.

Anderson et al. [2] have observed that a gliomatous transformation is more likely to occur if the demyelinating process involves the potentially active sub-ependymal plate area. They have also demonstrated contiguity between the demyelinated plaques and gliomas in each of their three cases. Similar contiguity was seen in another 11 cases reported by others [1], [3], [6], [7], [8]. Anderson et al [2] postulate this glial neoplastic transformation to be due to failure of homeostatic mechanisms controlling macroglial reaction. Likewise, in our case, the glioma was seen gradually merging with the plaques. The 'U' fibre sparing by demyelinating plaques, 'Schilders type' a feature in our case was also reported by Anderson et al. [2].

Multiple sclerosis was initially considered to be a primary defect of the oligodendroglia, but attention has now shifted to immunologically mediated destruction of the "myelin membrane" [25]. Immunocytochemical studies [26] have shown loss of myelin basic protein and one of the myelin associated glycoproteins in cases of MS. An increase in the oligodendroglial count at the periphery of MS plaques was reported by Ibrahim and Adams [27]. Further evidence and mechanism involved in such a proliferation was provided by the work of Merrill et al. [28]. They hypothesised that the perivascular mononuclear cell infiltration around plaques could release soluble mediators, which in turn, may cause astroglial and / or oligodendroglial proliferation. They have demonstrated in vitro, that T-cell medium from patients with MS induced both astrocytic and oligodendroglial proliferation in primary rat glial cell cultures. Oligodendroglial proliferation identical to descriptions given above was also a feature in our case.

Considering the relatively large incidence of neuro-ectodermal tumours, one would expect a far greater number of cases with associated MS if the Tumours were to mediate an allergic demyelination. Hence it is felt that demyelination is the primary process and that the glial tumour is a secondary phenomena.

Silent and atypical cases of MS are a rare occurrence with only 18 cases reported in literature [15]. Phadke and Best [15] reported 12 cases and classified them into 3 broad groups:

(a) cases with no known previous history of neurological illness
(b) cases with a history of neurological illness in whom a diagnosis of MS was never considered and
(c) cases with a history of neurological disorder in whom a diagnosis of MS was neglected or considered unlikely.

Our case with no previous neurological ailment corresponds to group 'a'.

Review of literature has enlightened us about the probable mechanisms involved in the initiation of glial neoplasm by the demyelinating plaques, but this alone cannot explain the low incidence of an association between the two. In future, with the advent of CT Scan and evoked potential studies it is unlikely that silent cases of MS will escape detection.

Acknowledgements

We are grateful to the Director, NIMHANS for allowing us to publish this article. We also thank Mr. Kumar and Mr. B G Rajaram for their technical help and Mr. S Vinayagam for the secretarial assistance.

