THE PROGNOSIS OF MEDULLOBLASTOMA IN CHILDREN

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The medulloblastomas comprise approximately 18 per cent of brain tumors in children. They are generally regarded as malignant neoplasms with a hopeless prognosis. However, a review of 61 cases seen at the University Hospital from 1938 through 1958 has given us a basis for some optimism.

REVIEW OF LITERATURE

The term medulloblastoma was introduced to distinguish this neoplasm as a specific tumor entity by Bailey and Cushing in 1925. Cushing had operated upon tumors of this type as early as 1903. Bailey and Cushing believed that a fatal outcome was inevitable, but that radiation therapy was conclusively beneficial in prolonging the average postoperative survival. This method of treatment had been used since 1919. Noting an incidence of 6 cases of spinal meningeal metastases among their total of 61, they extended the field of irradiation to include routinely the spinal axis in 1927. Their goal of operation was to unblock the aqueduct, rather than to attempt gross total removal of the tumor.

Subsequent reports have been in substantial agreement with the early views of Bailey and Cushing regarding treatment and prognosis. The futility of attempting cure by radical operation has become well established. On the other hand, irradiation without operation has been condemned. Irreparable damage may occur during the delay necessitated by trial irradiation of a radioresistant, benign tumor incorrectly diagnosed. Furthermore, irradiation without prior decompression risks a fatal edema. The possible advantage of avoiding operative dissemination of tumor cells through the subarachnoid space has assumed less importance since it has been shown that seeding may occur even without operation.

Survivals longer than 5 years have been reported sporadically. In some of these cases the diagnosis has been disputed or actually changed. The matter is further complicated by the failure of many authors to confine their reports to tumors occurring in children, since similar tumors in the adult have been thought to have a more favorable prognosis. Bailey believes that the medulloblastoma occurs only in children under 15 and that the leptomeningeal sarcoma has often been confused with it in the adult. While this may be a matter of opinion, we feel that analyses clearly distinguishing between cases in children and in adults are more meaningful.

The most optimistic report other than our own is that of Paterson and Farr. In 1953 they reported 6 children with 5-year survivals among 21 operated upon and irradiated.

PRESENT SERIES

There were 61 patients, ranging in age from 9 weeks to 15 years, with a median age of 5 years. Of these, 36 were males and 25 were females.

Four died prior to operation. One girl presented initially signs of a spinal cord tumor; she died 5 months following laminectomy. Fifty-six posterior fossa operations were carried out, with an operative and postoperative mortality of 11 (20 per cent). The
parents of 1 child refused irradiation. Three others were irradiated elsewhere. One of these died after 8\frac{1}{2} months; 1 died after 20 months; and the third is alive after 14 years, but is severely retarded.

Forty-one patients received postoperative irradiation at the University Hospital. The aqueduct had been cleared at operation in every case.

Of these 41 patients, 28 are now dead. The average survival time was 18 months, the median 12 months. Among these 28, there were 2 cases of long survival. One patient had onset of focal seizures 7 years postoperatively. Biopsy of the right temporal lobe revealed gliosis consistent with radiation damage. Seizures were well controlled for several years before he deteriorated and died after 13 years, 11 months. The other patient did well for 1 year, but then seizures developed and she became helpless until she died after 15 years, 10 months. No autopsy was performed in either case.

Thirteen patients are still alive. Of these, 11 have survived for periods ranging from 5 to 17 years without known recurrence, comprising \( \frac{28}{100} \) per cent of those irradiated at least 5 years ago. Six have survived longer than 10 years, comprising \( \frac{21}{100} \) per cent of those irradiated at least 10 years ago.

It is probably premature to suggest that any of these patients has been cured, although a survival of 17 years would suggest it. The 2 patients dying after 13 and 15 years respectively did not have postmortem examination to prove the absence of neoplasm.

Among the 11 patients with 5-year survivals, 2 are mentally retarded and have seizures, and 4\* others are mentally retarded (although 1 of the latter is able to operate a motel). Five (13 per cent of those irradiated) are essentially normal: 2 with no abnormality at all have survived for 5 years and for 15 years, 3 months; the other 3, with some residual but nonprogressive ataxia, have survived for 7 years, 5 months, 10 years, 7 months, and 12 years, 11 months.

Because of the high incidence of mental retardation and seizures, possibly attributable to radiation damage to the brain, the method of treatment was changed in 1950. Prior to this, concentrated doses were administered in short periods of time to successive segments of the cerebrospinal axis.\( ^{10} \) The newer method is a more protracted fractional irradiation of the entire ventricular system, including the primary site, supplemented with modest doses to the spinal axis concurrently.\( ^{41} \)

Thirty patients were treated by the former method. Of these, 6 are still alive without recurrence (20 per cent); 3 are essentially normal (10 per cent).

