THE VALUE OF STREPTOMYCIN IN THE SURGICAL TREATMENT OF INTRACRANIAL TUBERCULOMA*

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Although the incidence of intracranial tuberculoma has greatly diminished in recent years, there are some countries where these lesions still represent an important neurosurgical problem. The subject has been discussed at recent meetings of the Spanish-Portuguese Society of Neurosurgery (Barcelona, April 1948) and the Society of British Neurological Surgeons (Dublin, July 1948). In Portugal and Spain the incidence of intracranial tuberculoma is very high, and Imaginario (1949) found that they represented 6 per cent. of the intracranial tumours verified in Lisbon. In Ireland, Lanigan (1948) mentioned a frequency of 5 per cent. of the brain tumours of McConnell's series, and according to the figures of Asenjo and others (1947), the proportion is even higher in Chile and in Mexico.

In the last two years we have collected sixteen verified intracranial tuberculomata in our own material in Madrid, which represent nearly 10 per

cent. of our cases of expanding intracranial lesions.

Experience of the surgical treatment of intracranial tuberculoma has been on the whole disappointing. In the majority of cases where a tuberculoma was totally or partly removed tuberculous meningitis developed in the course of a few months and ended fatally. This bad prognosis was especially true of tuberculomata of the posterior fossa. Fear of spreading the tubercle bacilli into the cerebrospinal fluid led many neurosurgeons to practise simple decompressions. But even after such restricted operations there was a high late mortality. On the other hand it is often difficult to recognize the tuberculous nature of the lesion until a removal of tissue has been carried out. Thus some neurosurgeons prefer radical operations in spite of the risks of spreading the disease to the leptomeninges. Although in the literature there are isolated examples of recovery following removal of tuberculomata from the cerebellum and cerebral hemispheres, the mortality rate has been on the whole very high, over 50 per cent. in some series.

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TABLE
RESULTS OF TREATMENT IN TEN CASES OF CEREBRAL TUBERCULOMA

Localization	Surgical treatment alone			Surgical treatment and intrathecal streptomycin			Surgical treatment and streptomycin (intramuscular and intrathecal)	
	No. of cases	Recoveries	Causes of death	No. of cases	Recoveries	Causes of death	No. of cases	Recoveries
Infratentorial ..	2	0	Postoperative tuberculous meningitis	1	0	Generalized tuberculosis but not in meninges	4	4
Supratentorial ..	1	1	—	—	—	—	1	1
Multiple	1	0	Increase of intracranial pressure after ventriculostomy	—	—	—	—	—

FIG. 3.—Chart showing the changes in cells and total protein of the cerebrospinal fluid following the removal of a subtentorial tuberculoma and the treatment with streptomycin during the post-operative period.

The attitude of the neurosurgeon towards these lesions has been completely changed in the last two years by the use of streptomycin. The situation can be compared to the change brought about by penicillin in the surgical management of pyogenic brain abscesses. It seems that the spread of tuberculosis to the meninges can be prevented by streptomycin, and therefore the neurosurgeon can attempt the radical removal of cerebral tuberculomata without his previous fears.

From our material of sixteen cases of tuberculomata we present the results of treatment in the first ten cases for comparison of those operated on with and without streptomycin. The immediate and late results can be studied in this group, as they have been followed up from one to one and a half years after operation. The other six patients, who are not included in this report, all had tuberculomata of the cerebellum. Two of them died as a result of the operation, and the other four, also treated by streptomycin, are not included because the follow-up period has not yet been long enough to assess the result.

The Table gives a summary of our results in the first ten cases.

It is a striking fact that five cases of cerebral tuberculoma treated surgically and with streptomycin, given both intramuscularly and intrathecally, recovered completely, especially as in four of these the tuberculoma was in the posterior fossa; the results compare very favourably with those previously obtained in cases which were treated by operation

only. Owing to difficulties in obtaining sufficient supplies of streptomycin one of our early cases was given the drug intrathecally only, and although this patient died three months after the operation from generalized tuberculous meningitis, there were no signs of meningitis at autopsy.

Surgery

The surgical removal of tuberculomata is sometimes very easy when they are not deeply situated. Sometimes they are large, but can be removed intact without great difficulty. The bed of the tuberculoma is usually formed by degenerated brain tissue with slight vascularization which is aspirated during removal. But the surgical problem is not always so simple. Sometimes the lesions of the cerebellum are very deep, growing towards the fourth ventricle or higher up in the area of the tentorium and brain stem, and there may then be great difficulty in removing the tuberculoma. In those deeply situated lesions of the posterior fossa it is necessary to carry out a piecemeal removal in the same way as is done with tumours. There does not seem to be any obvious difference between the ultimate results of total or piecemeal removals, and in this series of the four recovered infratentorial tuberculomata two were removed in one piece and the other two in fragments, although every effort should be made to do the removal in one piece where conditions permit. Figs. 1 and 2 show some of the tuberculomata of our series.

