Diagnosis and Neurosurgical Treatment of Tuberculous Disease of the CNS

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A. The Brain

Summary

The tuberculoma is a space-occupying lesion encountered frequently by all Indian Neurosurgeons. Some features indicate the possibility of such a lesion. These are: tuberculous disease in the past or contact with a tuberculous patient, a positive Mantoux test, pyrexial onset of the disease and frequent history of seizures. The radiological features are not diagnostic, but the presence of multiple, enhancing lesions on the CT scan in a young patient, strongly suggest tuberculomas. Surgical excision of the lesion is recommended, partial near vital areas, and sometimes, with tuberculomas in areas like the thalamus and brain stem only medical therapy is advisable. Long-term medical treatment is necessary. Towards eradication of the disease all those close to the patient need to be examined for early detection of asymptomatic tuberculosis.
Keywords: Computed tomography, tuberculomas, tuberculosis.

Introduction

The tuberculoma, though a bacillary granuloma, has many of the features of a benign neoplasm, such as encapsulation, a slow rate of growth, low recurrence rate, an occasional tendency to calcify and to undergo necrosis or even cystic degeneration. In regions where tuberculomas are prevalent it would, therefore, not be illogical to classify them with brain tumours. World-wide in distribution, from the Poles among Eskimos, to the Equator, they are more concentrated in populous developing nations such as ours, but are also observed to occur sporadically in the more advanced countries, mainly among immigrants (1).

Indian neurosurgeons, who must have collectively treated well over a thousand such cases in the last few decades, rate their incidence between 8 – to 22%, the lower figure pertaining to Calcutta and the higher to Bombay (Table 1). This disparity in incidence would be easier to comprehend if a rural and an urban region were being compared, but not in the case of two equally densely populated industrialised cities like Calcutta and Bombay where the difference, perhaps, may be attributed to the relative availability, accessibility and acceptance of the neurosurgical services by the poorer sections of the local community (1, 2, 3).

Anatomical sites

Though commonly occurring within the cerebral or cerebellar hemispheres, tuberculomas may be found at unusual sites within the cranium, such as the dura mater, subdural space, the orbital fissure, the pituitary gland, or within any part of the ventricular system or the subarachnoid space (1, 2, 3, 5, 6). Their infratentorial location is somewhat commoner than the supratentorial. There may be multiple tuberculomas, a feature more often observed in the post mortem examination by the pathologist than the surgeon, but with the CT scan, the clinician is now beginning to see many more of the multiple lesions.

Sex and Age

In most older series a greater prevalence has been recorded in males, but more recent series show this trend has reversed, with females just outnumbering males. What needs emphasis is that the disease is essentially of the young with 50% of the cases occurring in children under 10 years and 80% in the under 25 age group. A slight male preponderance is ob-

Table 1. Brain Tumour Incidence (1957–1981)

Diagnosis	1957–1963	Number 1957–1970	1957–1972	1972–1981	Total
Gliomas	107	338	423	499	922
Tuberculomas	114 (30.5%)	228 (22.8%)	260 (21.6%)	142 (12.3%)	402 (17.1%)
Meningiomas	43	94	110	124	234
Metastatic tumours	19	92	109	56	165
Pituitary tumours	29	71	83	140	223
Acoustic neurinomas	23	68	84	87	171
Quadrigeminal plate tumours	12	33	38	10	48
Brain tumours miscellaneous	6	21	34	42	76
Cholesteatomas	5	16	18	23	41
Haemangioblastomas	4	15	18	15	33
Vasoformative tumours	5	10	10	–	10
Colloid cysts third ventricle	3	8	8	7	15
Chordomas	3	6	6	2	8
Total:	373	1,000	1,201	1,147	2,348

served up to the age of 15 years, but thereafter females outnumber males (1, 2, 3).

Tuberculous foci and contacts

A patient may have obvious tuberculous disease of other organs as well. Rarely, even while under treatment, additional foci of disease are seen to crop up. To assist the drive for tuberculosis eradication all relatives and close contacts should be located, examined and treated. At the same time, in communities prone to tuberculosis, it should be worth remembering that not all brain tumours are necessarily tuberculomas.

