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Intracranial Tumours in Childhood - A Follow-up study

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Abstract

One hundred histologically confirmed intracranial neoplastic lesions in children under twelve has been analysed retrospectively. They constitute 13.4 % of all intracranial neoplastic lesions operated in this Institute from 1975 to 1980. The data is generally consistent with other reported large series. The maximum age incidence is between 5 and 12 years. Gliomas are the commonest tumour. The high grade gliomas tend to occur more frequently during the first quinquennium of life. Certain unusual presentations like fever, focal seizures in posterior fossa lesions and limb ataxia in supratentorial tumours have been emphasized. The mortality in relation to clinical presentation is discussed.

Key words -
Paediatric neoplasia,
Tumours of brain

Intracranial neoplasms are one of the most challenging problems of clinical diagnosis and management in modern paediatric practice, accounting for 40-50% of all solid tumours of childhood [4]. Unfortunately information on this subject from India is scanty, though enormous data is published from abroad. In the few published series from our country the authors [2], [21], [23], [27] have included the non-neoplastic lesions like extradural haemotomas, abcess, tuberculoma etc., in their study, thus diluting the true incidence and problems encountered in diagnosis and therapy of tumours. Only two series dealt purely with intracranial neoplasms of paediatric age group [3], [24].

This paper reviews our experience with 100 consecutive cases of intracranial neoplasms in children under 12 years of age at the National Institute of Mental Health & Neuro Sciences, Bangalore (NIMHANS), during the past six years, (i.e., 1975 to 1980). Children above 13 years of age are excluded from the present study since "the clinical picture in them is more or less similar to that in adults" [28].

Material and Methods

One hundred cases of histologically confirmed primary neoplasms of the brain in children under 12 years of age, who had undergone surgery, either therapeutic or diagnostic, at NIMHANS between 1975 and 1980 are analysed. They constitute about 13.4 % of all intracranial neoplasms seen in this Institute during that period. Their clinical profiles and histological features of tumours resected were studied. The histopathological material was reviewed by one of the authors (SKS) for the sake of uniformity in the diagnosis. All the surviving patients were followed-up either by correspondence or at the out-patient department. The clinical data at maximum follow-up was taken into consideration for evaluation of the quality of survival. The patients were classified into the following five groups for evaluating the quality of survival:

(A) Normal child
(B) Minimal neurological deficits
(C) Able to take care of daily needs with moderate neurological deficits
(D) Confined to bed with normal sensorium
(E) Confined to bed with altered sensorium.

Observations

Topography and histological pattern of the tumours are shown in Tables I and II respectively. A striking feature regarding anatomical location of the tumours was that majority (68 %) of them were concentrated near the midline of the brain.

Table I - Tumours in Childhood Histopathology

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Table II - Tumours in Childhood Location

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Age and Sex Distribution

The youngest patient in the series was 11 months old. Low grade gliomas (Grades I and II of Kernohan's classification [15]) showed two peaks of incidence at the age of 6-7 years and 11-12 years. Majority (66.6%) of ependymomas occurred below the age of seven years, the youngest one being one and a half years old. On the other hand 93.5% of medulloblastomas and all craniopharyngiomas were seen after the first quinquennium. The craniopharyngiomas showed two peaks, one at 6th and another at 12th year. There has been a male preponderance (65%) in this series. No case belonging to neonatal period was seen.

Duration of illness

At presentation the duration of illness varied between four days to three years. Amongst low grade gliomas it ranged from fifteen days to three years with a mean of 8.8 months. Seven out of 23 cases had the presenting symptoms for less than one month. A shorter duration of illness (average 3-4 months) was noted in high grade gliomas (Grades III and IV of Kernohan's classification [15]) although an isolated case of two years had also been recorded. The average duration for medulloblastomas was 3.2 months (range 1-8 months) while for craniopharyngiomas it was 8.1 months, the minimum being 4 days.