FIG. 1.—Examples of four tuberculomata removed in toto from the cerebellum.

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FIG. 2.—Specimens of four tuberculomata which were removed in pieces due to their deep situation in the brain tissue.

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FIG. 4.—Another example of the variations of the number of cells and the amount of protein in the fluid during the treatment with streptomycin after the operative removal of a tuberculoma.

Postoperative Treatment with Streptomycin

The postoperative treatment with streptomycin was carried out by intramuscular and intrathecal injections. The drug was given intramuscularly in daily doses of 1 g. during periods varying from forty-three to seventy-eight days. The injections into the cerebrospinal fluid were given by the intraventricular or lumbar route for thirty-five to sixty days after the operation, usually in doses from 50 to 100 mg. daily during the first four weeks of treatment, and afterwards every other day. Studies of the cerebrospinal fluid were made during the course of the treatment, and in most cases a progressive diminution of the number of cells and the amount of protein was observed (Fig. 3), but these values may show some irregular variations (Fig. 4) which may be due to the action of the drug injected in the cerebrospinal fluid, and perhaps to other factors such as the presence of blood in the cerebrospinal fluid. However, the general tendency was towards a slow return to the normal cell and protein content, while the figures for chlorides and glucose in the spinal fluid have not been noteworthy in our cases.

In general our tendency has been gradually to reduce the length of postoperative treatment with streptomycin after the removal of tuberculomata. In our most recent cases, which are not included in this communication, we have given daily intramuscular doses of 1 to 2 g. for one month, and 50 mg. intrathecally during each of the first ten days, followed by injections of 50 mg. every other day for the next ten days and then three times a week in the final ten days. The cerebrospinal fluid is examined every ten days during the treatment and one month afterwards. This general short plan is of course modified according to the peculiarities of each case. A study of the reaction of the patient to high dilutions of tuberculin may also provide useful information.

We believe that our experience shows conclusively the great value of streptomycin in avoiding postoperative tuberculous meningitis after the removal of intracranial tuberculomata. This highly protective effect is of immense value in the surgical attack on these lesions. However, the evolution and final outcome of the individual case with an intracranial tuberculoma depends on several factors: first, the

site of the lesion and the possibility of removing it without great surgical risk; secondly, whether the lesion is single or multiple. It seems that tuberculomata are more often solitary than multiple. In thirty cases studied by Imaginario, twenty-four were solitary; and, of these, sixteen were in the cerebellum. We have seen autopsies in five cases of cerebral tuberculomata, and four of these were solitary lesions of the cerebellum. Finally, the general condition of the patient and the presence of active tuberculous lesions in other organs is of extreme importance, for a patient may be cured of an intracranial tuberculoma and the meningeal spread prevented by streptomycin, but may yet die later of other tuberculous lesions. It is also very probable that some patients from whom we remove tuberculomata which give focal or intracranial pressure symptoms may have other silent tuberculomata which may cause late complications.

Summary

The surgical treatment of intracranial tuberculomata has in the past been very unsatisfactory, as most cases developed fatal tuberculous meningitis shortly after the operation.

In Spain tuberculomata are still very frequently found, and in our experience represent nearly 10 per cent. of brain tumours and other expanding lesions. From a group of sixteen cases of tuberculomata, the results are given of the first ten cases with a

sufficiently long follow-up period. Four patients received only surgical treatment, with one recovery in a supratentorial tuberculoma; two of these patients died of postoperative tuberculous meningitis, and one of increased intracranial pressure. In another case streptomycin was not given by the intrathecal route until after the operation, and, although the patient died several months later of generalized tuberculosis, the meninges were free from the disease.

In the next five cases of this series the tuberculomata were removed completely, and for a period of two to three months afterwards the patients were treated with intramuscular and intrathecal streptomycin. All these five cases have recovered and have remained well for periods of one to over one and a half years after operation. In four the tuberculoma was in the posterior fossa.

Our results clearly demonstrate that streptomycin has changed the outlook in the surgical treatment of intracranial tuberculomata and prevents the postoperative spread to the meninges. Under the protection of streptomycin we can now be more radical in our surgical approach to these cases.

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