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PEDIATRIC BRAIN STEM TUMORS: ANALYSIS OF 25 CASES

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SUMMARY

The charts of twenty-five pediatric patients with brain stem tumors diagnosed between March 1977 and December 1980 have been reviewed. Ages of patients ranged from 22 months to 17 years. The use of computed tomography (CT) was found to have been valuable in diagnosis and follow-up, as well as in the design of radiation therapy portals. Radiotherapy and combination chemotherapy with VM26 (4'-1 demethyl-epipodophyllo-toxin B-D-thenylidene glucoside) and CCNU (1-2-chloroethyl-methyl-3-Cyclohexyl-1-nitrosourea) were the treatment modalities employed. The three-year survival rate for this group of patients was 29%.

UNITERMS: *Brain neoplasms, VM26, CCNU, Vincristine, Childhood, Radiotherapy, Brain Stem Tumors.*

INTRODUCTION

The Brain-stem tumors account for 5-20% of intracranial tumors of childhood[2, 5, 7, 9, 11, 16]. These tumors arise in the region of the midbrain, pons and **medulla oblongata**[3, 9, 12].

Brain stem tumors pose a diagnostic and eventually therapeutic problem to the clinician. Recently, computed tomography has become the primary radiologic method for diagnosing brain stem tumors. Until the advent of computed tomography, pneumoencephalography and ventriculography were the procedures of choice for evaluation of lesions in the brain stem.

Surgical exploration is rarely indicated due to the anatomical position of this type of tumor[6, 14], being too close to vital structures.

Classicaly, they are treated with radiotherapy with a 5 year survival rate of 20-41% being reported[10, 15].

This paper reports on a study performed at the Institut Gustave-Roussy of 25 patients with pediatric brain stem tumors treated with a combination of radiotherapy and chemotherapy with VM26 and CCNU.

MATERIAL AND METHODS

From March 1977 to December 1980, 25 patients were treated for brain stem tumors at Institut Gustave-Roussy – Villejuif – France.

The results of the present series, reviewed in june 1981, were compared to other treatment protocols used before 1977. Up to that date patients were treated with radiotherapy alone or radiotherapy plus chemotherapy using Vincristine (VCR).

Ages ranged from 22 months to 17 years, with a mean age of 7.6 years. There were 14 boys and 11 girls.

The most frequent neurological signs were pyramidal tract signs (21 patients), ataxia and incoordination (18 patients) and cranial nerve abnormalities (16 patients). Dysphagia was reported in 7 patients. Personality changes and insomnia were seen in five patients. It is rare to find oedema on **fundus oculi** examination. Only one patient had oedema at fundoscopy.

Computerized tomography (18 patients), pneumoencephalography (17 patients), angiography (nine patients) and ventriculography (five patients) were the most frequent neuroradiological procedures employed.

The computed tomography picture was characterized by hypodense image (13 patients), pontine thickening (three patients), pontine thickening and hypodense image (one patient). On patient had a normal CT scan and the pneumoencephalography revealed a mass in the pons with displacement of the fourth ventricle.

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Seven tumors were localized in brain stem only. Often the tumor extended to other structures, predominantly adjacent tissues such as 4th ventricle (eight patients), cerebellum (five patients), floor of the 3rd ventricle (two patients), aqueduct of Sylvius (one patient), cervical spinal cord (one patient) and mixed nerves (one patient).

Six patients underwent a surgical exploration done elsewhere. Five of them had their diagnosis confirmed histologically. Four had a grade I/II astrocytoma and the other patient was a grade III astrocytoma.

Radiotherapy was delivered through localized parallel opposed fields to the region of the tumor, using a Cobalt-60 tletherapy unit. The prescribed tumor dose was 55 Gy in 5 1/2 weeks.

Prior to irradiation, all patients were started on corticosteroids.

Chemotherapy consisted of a combination of VM26, 60 mg/M², given I.V. on days 1 and 2, and CCNU, 120 mg/M², given orally on day 3. Treatment courses were repeated every six weeks for a total of one year. It was started concomitantly with radiation in 14 patients. In 11 patients it was given following radiotherapy. Only seven patients received a full course of chemotherapy for one year or more. The others neither completed the stipulated time nor received all the drugs scheduled. This happened either by progression of the disease or by side effects (thrombocytopenia, severe nausea and vomiting or septicemia).

The actuarial overall survival was calculated according to the Kaplan-Meier method[13], from the beginning of radiotherapy.

RESULTS

The overall actuarial survival was 29% at 3 years (Figure 1). Survival seemed to correlate well with clinical improvement following therapy. Those patients who showed a response to treatment, survived an average of 20.5 months, while those who did not, survived for an average of only two months. Median survival was 14 months.

Patients who responded to treatment had experienced symptoms for a longer period of time than patients who did not respond (5 months vs 1 month). These findings are similar to those reported by Panitch et al[11].

Usually, patients would present clinical improvement of neurological signs in the first 3 months after treatment. The average duration of remission was around 12 months.