Symptomatology

In 31 patients the symptoms started with fever, of which two were provisionally diagnosed and treated as cases of tuberculous meningitis. Trivial fall was the landmark at the onset of the presenting symptoms in five cases. In many instances (20%) the usual complaint presented by parents was that the child was ill or he was not his normal self. In an energetic child, who had an astrocytoma in the dorsal midbrain to start with, there was slowing down and later regression of the motor skills. Sixteen patients were presented in a state of altered sensorium of which 5 had posterior fossa lesions. Four cases with posterior fossa mass had head tilting to one side. A two year old child presenting with delayed milestones and irregular fever, was found to have a midbrain glioma. Vomiting was a predominant and early symptom in all ependymomas and medulloblastomas. In case of ependymomas vomiting was usually associated with marked giddiness (63.6%), in contrast to only vomiting in case of medulloblastoma. Two cases with medullablastoma and one with astrocytoma in the cerebellum had focal seizures becoming generalized. The visual disturbances noticed were in the form of diminished, blurred or double vision. This was the major symptom in ten cases with craniopharyngioma. The other two cases of craniopharyngioma had diabetes insipidus. Certain uncommon features like change in facial expression, mood, poor scholastic performance, constipation, irritability and pain etc., were recorded in a few isolated cases. In 13 % of cases the clinical symptoms were totally vague which would not fit with any of the 'childhood problems'.

Table III - Symptomatology

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Physical Signs

The characteristic 'woe begone facies' was recorded in three cases. 83.33 % of craniopharyngiomas showed primary optic atrophy. Cranial nerve involvement (3rd, 6th and 7th) was seen equally in both supratentorial and infratentorial lesions. Enlarged head size with clinical evidence of hydrocephalus was recorded in 28% of patients.

Table IV - Signs

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Investigations

All the patients were subjected to conventional neuroradiological investigations and mass lesion was confirmed radiologically. Eighty three percent of craniopharyngiomas showed classical suprasellar calcification. In majority of cases the skull X-ray showed evidence of raised intracranial pressure in the form of sutural distasis (52%), posterior clinoid erosion (16%) and beaten silver appearance (18%).

Management

In all cases of posterior fossa tumours, preliminary ventriculoperitoneal CSF shunt was done. Radiation therapy (RT) was routinely given to all except in cases of low grade astrocytoma (Grades I and II). The dose varied depending on the tumour type (astrocytoma 5500-6000 r, brainstem tumours 4500-5500 r, craniopharyngioma 5500 r, medulloblastoma 3500-4000 r for craniospinal axis and additional 1000-1500 r to posterior fossa, 4500-6000 r in other cases). This was given over 4 to 6 weeks (800-1000 r weekly if tolerated) starting soon after healing of the operative wound (during second week in most cases). The dose was further modified depending on the age.

In supratentorial gliomas, sufficient intratumoural decompression was performed. Cystic astrocytoma of the cerebellum was excised as much as possible, along with their mural nodule. In case of intrinsic brainstem lesion only biopsy was taken.

Surgical decompression was done to open CSF pathway for medulloblastoma. One patient was given a second course of radiation therapy two and half years after the first course, following surgery. He received chemotherapy (cyclophosphamide, methotrexate and vincristine) during the next one and half years for recurrence.

A more aggressive approach was followed for ependymomas. In this group excision was performed in one case, subtotal in five cases; and in rest of the six cases only partial excision was done.

The approach differed in each case of craniopharyngioma being dictated by various factors like extent of tumour, cystic or solid and finally the tumour adherence to the hypothalamus. Only aspiration of the cyst and biopsy was done in one case, partial excision in six cases and sub-total excision in four cases. One had total excision.

Follow-up and Prognosis

Twenty-one patients in the present series died during the post-operative period. The various causes responsible for such deaths were meningitis, cardiopulmonary arrest, seizure phenomenon and other causes not related to surgery. Out of sixteen patients who presented in altered sensorium, eleven patients died.