Clinical presentation

Features helpful in distinguishing tuberculomas from other brain tumours are a pyrexial onset, or rapid enlargement of skull in infants, a high frequency of convulsions even in cases with cerebellar involvement, a positive Mantoux test and a raised sedimentation rate. In patients who have previously suffered from tuberculous meningitis the lesions are often cerebellar, or deep-seated within the basal ganglia of brain stem. The usually reliable localizing features of brain tumours such as intracranial calcification, hemiparesis or focal convulsions can prove misleading the presence of multiple tuberculomas, where the larger lesions may be in a relatively silent area and may be revealed unexpectedly by radiological contrast studies (3) or by isotope or CT scan.

Some of the unusual ways in which patients with tuberculomas are known to have presented are with a scalp swelling or sinus, a cerebrospinal fluid rhinorrhoea, exophthalmos, trigeminal neuralgia, or with the signs and symptoms of a pituitary, or an acoustic nerve tumour (1, 2, 6).

Pathology

The brain tuberculoma is always secondary to a focus in the body, most commonly from haematogenous spread. The usual mature tuberculoma is a well-defined nodular avascular mass with a caseating core and crenated margins surrounded by collagen or granulations. In its immature form, multiple small tuberculous follicles are seen embedded within oedematous brain. Well over half are attached at some point to the dura. When the dural attachment is wide it may resemble a meningioma *en plaque*. Cerebellar folia covering a tuberculoma may appear glassy and cystic due to local oedema.

Microscopically, the tuberculoma is a conglomeration of typical tubercle follicles surrounded by degenerated nerve cells and fibres, thrombosed vessels, gitter cells and in some cases swollen astrocytes and oligodendroglial cells. There may be associated infarcts from widespread occlusive and necrotic vascular changes.

Tuberculomas do sometimes undergo calcification and on very rare occasions are known to ossify. The presence of calcareous salts, perhaps induces a metaplasia of connective tissue cells into osteoblasts.

A tubercular abscess is a separate entity which needs to be distinguished from a caseous softened tuberculoma. Unlike the latter the wall of an abscess shows only chronic inflammatory changes and its tubercular origin is revealed by the detection of tubercle bacilli within the pus.

An even more interesting change in a tuberculoma

observed by us, and reported for the first time, is a cystic transformation causing it to be mistaken for a cystic astrocytoma. The fluid may be clear yellow or cloudy green, as much as 100 ml in quantity and may contain tubercle bacilli (1,4).

Radiological Features

Calcification in tuberculomas has been found to vary from two to six per cent, with the sole but striking exception of the Eskimos and the North American Indians in whom nearly 60 per cent are known to calcify. Tuberculoma calcification is generally patchy, varied in density and cannot be easily distinguished from other forms of tumour calcification.

In the detection of tuberculomas by contrast studies minimal angiographic or ventriculographic displacements are significant and are often associated with large masses. Angiographic features are a reduction in the calibre of vessels in the vicinity of the mass, avascularity, and only rarely, a faint blush in superficial tumours adherent to the dura (1,2,3).

In the CT scan tuberculomas appear as strongly enhancing, often multiple, irregular masses, sometimes showing both ring and central enhancement.

Treatment

The surgical method was the only one available to the great neurosurgeons of the past century like Wernicke, Hahn, Horsley, MacEwen, Krönlein and Krause, and to our forebears up to the middle of this century, until the discovery of streptomycin, para-aminosalicylic acid (PAS) and isoniazid (INH) (1,2). Those earlier operations were often performed in multiple heroic stages, aimed at total excision of the mass with some surrounding normal brain, which provided the only chance of success (1,2). Cerebellar tuberculomas proved to be far more lethal than the cerebral, because of the higher postoperative mortality from tuberculous meningitis. None of Harvey Cushing's patients in whom a cerebellar tuberculoma had been excised survived. At the same time, surprisingly, spontaneous cures were not unheard of and a few such authentic cases have been recorded in the older literature (1).

A sharp decline in the postoperative mortality to around 10% followed the introduction of triple therapy (streptomycin, PAS, INH) and corticosteroids. Partial excisions, which were previously condemned, are now being recommended for the very large cerebellar tuberculomas, where a rim of tumour adjacent to the brain stem and often adherent to the tentorium is allowed to remain, to prevent gross internal shifts. Again, wherever important structures are involved, partial excisions are preferred. Shunting devices are employed whenever relief of hydrocephalus cannot be satisfactorily achieved by other means.