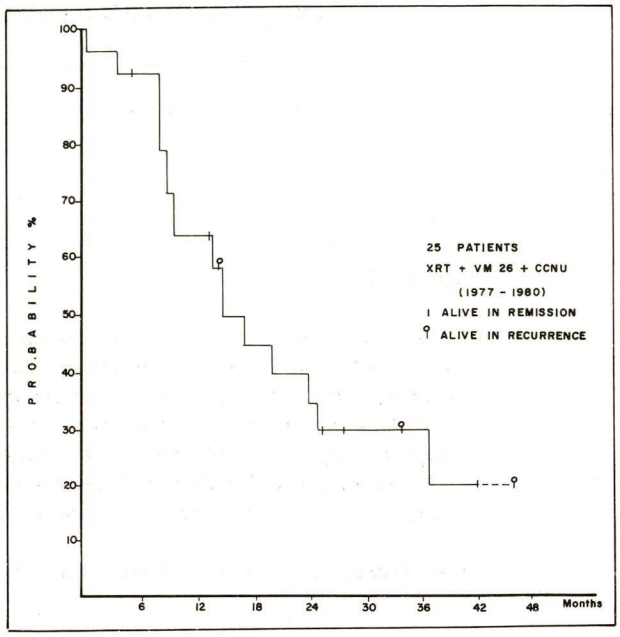

FIGURE 1 — Actuarial survival curve.

At the end of 3 years, 17 patients were dead, 5 were alive and well and 3 patients were alive but with recurrent disease. In most of the patients (76%) recurrent disease appeared within the first year. A second course of radiotherapy was delivered (tumor doses of 20 to 25 Gy). In addition to radiotherapy, they also received Procarbazine, 150 mg/M², given orally for 10 days, once every six weeks. The results of this second treatment were very poor and only three patients were alive, with disease, at the end of three years.

Treatment related complications occurred in two patients. One developed a deficiency in growth hormone 15 months after therapy; another one had a bony age of 4 years when he was 6 year old.

DISCUSSION

Primary brain stem tumor is a relatively rare intracranial neoplasm[2, 5, 7, 9, 11, 16]. The typical clinical presentation of the brain stem tumor is characterized by the insidious onset of multiple cranial nerve palsies, corticospinal tract involvement and ataxia, commonly in the absence of raised intracrannial pressure[4, 5, 14].

Tumors in these locations are seldom biopsied and the majority of the patients are treated with radiotherapy without histological confirmation.

Brain stem tumors often extends to other structures, predominantly adjacent tissues such as midbrain, floor of the 3rd ventricle, aqueduct

of Sylvius, 4th ventricle, cerebellum and cervical spinal cord[7].

Computed tomography has replaced air contrast studies as the primary radiographic modality in the diagnosis of lesions of the brain stem[1]. CT studies have become a prerequisite for delineation of the tumor in setting up radiotherapy portals being also useful in postradiotherapy evaluation. The computed tomography picture is characterized by pontine thickening, hypodense image without contrast and a mass in the pons with upward and backward displacement of the aqueduct and fourth ventricle.

The brain stem tumors at Institut Gustave-Roussy were treated exclusively by radiotheraphy until 1971[6]. Clinical improvement had been observed in 75% of cases. Improvement was temporary and the average duration of remission was 6 months. Survival at 18 months for 96 patients treated from 1944 to 1971 was 27%.

From January 1973 to February 1977, Vincristine was added to radiotherapy. A total of 47 patients received this combined treatment. Overall survival at 3 years was 34%. In march 1977, we began a new protocol in which VM26 and CCNU were also given together with radiotherapy. The rationale was to use a drug that can cross the blood brain barrier to try to improve these dismal results. Unfortunately, this did not prove to be the case. The results obtained are similar to those of patients treated exclusively by radiotherapy[7, 8].

Brain stem tumors remain a great challenge to the oncologist.

There was no significant difference in survival among the three treatment protocols used at our institution.

New treatment modalities (radiation sensitizers, neutrons or other heavy particles) need to be explored in light of the dismal results as discussed above so that we can show some real improvement in patient survival.

SUMÁRIO:

Os prontuários de 25 crianças com tumores de tronco cerebral diagnosticadas no período de março de 1977 a dezembro de 1980 foram revistos. A idade dos pacientes variou de 22 meses a 17 anos. O emprego da tomografia computadorizada (CT) foi de grande valor no diagnóstico e seguimento, como também na determinação dos campos de tratamento pelas irradiações. Radioterapia e quimioterapia com associação de VM26 (4'-1-demethyl-epipodophyllotoxin β-D-thenylidene glucoside) e CCNU (1-2-chloroethyl-methyl-3-Cyclohexyl-1-nitrosourea) foram as modalidades de tratamento utilizadas. A sobrevida actuarial em 3 anos foi de 29%.

UNITERMOS: *Tumores cerebrais, VM26, CCNU, Vincristina, Infância, Radioterapia, Tumores de tronco cerebral.*

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