Table V - Analysis of Post-Operative Mortality

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Included under the deaths during the immediate post-operative period of one week were five cases, one each, of haemangioblastoma, choroidplexus papilloma, lymphoma, pituitary adenoma and pineal yolk sac tumour. The first two patients died of respiratory arrest, the third on the operation table due to uncontrolled hypotension while the last patient died as a consequence of post-operative meningitis. The fourth patient with pituitary adenoma (chromophobe) developed generalised seizure soon after surgery followed by hurried respiration, hypotonia and hyper-pyrexia and died on the second day. At autopsy a large tumour measuring 3" × 4" compressing the optic chiasma, hypothalamus and temporal lobe was found.

Seventy-nine patients were followed-up for periods varying from 2 months to 10 years.

Sixteen patients with low grade astrocytoma were going to school although five of them had minimal neurological deficits (Table VII, groups A, B). The seventeenth patient (group B) with low grade astrocytoma was reexamined for recurrence four years later and succumbed following second surgery. Another patient died five months after surgery. One patient who was in grade C at the time of discharge has written a letter 8 ½ years after the initial diagnosis that he is doing well but for persistent impaired vision. The mean follow-up period in this group was 32.8 months.

Five out of thirteen cases with high grade astrocytoma died within six weeks after surgery. Among the survivors, five were followed-up for more than 20 months. The average follow-up of the entire group was 37.7 months. One of these patients is leading a normal life ten years after surgery (B).

In the medulloblastoma group, five patients died during their hospital stay following surgery. Among the 26 survivals, one died eight months (C) later due to complications of shunt surgery. The only patient who had received both radiotherapy and chemotherapy died four years (A) after surgery. He developed paraplegia and had definite evidence of seedling in the spinal axis. Another patient lived for five years & eight months after surgery and radiotherapy with minimal neurological deficits, later died of recurrence. Nine patients are alive for more than two years after surgery and are leading normal life (A). Three patients have been well for the past six years (A & B) without any neurological or mental deficits. The average follow-up for this group was 23.72 months.

Three of the patients with ependymoma died during the post-operative phase; one due to uncontrolled ventriculitis, another due to hepatitis and the third as a consequence of aspiration pneumonia.

Two patients with craniopharyngioma succumbed to death. The only patient where total excision was achieved, died on the eleventh post-operative day. Autopsy showed hypothalamic damage. One isolated case where aspiration of cyst and biopsy was done, died five months after diagnosis (A) due to infective hepatitis. Out of the four patients who had subtotal excision of the tumour, one expired during the first post-operative day due to cardiac arrest, another required re-exploration for recurrence of tumour nine months later (C) and died following second surgery. Of the remaining two, one expired six months (D) later and the other was going to school 2 years later (B). Among the six cases where partial removal of the tumour was achieved, one died after a second exploration for recurrence five months after (A) the first surgery; one is leading a normal life as seen in 3 years later (A), another is leading a normal life with minimal neurological deficits four years (B) after surgery. The rest of the three had moderate neurological deficits but are able to take care of themselves, when seen 3 years, 7 years and 16 months later respectively (C).

Table VI - Outcome in relation to Clinical Presentation

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A B C D E indicate the outcome scale as noted in the text. M indicates mortality.

Table VII - Tumours in Childhood -Mortality and Follow-up Data

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Figures in parentheses indicate the duration of follow-up in months

Discussion

The incidence of intracranial neoplasms in children at our centre is low (13.4%) when compared with that of Dastur and Lalitha [7] (17.4%). This may be due to the fact that only children up to the age of 12 years have been taken into account in the present series. This will be probably comparable with the above mentioned series, as well as that of Kastura [14] (18 %), if children up to 15 years of age are considered. The ratio of 1:1.56 between supra and infratentorial location of tumours is in concurrence with other available Indian [2], [21], [23], [25] and Western series [4], [9], [11], [32] except that of Balasubramanyam and Ramamurthi [3] who reported a ratio of 1:0.7. There has been no left or right sided preponderance. This is a striking feature as compared to previously reported left and right sided preponderance by Rubinstein [29] and Yates et al [32] respectively. Sixty-two percent of the tumours were either nearer to or in the midline. The ventricular system was directly involved in 46 % of tumours as against 41% recorded by Koos and Miller [17]. The observation possibly explains the early obstruction of CSF pathway and bilateral signs without lateralization. Similar observations have been recorded by Raja Reddy [28]. In contrast to the global distribution in the present series, Koos and Miller [17] reported the common involvement of frontal lobe (39%) in children.

