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Hydrocephalus - Pathological Changes in Pre and Post Shunted Brains in Cases of Post Infective Hydrocephalus

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Abstract

In paediatric age group the pathological changes in post infective hydrocephalic brains before and after shunt surgery was studied in autopsy material. The degree of ventricular dilation, the extent of ependymal loss were found to be variable. In the initial stages subependymal oedema was prominent, while at later stages gliosis predominated. Many epitheloid cell granulomas were observed projecting into the ventricle breaching the ependyma. Following shunt surgery, in hydrocephalics of long duration, though the intraventricular pressure was relieved, there was no significant structural restitution of the cortical mantle. A more detailed neuroanatomical studies need to be conducted for a proper correlation of the relationship between the structure and function of the cortical neuronal circuitary.

Key words -
Hydrocephalus,
Post meningitic hydrocephalus,
Shunt surgery,
Pathology of hydrocephalus

Neurotuberculosis still continues to be a major cause of mortality and morbidity in many countries of Asia and South America. Hydrocephalus is one of the commonest pathological sequelae to chronic tuberculous meningitis, a disease widely prevalent in our country. Thinning of the cortical mantle due to obstructive hydrocephalus, secondary to inflammatory basal exudate is observed in nearly two thirds of the children and about half of the adult cases of this chronic meningitic process [1]. Attempts have been made to correlate the cerebral mantle thickness to intellectual performance and evaluate the efficiency of shunt procedure in restitution of the thinned out brain tissue to normalcy [2], [3], [4], [5]. In spite of detailed studies about the pathological aspects on tuberculous meningitis in humans [1], [6], the data is incomplete and sketchy on the effect of hydrocephalus, especially the post infective variety, on the cortical mantle, particularly with respect to the sequential changes in the cortex with time and their reversibility following surgery. In view of the fact that a predictably controlled and uniform model system is difficult to achieve in human beings, various animal experimental models are evolved to study this problem and their results are extrapolated on to human beings [7], [8], [9], [10]. The dynamics of human skull and brain are different from those of the various experimental animals. Similarly the skull of the adult offers greater resistance to the expansion of the brain to counter the rising intraventricular pressure, in contrast to children. These differences need to be kept in mind while evaluating the effect of hydrocephalus

on the brain and the associated functional derangement.

This study is undertaken to observe the pathological changes in the brain following hydrocephalus and the effect of shunt surgery on these changes. At National Institute of Mental Health & Neuro Sciences, Bangalore, nearly 70 per cent of hospital deaths are autopsied and nearty one fifth of them are cases of tuberculous meningitis in various stages of pathological evoluti6n. This report describes the histological changes observed inpost infective hydrocephalus, before and after shunt surgery.

Material and Methods

From the autopsied cases from January 1979 to March 1982, a sample of 10 of tuberculous meningitis with basal exudate, in paediatric age group were selected randomly. Similarly 6 cases of T. B. M. of the paediatric age who had undergone shunt surgery were taken. A case of Dandy Walker's anomaly, who had also undergone shunt surgery was added, as the non infective hydrocephalic case for the sake of comparison.

The duration of illness, from the onset of symptoms as informed by the parents, till the time of death was noted. The routine laboratory investigations and the radiological studies (whenever available) were analysed. The formalin fixed brains were carefully examined noting the degree of basal exudate, the vascular involvement, oedema and' other ischemic lesions. For the present study attention is confined to the basal exudate, the degree of ventricular dilatation and changes in the cortical mantle. The basal exudate when appeared as a thick plaque over the optic nerves interpedunculor fossa, and pons, obliterating the cisterna ambiens and obscuring the cerebral vessels was graded as severe, while only a few tubercles over the leptomeninges and slight meningeal thickening represented the mild degree and intermediate stage in between these two was considered moderate. The ventricular dilatation was also arbitrarily graded from mild to mild-moderate-severe, noting the maximally affected part. The general pathological features of the cerebral cortical mantle, the ventricular lining and the deep nuclear masses were also noted.

Tissue blocks were taken at different levels. Paraffin processed sections were stained with H.E., LFB-PAS for myelin and PTAH for glial fibres. A few sections were stained with Masson's -Trichrome to evaluate the stromal response and BielSchowski's Silver impregnation to study the axis cylinders. The various histological features were graded depending on the severity to attempt a correlation with the chronology of the illness.

Results

Non shunted group (Table I, page 30):

In this group of 10 cases, the duration of illness varied from 10-180 days from onset to death. They all had fairly uniform degree of basal exudate covering the various anatomical structures. In two of them outlet block was observed, while in 4 irregular fibrous and fibrinous tags were seen traversing the IV ventricular cavity and partially obstructing the CSF pathway; cisterna ambiens was consistently obliterated in all the cases.