Tuberculomas of the brain stem and basal ganglia and some cortical tuberculomas can be successfully treated by medical measures alone. This is being increasingly achieved with the help of serial CT scans which show whether the response to treatment is satisfactory or otherwise.

To complete a full course of the necessarily prolonged medical treatment, which may exceed a year, patients need constant encouragement and sometimes financial assistance. For patients with supratentorial tuberculomas the importance of prolonged intake of anticonvulsants cannot be stressed enough. At the same time there is need for regular and careful supervision of the patient for the onset of drug toxicity.

A more determined effort to culture tubercle bacilli and to discover resistant strains is recommended if we are to derive the maximum advantage from drug therapy and the newer drugs pyrazinamide, ethambutol and the rifampicin. With more effective tuberculosis control it is hoped that the tuberculoma will disappear from the neurosurgical scene, even though, for the neurosurgeon, it might mean denial of an opportunity to effect a simple surgical cure.

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B. Spinal Cord and its Coverings

Summary

Tuberculoma of the spinal cord is uncommon in comparison to that of the brain. There were six within the spinal cord in comparison to 260 in the brain. Tuberculosis of the coverings of the spinal cord comprises arachnoiditis, subdural granulomas and extradural granulomas. The last type is divided into four groups. i) With vertebral body involvement (Pott's disease of the spine). ii) With vertebral arch involvement. iii) Without osseous involvement. iv) Without osseous or dural involvement, but within epidural fibrofatty tissue. All the types of spinal cord tuberculosis except that with osseous involvement are uncommon.
Keywords: Arachnoiditis, intramedullary tumours, spinal tuberculosis, tuberculosis.

The Spinal Cord

The first description of what was probably a spinal cord tuberculoma has been generally attributed to E.R.A. Serre (25) in 1830, but his case, according to Jenkins and Hill (13) was one of an 'intradural' tuberculoma. The earlier writings of John Abercrombie (1) (1828) show that not only he, but many of his contemporaries were familiar with tubercles of the cord and its membranes, which were described by them as being of the size of a nut or a nutmeg, occurring either "betwixt the dura and the arachnoid" or within the substance of the cord, and sometimes associated with similar tumours in the cerebellum and other organs. Spiller's discovery in 1905 of two cord tuberculomas, in each spinothalamic tract, from which the operation of Cordotomy for relief of pain was devised, was mentioned earlier in Part A.

In his "Surgery of the Brain and Spinal Cord", 1910 Krause (16) of Germany, described the case of a young man on whom he had operated for a cord tuberculoma. The patient, 32 years of age, had become paraplegic with sensory loss up to "the xiphoid line", which led Krause (16) to suspect involvement of the fifth dorsal segment: ". . . dura was found very tense. Longitudinal incision into it caused the spinal cord to bulge forward and a bloody liquid drained off in moderate quantities. A greyish-red, tumorlike flat swelling was now seen on the pia . . . After removal of these grey-red tumour-masses, the cord appeared slightly excavated and yellow." These descriptive passages leave one wondering whether the disease was leptomeningeal or intramedullary. His full-page coloured illustration of the cord (Plate LXI) does show, in multiple areas, a certain nodularity, suggestive of cord substance involvement, but other changes such as pin or millet sized surface nodules and arachnoiditis are also seen. Death occurred 16 days after the operation: by then the wound was well-healed.

Just about this time, across the Atlantic, an almost identical case was treated by Krauss and McGuire (17) of USA. Their patient was a man of 36 years, who had an attack of influenza in the spring of 1907 and developed weakness, chest pains and pleurisy in the summer. By winter weakness had progressed to paraplegia, with an upper sensory level at the fourth dorsal segment. He was also found to be suffering from tuberculosis of the testis, and loss of body weight. After laminectomy a tumour of the cord "was shelled out with perfect ease" using "the blunt end of a dressing forceps". Though haemorrhage was slight he "left the table in very poor condition" and died one hour later. The tumour was 2×1.5 cm in size, with a glistening white homogenous surface, revealing microscopically a tuberculoma, while "a section stained with carbol fuchsin showed a few tubercle bacilli".

But success was not long in the offing. In 1916, Elsberg (10), in his monograph on Surgical Diseases of the Spinal Cord, relates how a tuberculoma "will almost "pop" out of the cord after the incision has been made". Unfortunately, such case of excision is by no means a regular feature. His patient recovered and as Anderson (2) has recorded, was alive 8 years after the operation.

