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DNA CONTENT—A PROGNOSTIC FACTOR IN CHILDHOOD MEDULLOBLASTOMA?

The treatment results in pediatric brain tumors, especially medulloblastoma, still lags behind the remarkable positive achievements obtained in most other types of childhood cancers. Based on some encouraging results from CCSG and SIOP studies, a treatment modality consisting of combined chemotherapy, surgery and irradiation has been introduced for the treatment of highly malignant brain tumors, replacing the traditional approach of surgery and irradiation (1, 2). Very aggressive chemotherapy followed by bone marrow rescue has also been suggested for advanced cases. Identification of the parameters related to the prognosis is important for deciding on the intensity of chemotherapy to be used. Prognostic significance has been reported for several histologic and clinical features, i.e. tumor size and extent, CSF cytology, age at diagnosis and extent of resection (3). Predicting the outcome, based on these parameters, is still rather uncertain, and therefore the search for additional prognositc variables is ongoing. DNA content is known to be a valuable prognostic factor in acute leukemia and neuroblastoma (3). Studies of tumor cell DNA content have suggested that DNA aneuploidy and conversely DNA diploidy may be favorable features in medulloblastoma (4, 5). Schofield et al. (6) have recently reconfirmed DNA aneuploidy to be a relatively favorable factor in medulloblastoma, especially amongst patients with a disseminated disease at the time of diagnosis.

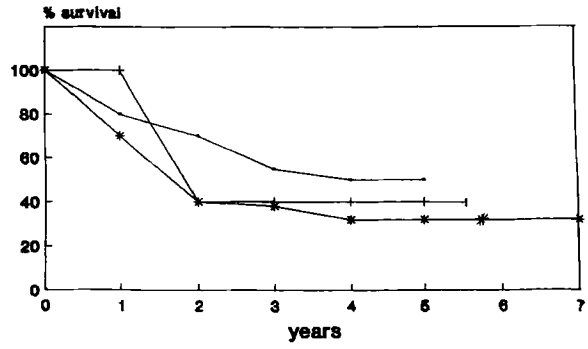

Figure. Patient survival according to DNA pattern of the tumor. —•— Tetraploid (n = 5); —|— aneuploid (n = 5); —*— diploid (n = 11).

Twenty-six patients with medulloblastoma, who were treated at the Sheba Medical Center between 1982 and 1990, were studied. Median age was 5 years. Therapy consisted of radical surgical resection, radiotherapy and chemotherapy according to Pendegrass et al. (7). Using the technique described by Hedley et al. (8). We analysed cells from paraffin-embedded pathological blocks and estimated the DNA content by flow cytometry (FACS). Three sections were cut from each block to reduce sample error. Adequate tissue for DNA content analysis was available in 21 cases only.

Our results showed no statistically significant differences between survival in the three groups of DNA ploidy (diploidy, aneuploidy, tetraploidy) according to the Mantle-Cox-test (Figure). The three groups were similar concerning age, tumor size and extent, degree of resection, and therapy.

Our results were thus disappointing but there seems to be a lack of consistency between different studies concerning the role of DNA content as prognostic factor in pediatric medulloblastoma. We feel that further extensive studies are required to elucidate the possible association between DNA pattern and prognosis and before it can be used as a guide for the choice of therapy.

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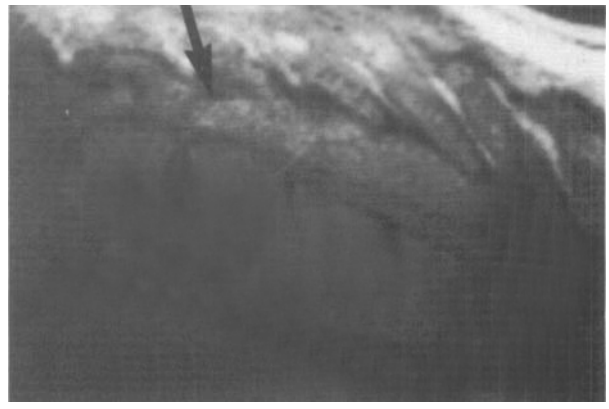

Figure. MRI revealing an extradural mass, compressing the spinal cord at Th 6 and 7.