Eight patients have been treated by the latter method and followed for at least 5 years. Five are still alive without recurrence (62 per cent). Two are essentially normal (25 per cent). Three are mentally retarded; 1 of these had a single grand mal seizure 5\frac{1}{2} years after irradiation. Of 3 patients more recently treated, 1 is dead after 4 months; 1 has a recurrence after 16 months; and 1 is doing well at 1 year. Patients treated within the past year are not included in this study.

Although the newer series is still too small to be conclusive, the over-all percentage of 5-year survivals has been increased.

There do not as yet appear to be any striking differences in late morbidity between the two series. However, it is likely that factors other than radiation damage may play a role in causing mental retardation and seizures. One of these may be the effects of hydrocephalus.\( ^{48} \)

There were no cases in which delayed deterioration followed the newer method of irradiation. On the other hand, there were 2 cases of patients now dead but with long survival in which delayed deterioration followed the older method.

**DISCUSSION**

Each of the 11 patients with long survival presented a typical clinical picture of medulloblastoma. There were 9 males and 2 females. The median age at the time of operation was 8 years, compared with 5 years for
the entire series; the median duration of symptoms was 6 weeks, compared with 8 weeks.

The only factor peculiar to those who died was the presence of spinal meningeal metastases, which uniformly denoted a poor prognosis. They were proven in 9 and probably present in an additional 6 cases. Five were not related to operative spread.

Repeated courses of irradiation did not seem greatly beneficial except in the case of 1 boy, now 11½ years postoperative, who was treated for recurrent symptoms after 2 years. However, he is retarded and has seizures.

No characteristic microscopical features were noted that would be of prognostic value. In particular, the number of mitoses was not helpful. While some might say arbitrarily that in cases of long survival the tumors \textit{a priori} are not medulloblastomas, such an argument would seem to us to be unreasonable. As with neoplasms in general, microscopic diagnosis should reflect the prognosis as accurately as possible. If tumors with poor and tumors with favorable prognoses cannot be distinguished from one another at the time of operation by expert pathologists, it would seem preferable to class them all together as medulloblastomas of different, unpredictable degrees of malignancy, rather than to change the diagnosis the day the patient survives 5 years. Otherwise, the practical purposes of microscopic interpretation is defeated.

However, we recognize that the microscopic diagnosis may not always be clear-cut. Illustrated are microscopic sections of the tumors in 5 cases in which postoperative results were exceptionally good. All of these were very kindly examined by Dr. Percival Bailey. Fig. 1 was thought by him to be typical of a medulloblastoma in hematoxylin and eosin stain, but more suggestive of an alveolar sarcoma in subsequent Perdrau stain for reticulin. Fig. 2 was thought probably and Fig. 3 and Fig. 4 definitely to be alveolar sarcomas. Fig. 5 was interpreted as a neurospongioblastoma. The difficulty in making accurate diagnoses on small biopsy specimens, often without benefit of special stains, was emphasized. The cases illustrated in Figs. 1–4 were examined by Dr. K. J. Zülch,
Fig. 2. Tumor from an 11-year-old girl, well and without recurrence, 10 years, 7 months postoperative. Hematoxylin and eosin, 160X.

Fig. 3. Tumor from a 4-year-old boy, well and without recurrence, 15 years, 3 months postoperative. Hematoxylin and eosin, 160X.
FIG. 4. Tumor from a 64-year-old boy, well and without recurrence, 7 years, 5 months postoperative, Hematoxylin and eosin, 160X.

FIG. 5. Tumor from a 12-year-old-boy, well and without recurrence, 5 years postoperative. Hematoxylin and eosin, 40X.
whose opinion it was that they are all medulloblastomas. It is the belief of Drs. K. Scharenberg and L. Liss that all tumors in this series are medulloblastomas.

The distinction of alveolar sarcoma from medulloblastoma, usually on the basis of the reticulin stain, is evidently a controversial subject. Those who recognize this group admit that it may be a difficult distinction to make. From a practical standpoint they have not noted any clinical features that would set it apart from the medulloblastomas. It is his opinion that "there is no real unanimity" as to the medulloblastomas. It is his opinion that "good autopsy material" rather than small bits from surgical biopsy must be studied by advanced methods to increase our knowledge of this tumor.

It is not our purpose here to enter this histologic debate. Rather, it is to present this thesis: that there are tumors that are or closely resemble the medulloblastomas; that given such tumors, when competent pathologists do not agree, the prognosis is not always hopeless.

SUMMARY AND CONCLUSION

Of 38 patients operated upon and irradiated 5 or more years ago, 11 (28 per cent) are alive without evidence of recurrence. Five (13 per cent) are essentially well. Considering only the 8 patients treated with the more recent method of irradiation, 5 (62 per cent) are alive for at least 5 years without evidence of recurrence, and 2 (25 per cent) are essentially well.

We believe that the unusually good results in this series may be attributed to radiation therapy. That there is an inherent biologic variability in the malignant potentiality of these tumors seems probable. Except for the presence of spinal metastases, no factors have been found to be of value in predicting the course in a given case. We therefore believe that we can honestly offer some hope to the parents of a child undergoing operation and irradiation for medulloblastoma.

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