Incidence

The relationship of cord tuberculoma to brain tuberculoma must now be examined. Out of 80 tuberculomas recovered from nearly 6000 necropsies by Wilson et al. (27) of Philadelphia, between 1925 and 1940, six were within the cord. Three were solitary, but in two there were associated tuberculomas in the cerebral cortex and in one in the cerebellum.

Most surgical series show the incidence of cord tuberculomas to be much lower. This infrequency of cord involvement is further emphasized by Lin's (18) review of all cases of intramedullary tuberculoma up to 1960. Out of 104 cases he was able to collect, 88 were post mortem specimens and only 16 were surgically excised, with successful results in seven. One additional case treated by him was also reported. In Arseni and Samitca's (3) 12-year series of tuberculomas, 201 involved the brain and only five the cord. In the Mathai and Chandy (19) series of 143 brain tuberculomas, they encountered only two cord tuberculomas within the same period. Ramamurthi (22) records only two cord tuberculomas as against 199 occurring in the brain. Information gathered from

other Indian centres up to 1968 shows that Natarajan* operated on two patients with tuberculomas of the cauda equina, while Dayanandarao and Subrahmanyam (7), and Bhagwati* had each operated on a single patient. Dastur* found cord tuberculomas in necropsies on two women, aged 32 and 35 years, who had been suffering from spinal arachnoiditis and meningitis. Mani et al. and Balaparmeswararao and Dinakar, in papers read at the 3rd Asian and Oceanian Congress of Neurology, Bombay, 1971, each recorded three intramedullary tuberculomas.

In our tuberculoma series, 260 were found within the brain and six within the cord. Four were in females and two in males, their ages ranging from 1½ to 50 years. Symptoms in our youngest patient, the 1½ year-old infant, began at the age of nine months; her case report was published in 1968 (6). In two of our cases the conus was involved and in four cases the dorsal cord. All were confirmed by surgical excision and biopsy with three patients making very good recoveries, one showing improvement, but two advanced cases remaining paraplegic.

The cord coverings

This section has been included only because on clinical and radiological grounds it is extremely difficult to differentiate tuberculous involvement of the cord coverings from that of the cord proper, the sole exception to this being a history of tuberculous meningitis in favour of the former possibility. Tuberculous disease may transgress all the anatomical planes from the bony vertebra to the pia arachnoid, but there are times when the lesions may be singularly discrete and confined to one anatomical plane only. This observation stems from our study of 74 cases of tuberculous paraplegia, from which all cases of Pott's disease of the spine had been excluded. The granulomas were extradural with minimal osseous involvement in 44 instances; extradural without any apparent bone involvement, either radiological or as observed at the time of surgery, in four: subdural but extramedullary in four: combined subdural and extradural in one; arachnoidal without dural involvement in 15; and intramedullary in six.

Arachnoiditis

Our 15 cases of tuberculous arachnoiditis were among a group of 53 cases of spinal arachnoiditis of varying aetiology, much of it obscure. All 15 had in the past suffered from tuberculous meningitis or pulmonary tuberculosis.

In an extremely well-planned study of 80 gravely ill patients suffering from tuberculous meningitis at the St. Mary's Hospital, London, between 1947 and 1953, Brooks et al. (4) found spinal blocks (Froin syndrome and a negative Queckenstedt response continuously present for more than three weeks) in 15 patients, of whom ten died. They reported 11 incidents, clinically diagnosed as transverse myelitis but without spinal blocks, in another ten patients and detected important clinical and prognostic differences between the two groups of the 'rapidly developing lesion'. In the former there were eight patients of whom six recovered, while in the latter there were two patients, both of whom died. Again, in the former, maximum disability was reached in 12 to 24 hours; the disorder was primarily of motor function, with mild or absent sensory and visceral disturbances; and signs of recovery appeared within six weeks. They demonstrated how thick and densely organized exudates could encase the entire length of the cord, cause arteritis and secondary vascular changes within it, with eventual mortality. Surgical relief of compression caused by localized arachnoidal granulomas, when the meningitis was in a quiescent stage, has in our hands yielded good results.

Rosen (23) and Bucy and Oberhill (5) each had a patient with arachnoidal granuloma treated successfully by surgery; in Rosen's (23) case the dura was involved. Slade and Glazer (24) mention that they came to learn later from Dr. Bucy that his patient, who had been doing well for three years, worsened and became paraplegic once again.