SPINAL CORD COMPRESSION IN MYELOFIBROSIS—A CASE REPORT

Extramedullary haemopoiesis (EMH) is a recognized, though rare, cause of spinal cord compression, occurring in a number of haematological conditions. Its optimal management, and particularly the role of radiotherapy, is unclear from the literature. We report a case of spinal cord compression due to extradural EMH in association with myelofibrosis, where good neurological recovery followed radiotherapy.

Case report. A 67-year-old previously well man was found to have hepatosplenomegaly and a leukoerythroblastic blood film, while attending a urologist with prostatism. Marrow/trephine biopsy confirmed the clinical diagnosis of idiopathic myelofibrosis and 4 months later an uncomplicated splenectomy was performed because of abdominal discomfort. The patient remained well with minimal transfusion requirements until one year later when he complained of tired, heavy legs. Formal neurologic assessment revealed no abnormality. Over the following months he developed slowly progressive weakness of both lower limbs, more marked in the proximal muscle groups. His mobility deteriorated, necessitating the use of a stick. These symptoms improved briefly following physiotherapy and blood transfusion. Eleven months after developing leg weakness, features of a myelopathy became apparent. Diminished power and exaggerated deep tendon reflexes in the lower limbs, with ankle clonus and extensor plantar responses were later found. A sensory level was detected in the mid thoracic distribution. At this time his mobility was severely impaired, although he had no bladder or bowel dysfunction.

The chest radiograph was normal. Magnetic resonance imaging of the spine (Figure) revealed an extradural mass, extending from the upper cervical to lower lumbar areas, compressing the spinal cord at the level of the 6th and 7th thoracic vertebrae. Biopsy of the abnormal tissue showed extramedullary haemopoietic tissue only. The patient received megavoltage radiotherapy to the site of compression with an incident dose of 25 Gy, delivered in five daily fractaions over one week. By the end of treatment there were early signs of neurological improvement and six weeks later this had continued such that he was independently mobile. The radiotherapy was well tolerated and caused no alteration in the peripheral blood count.

Discussion. Extramedullary haemopoiesis (EMH) is found in disorders characterized by chronic haemolysis, or a reduction in volume of functional marrow tissue, through loss of marrow space. Consequently it is found in a number of haematologic conditions, notably the haemoglobinopathies and the myeloproliferative disorders. The commonest sites of EMH are the liver, spleen and lymph nodes. EMH as a cause of spinal cord compression (SCC) was first reported in 1954 and since this time there have been further reports, most in association with thalassaemia. No large single-centre series exist, but a recent report reviewed 37 cases of SCC due to EMH in thalassaemia (1). A number of case reports have recorded the phenomenon in other conditions, including sideroblastic anaemia (2), sickle cell disease (3), polycythaemia rubra vera (4), and myelofibrosis (5, 6). The clinical presentation is with slowly progressive paraparesis and as in our case, symptoms may extend over a period of many months. Despite long-standing neurological deficit, such cases may still respond well to treatment (5). Acute presentations are also recorded (3). The age range at presentation is wide, due to diversity of the underlying disease processes. There seems to be a predominance of cases in males, a feature noted in several reports (1, 2), despite the absence of any significant sex association of the primary pathology. Clinical examination and radiological investigation commonly localize the lesion to the mid or lower thoracic spine. The narrow diameter of the spinal canal in this region may be relevant (7). The diagnosis is suggested by the clinical and radiological features and should be confirmed by biopsy. Treatment of most reported cases comprised surgery, radiotherapy, or a combination of both. While surgery alone may be effective (2, 7, 8), many cases receive postoperative radiotherapy, either because of persisting neurological deficit following surgery, or due to incomplete removal of haemopoetic tissue, which is often extensive and diffuse in nature (9). Spontaneous remissions have been occasionally seen (10). Several authors suggest radiotherapy alone as the treatment of choice. One group (9) reported 5 patients with EMH related SCC treated with radiation in whom good responses were obtained in all patients. One case recurred within 6 months of treatment but following further radiotherapy there was again complete resolution of symptoms. One case remained symptom-free 3 years after irradiation. Doses used were modest, most cases receiving between 10 and 18 Gy in a fractionated course. Another series documented 10 episodes of EMH related SCC in 7 patients (10). Treated with radiation alone, with doses of between 10 and 35 Gy, there was improvement in every case. Recovery was prompt, often beginning within a few days, usually complete, and recurrences at further sites were managed in a similar manner, again with good results. Radiotherapy is reported to be well