We did not find a single case under the age of eleven months, even though intracranial tumours during first year of life constitute 11 % of the childhood intracranial neoplasms [26]. Pandya [24] reported 13 cases below the age of 12 months in his series of 141 children with intracranial neoplasms. This could be because the cases in neonatal period succumb to death early before they had a neuro-surgical consultation and are rarely investigated for a space occupying lesion.

Low grade gliomas were seen after sixth year whereas high grade gliomas presented before the age as reported by Pandya [24]. The medulloblastomas on the other hand occurred after the fifth year, but for three cases similar to the observations of Koos and Miller [17] and Burno and Schut [4], Matson [22] and Farwell et al [9] recorded the peak incidence during the first hemidecade. Ten out of the 12 ependymomas presented below the age of seven years. Various other series reported a peak under 5 years of age [5], [8], [22]. In Balasubramanyam and Ramamurthi [3] series of 21 cases of craniopharyngioma, fifteen were under the age of ten years. Similar age incidence has been documented in other large series [13], [30]. In our material all the patients were between the ages of five and twelve years. There has been remarkable similarity of histological types with other reported series. We did not observe metastatic brain tumour (Table II). Unlike in Heiskanen's [11] series where medulloblastoma was the common tumour, gliomas were the commonest type of neoplasms in our material. This is consistent with most of the other reported series.

The non-specific symptoms or events like fever, fall or an unexplained illness appear to be important

[3] and usually preceded the precipitation of the crisis, and it was noted in 46% of our cases. The fever could be coincidental or be an associated phenomena due to hypothalamic involvement or third ventricular dilation resulting in disturbances in thermo regulation. In case of infratentorial ependymomas vomiting was associated with giddiness more often than in cases of medulloblastomas. This may be due to direct involvement of the floor of the fourth ventricle infiltrating the vestibular nucleus as well as area postrema by ependymomas, while the medulloblastomas are commonly seen in the cerebellum. Backus [1] had reported 12 % of patients with infratentorial tumours to have seizure. This fact is increasingly realised. In the present series, among the 6 patients with posterior fossa tumours presenting with seizures, three had focal seizures becoming generalized. This could be due to venous stasis, cerebral edema and hypoxia complicating upon the increased intracranial tension. A fact that needs to be taken into cognizance, while localising anatomically, is that 15.3% of supratentorial tumours had limb ataxia which can be explained by involvement of corticopontocerebellar connections which are concerned with integration of coordinated movement. More cases of supratentorial tumours presented in altered sensorium, than the infratentorial mass, since the latter probably deteriorate fast and die, thus having less chance of being brought to the hospital in altered sensorium.

The Collins [6] concept of period of risk for recurrence of embryonal tumours like medulloblastoma which states that "the patient is at risk during a period of time equivalent to his age at that time of diagnosis plus nine months of gestation," does not seem to hold good in the present series though McFarland et al [19] claimed 25% cure rate as per this concept. Occasional survival of cases beyond eight years need further study. Such random cases are reported in other series too. The number is too small for deriving any fruitful conclusion about ependymomas.

Though benign, the cranipharyngiomas carry a very unfavourable prognosis. Despite claims of excellent results by some, [12], [13], [20], [30] total excision has its inherent problems. Despite therapy, only three out of 12 children are leading a normal life.

Further detailed studies are needed for a meaningful evaluation of the incidence, clinical feature, the efficacy of diagnostic and treatment modalities of intracranial neoplasms in infancy and childhood.

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