1.Scherer H J, La glioblastoma en plaque

Beligique Neuro Psychiat Page: 38: 1-17, 1938
2.Milne H, Brodie, Michael W, Smith, Waterhouse J M H, Gliomatous transformation and demyelinating disease
Brain Page: 103: 603-622, 1980
3.Brihaye J, Perier O, & Stenuit J, Multiple sclerosis associated with a cerebral glioma
Neuropathology & Experimental Neurology Page: 22: 128-137, 1963
4.Mathews T & Mossy J, Mixed glioma multiple sclerosis and Charcot-Marie-tooth-disease
Archives of Neurology (Chicago) Page: 27: 263-268, 1972
5.Munch-Peterson C J, A case of disseminated sclerosis and glioma of the brain in the same patient
Acta Psychiatrica et Neurologica Scandinavica Page: 24: 599-605, 1949
6.Russell D S & Rubenstein L J, Primary tumours of neuroectodermal origin
In Pathology of tumours of the Nervous systems Eds. D S Russell and L J Rubinstein 3rd edition Lon Page: P.179, 1971
7.Reagan T J & Feiman I S, Multiple cerebral gliomas in multiple sclerosis
Journal of Neurology, Neurosurgery & Psychiatry Page: 36: 523-528, 1973
8.Currie S & Urich H, Concurrence of multiple sclerosis and glioma
Journal of Neurology, Neurosurgery & Psychiatry Page: 28: 271-312, 1950
9.Zimmerman H M & Netsky M G, The pathology of multiple sclerosis
Research publications of the Association for Research in Nervous and Mental Disorders Page: 28: 271-312, 1950
10.Barnard R D & Jellinek E H, MS with amyotrophy complicated by oligodendroglioma - History of recurrent zoster
Journal of Neurological Sciences Page: 5: 451-455, 1967
11.Boyazis R M, Martin L, Bouteille M et al, Images histochimiques et ultrastructurales dans un case de sclerose en plaques associ'ee a un spongioblastome
Rev. Pathol. Nerv. Mentale Page: 88: 1-19, 1967
12.Aubert L Arroyo H, Daumas B, & Tripiper M E, 'Un-cas d' association entre sclerose en plaques et glioblastoma cerebral
Review of Neurology Page: 119: 374-376, 1968
13.Koya G, Suzuku M, Bab M, & Iwabuchi T, An autopsy case of concurrence of MS and glioma
Hirosaki Med. J. (Jpn) Page: 294: 588-595, 1977
14.Giordana M T, Association between MS & oligodendroglioma case report
Italian Journal of Neurological Sciences Page: 2: 403-9, 1981
15.Phadke J G & Best P V, Atypical and clinically silent multiple sclerosis : a report of 12 cases discovered unexpectedly at necroscopy
Journal of Neurology, Neurosurgery & Psychiatry Page: 46: 414-420, 1983
16.Gourie Devi M, & Nagaraja D, Multiple sclerosis, East and West
(Eds) Yoshigoro Kuroiowa Leonard T Kurland, Kyushu University Press, Fukoka Japan Page: 135-147, 1982
17.Dastur D K, & Singhal B S, Two unusual neuropathologically proven cases of multiple sclerosis from Bombay
Journal of Neurological Sciences Page: 20: 397-414, 1973
18.Shankar S K, Gourie-Devi M, Nagaraj D, Vasudev Rao T & Sarala Das, Neuromyelitis optica - Report of an autopsy proven case from South India
Journal of Association of Physicians of India Page: 52: 371-373, 1984
19.Nair K R & Saharanam K V, Multiple sclerosis in Malabar

Journal of Association of Physicians of India Page: 26: 899-903, 1978
20.Mathews N T, Mathai K V, Abraham J & Taroi G M, Incidence of pattern of demyelinating diseases in India
Journal of Neurological Sciences Page: 13:27-38, 1971
21.Chopra J S, Radhakrishnan K, Sawhney B B et al., Multiple sclerosis in North West India
Acta Neurologica Scandinavica Page: 62: 312-321, 1980
22.Barucha E P & Umarji R M, Disseminised sclerosis in India
Inst. J. Neurol Page: 2: 312-321, 1980
23.Singhal B S & Wadia N H, Profile of multiple sclerosis in the Bombay region on the basis of critical clinical appraisal
Journal of Neurological Sciences Page: 26: 259-270, 1975
24.Dastur D R & Lalitha V S, Pathological analysis of intercranial space occupying lesions in 1000 cases including children. Part -2 Incidence, types and unusual cases of gliomas
JNIS Page: 8:143, 1969
25.Mc Farlin D E, & McFarland H F, Multiple sclerosis (1st of 2 parts)
New England Journal of Medicine Page: 1183-1188, 1982
26.Itoyama Y, Sternoberger N H & DeF. Webster H et al., Immuno cytochemical observation on the distribution of myelin-associated glycoprotein and myelin-basic protein in MS lesions
Annals of Neurology Page: 7: 167-77, 1980
27.Ibrahim M Z M & Adams C W M, The relationship between enzyme activity and neuroglia in plaques of multiple sclerosis
Journal of Neurology, Neurosurgery & Psychiatry Page: 26: 101-110, 1963
28.Menrill J E, Ellison G W, Groopman J E, Hofman H & Golde D W, *Astrocytic and oligodendroglial cells proliferate in response to human T-lymphocyte-derived factors, (Paper presented in the 35th Annual Meeting Program, American Academy of Neurology, California, April 1983)*