The exudate was essentially of exudative type, pools of fibrin enclosing various structures The

underlying vessels showed vasculitis and granulomatous inflammation. There was minimal evidence of organisation of the exudate and fibrosis even as late as 180 days of illness.

The ventricular dilatation was variable in degree and no correlation was found between the degree of dilatation, CSF protein and inflammatory cell content, in this small sample of cases. In both the cases with outlet block, the whole of the ventricular system was dilated, the lateral ventricle along the horns showing the maximal effect.

On histological examination, the ependyma at various places showed patchy loss. The lining epithelium was cuboidal to columnar, similar to the cases with no ventricular dilation. Even in the cases with significant hydrocephalus, there was no total enudation or absence of ependyma. In the immediate subependyanal zone, many active epitheloid cell granulomas were observed projecting into the ventricular cavity 'like mushrooms' elevating and rupturing the overlying lining, the ependyma being present along the everted margins (Fig.1). These granulomas were conspicuous by their absence in cases, where there was no hydrocephalus. In the case with duration of illness of 180 days, instead, glial granulations were seen projecting out.

Table I - Hydrocephalus - Non Shunt Group - Histological Features

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.***Tuberculous granulomas projecting into the ventricular cavity rupturing the ependyma H. E. ×24***

Subependymal oedema and spongi change was evident from 10th day of illness onwards, reaching a maximum by 3rd week. Fibrillary astrocytic proliferation was evident from 10th day though less prominently, coexisting with oedema. Later the oedema tended to reduce, the gliosis becoming prominent. As the oedema reduced, the ventricles were lined by thick gliotic subependymal astrocytes near the cavity and protoplasmic astrocytes away from the cavity. No appreciable degenerative changes were seen in the white matter, the overlying cortical grey, the. basal ganglia and the brainstem nuclie. In spite of the ventricular dilation, the thickness of the grey matter was fairly well maintained.

Shunted group (Table II, page 30):

Followmg ventriculoperitoneal shunt, in the case with 20 days of duration of illness and radiologically moderate ventricular dilatation (+ +), the ventricle size collapsed within 12 hrs, but the patient died of other neurological complications. Both subependymal oedema, gliosis, and ependymal breaks were observed, similar to the non-shunted group of comparable duration. The elastic compliance of the cortical mantle to shunting in reducing the ventricular size was variable. In cases with longstanding shunt of 7 months and 1 year, the ventricle size reduced with some residual dilatation. In both variable amount of subependymal oedema and significant gliosis were observed.

The case 4 and 7 of this group need special consideration. In both of them the basal exudate was negligible and had severe degree of hydrocephalus involving the whole length of the ventricular system. The cerebral cortical mantle was reduced to a thin ribbon of 2 - 4 mm thickness, the white mater being compressed markedly (Fig. 2, 3). Both of them had outlet block-one of them was the result of congenital anomaly, while the second was post inflammatory as confirmed by a granulomatous lesion in the lateral ventricle and at the outlet. In both, the lesion had started very early in life, when the myelination was in the process of forming. In both the shunt surgery was done, but did not bring out appreciable change in the ventricular size.

.***The cerebral cortical thickness in an age matched control brain (indicated by vertical bar) H. E. ×30***

.The thinning of the cortex involving both the grey and white matter (vertical bar to indicate thickness). Note the band of gliosis towards the ventricular aspect (V) H. E. ×30 (Case -4 shunted group)

Table II - Hydrocephalus-Post Shunt Group-Histological Features

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Case 7 - Dandy Waler's anomaly

Histologically, the lining ependyma was absent in most of the areas, but for a few places where tall columnar epithelium was seen, covered by plaques of fibrillary gliosis. The immediate subependymal zone was oedematous containing a few astrocytes. Next to it, a continuous compact band of gliosis, like a ribbon, was seen, which became loose at the angles of the ventricles. This feature was seen both in the lateral and IV ventricles, compressing the parenchyma. In case 4, the deep white matter of corona radiata, beyond the gliotic band showed focal destruction and gitter cell proliferation. Silver stains revealed dystrophic axonal bulbs diffusely (Fig. 4) but more near the zones of gitter cell reaction. In the rest of the areas active destruction or demyelination of the white matter was not found. The cortical grey matter was also thinned out, at small areas being represented by a band of glial cells and a few neurons. The IV ventricle outlet obstructing membrane of the post meningitic case had chronic inflammatory infiltrate along with gliosis and thickened meninges.

.Zone of white matter distruction showing black dystrophic axonal bulbs in the midst of glitter cells (Case - 4 non-shunted group) Bielschowski's ×150

Discussion

In the nonshunted group, the basal exudate was essentially of similar degree in all the cases, though the duration of clinical symptoms varied from 10 days to 3 months. The cerebral vessels revealed distinct granulornatous response which usually takes 3 weeks to develop. This brings to light the problem of determining the exact duration of illness and the time taken in the evolution of hydrocephalus. The degree of dilatation was variable depending on the site and degree of block and the functional status of the CSF dynamics at different levels.