Subdural granulomas

These are generally of the diffuse type, with the dura thickened all around and the granuloma surrounding the cord. Within recent years cases of this type have been documented by Dibble and Cascino (9), Jakoby and Koos (12), and Jenkins and Hill (13). Surgical relief of compression does appear to be the treatment of choice, but Parsons and Pallis (21), disputing this have related how they depended on steroids and anti-tuberculous drugs alone in one of their patients, whom they had reason to suspect had a granulomatous compression of the cord and who finally made a good recovery.

The localized type of subdural granuloma is rather an interesting entity. Slade and Glazer (24) reported one such case of a circumscribed lesion, $2 \times 1 \times 1$ cm, which was "inside of the dura, but outside of the arachnoid" and direct smear from its cut

* Natarajan, M.: Personal communication, 1967.
Bhagwati, S. N.: Personal communication, 1968.
Dastur. D. K.: Personal communication, 1968.

surface was positive for acid-fast bacilli. Included in their report is an excellent photograph of the surgical specimen. Arseni and Samitca's (3) cases were also of this type. Such lesions, specially when they become sclerotic, may be mistaken for meningiomas.

Extradural granulomas

Depending on their sites of origin they may be divided into four groups.

1. With vertebral body involvement (Pott's disease of the spine). As Kocen and Parsons (15) have stated this is an easily recognizable disorder and is therefore not likely to be mismanaged. Recent contributions to the many excellent reviews already available were made by Ginsburg et al. (11) and Mathai and Chandy (19) in 1967. The present trend is to favour the anterior or anterolateral approaches, which provide direct access for thorough excision of the disease affected areas, and for the insertion of bone grafts to lend stability, bring about quicker union and promote speeder rehabilitation.

2. With vertebral arch involvement. This type of case may be easily mistaken for epidural metastases, especially when associated with radiological abnormalities in the lungs or mediastinum (15, 16). The vertebral arch lesions, though radiologically or surgically obvious, are generally quite small or may escape detection unless a necropsy were available. In the lumbar region they may simulate prolapsed intervertebral disc (8, 15, 26).

3. Without osseous involvement. These granulomas, believed to be haematogenous in origin, are attached to the dura, but sometimes ever so lightly, as to strip off it easily during dissection. They tend to surround the dura and may spread over many segments. At no time during life do they produce radiological evidence of bone involvement, which is the only criterion employed for giving them a separate identity. The general reluctance to accept this is reflected in the paucity of reported cases of this type in the literature. In 1960 Arseni and Samitca (3) reported a single case and in 1962 Johnston et al. (14) were able to find only seven reported cases in the medical literature of the previous 70 years, to which they added two of their own patients and concluded that promptness of surgical decompression was more important than drug therapy in influencing neurological recovery. In a report appearing in 1966 Milnes (20) described three more cases and a year later, in another report, Mathai and Chandy (19) described five cases of this type, by now familiar to most Indian neurosurgeons.

4. Without osseous or dural involvement but within epidural fibrofatty tissue: Unlike the previous three groups, the justification for including this fourth group rests upon a solitary case described by Decker et al. (8). Their patient, a labourer aged 67 years, had backache and sciatica of three months duration, aggravated by straining and movements of the spine. He had been in good health excepting for a scrotal hydrocele operation five years earlier. A disc prolapse at L5-S1 was diagnosed but exploration of this space showed no involvement of bone, disc or posterior longitudinal ligament. Under the S1 root was a blue-grey mass exuding purulent material, which was excised; the dura was found intact and healthy. Histologically, a non-specific granuloma amidst epidural fat was found, but from the pus acid-fast bacilli were isolated and guinea pig inoculation demonstrated a virulent strain of M. tuberculosis. With treatment the patient did well, but intensive search for a tuberculous focus proved unavailing.

This case is cited to support the earlier statement that in tuberculosis quite remarkably discrete lesions may be found in every conceivable anatomical plane of the spinal cord and its coverings.

Having reached the end, I must now admit that Kocen and Parsons' splendid coverage of the subject (15) often had me wondering whether it was after all necessary to write Part B of this review. In view of their relatively small case material (gathered over a period of only four years) it was all the more remarkable that their perspective should have been so wide-ranging and comprehensive, and their conclusions so well-founded.

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