The histological features in the white matter of the brain in which there was significant ventricular dilatation was not nearly as dramatic as the appearance to the gross examination. The brunt of the intraventricular pressure and the resulting thinning was observed maximally at the angles of the ventricles and the corpus callosum. The ependymal loss was patchy even in cases with significant ventricular dilatation, contrary to the reports of Penfield [11] and Rowlatt [12] in human material. The subependymal oedema was the initial feature while the gliosis predominated in the later stages, though the glial reaction was observed even in the initial phase. This was in variance to the observations in various experimental animals [7], [8], [9]. Probably this could be attributed to the problems in establishing the exact chronological sequence of events in human material unlike the controlled experiments on laboratory animals. The non-shunted group showed numerous sub pendymal granulomas disrupting the ependyma. They could probably act as a source of tuberculous infection similar to 'Rich's focus'.

The presence of subependymal oedema, even in areas with intact ependyma raises the doubt about the exact role of ependymal breaks or gaps, on the trans ependymal spread of CSF and thus initiating

oedema [8].

As there was no active tissue damage in large majority of cases, it seems likely that the thinning of the cerebral mantle to a large extent is the result of simple pressure from inside. In human infant in whom the sutures are not fused, the ventricular expansion is unimpeded and it is they who suffer greater cortical stretching. It is possible that the state of myelination and the amount of allowable cranial expansion determine the degree of damage. However the data is incomplete in human beings.

The advent of ventricular shunt has created an impression that hydrocephalus is a reversible process. Clinical experience from serial ventriculograms in patients have demonstrated an increase in mantle thickness occurring usually over several weeks. However, no study is available demonstrating the anatomical changes in the mantle thickness, especially those occurring within the first few week's following the ventricular shunting in postinfective hydrocephalus. In our material the ependymal breaks observed in the early stages persisted, even after relieving the ventricular pressure by surgery, so also the subependymal oedema and gliosis. These features were still present even 1 year after shunting. Probably it is necessary to study many more cases, who had shunt tube over weeks and the ventricular size has returned to normal or near normal state, for a proper evaluation of the reversible anatomical changes in hydrocephalic patients.

The cases 4 and 7 were comparable in many respects, though different aetiologically. Both had the onset of clinical features almost at the same age and progressed to have severe degree of ventricular dilatation. They had a dense band of gliosis in the subependymal zone, the rest of the white matter showing astrocytosis. Case 4 also revealed focal gitter cell response and dystrophic axonal bulbs indicating active tissue destruction and disruption of axons in long standing cases with marked intraventricular pressure. The shunting procedure probably has relieved the intraventricular pressure, but did not facilitate the restitution of the cortical mantle to normal thickness even after weeks of surgical procedure, suggesting the permanency of the lesion.

Several studies have attempted a correlation of the final cortical thickness following shunt procedure and intelligence [3], [5], [13], [14] the results being variable. These discrepancies were understandable as hydrocephalus mostly affects the white matter, with remarkable sparing of the grey matter. The measurements of the mantle thickness reflects primarily the loss of white matter and hence poorly correlates with the parameters indicative of grey matter performance. Initially as hydrocephalus develops, little functional impairment is noted, probably because many of the axons are expendable. However severe loss of axons with dystrophic changes will disrupt the interneuronal communication eventually functional and intellectual impairment. Case 4 in our material in the post infective-shunted group showed such axonal changes and could have had the predictable changes if survived. Because of the inherent impracticability of estimating and assessing the site and degree of axonal damage, these correlations remain only partial and lot more study is needed to understand the basic process. In addition, the manner in which these parenchymal changes interfere with CSF dynamics is not known.

Conclusions

1. In hydrocephalic brains, the degree of ependymal loss is variable and there is no definite evidence of regeneration of it, following the shunt surgery.
2. In the evolution of parenchymal changes following hydrocephalus, the subpendymal oedema and

astrocytic proliferation are seen together, while at a later stage, gliosis predominates.
3. Subependymal granulomas projecting into the ventricle disrupting the lining could behave like the Rich's focus in maintenance and spread of the disease.
4. Following the shunt surgery the degree of return of the ventricular size of normalcy is variable and restitution is minimal if the ventricular size is large and has occurred early in life.
5. The subependymal parenchymal changes observed persisted even after shunting, though there was variable degree of restitution of the cortical thickness.
6. In longstanding hydrocephalus, the destruction of the stretched axons and their disruption could contribute to various neurological and intellectual derangement.
7. More detailed study is needed using human material, to evaluate the neuronal changes, their dendritic arborisation and the synaptic density in hydrocephalic brains for proper understanding of the structural and functional interaction.

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