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CLINICAL INVESTIGATION **Brain**

LONG-TERM INTELLECTUAL OUTCOME IN CHILDREN WITH POSTERIOR FOSSA TUMORS ACCORDING TO RADIATION DOSES AND VOLUMES

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Purpose: To analyze the relationship between craniospinal irradiation (CSI) and intellectual outcome in children with posterior fossa (PF) tumors.

Methods and Materials: A neuropsychological evaluation was performed retrospectively in 31 children, aged 5–15 years, who had received radiotherapy for PF tumors, and who had been off therapy for at least 1 year. Factors evaluated for impact on intellectual outcome were: socioeconomic status, disease presentation, histology, complications, chemotherapy, age at radiotherapy, interval between radiotherapy and testing, and radiation doses and volumes. Patients were divided into 3 subgroups according to the CSI doses (0 Gy [i.e., PF irradiation only], 25 Gy, and 35 Gy), with 11, 11, and 9 patients, respectively.

Results: Long-term cognitive impairment occurred in most of the patients, even after PF irradiation only. Moreover, there was a significant correlation between the full-scale IQ score (FSIQ) and the CSI dose, with mean FSIQ scores at 84.5 (SD = 14.0), 76.9 (SD = 16.6), and 63.7 (SD = 15.4) for 0 Gy, 25 Gy, and 35 Gy of CSI, respectively. A marked drop in verbal comprehension scores was noted in children who had received the higher dose.

Conclusion: This preliminary study further supports the rationale for de-escalation of CSI doses and volumes in standard-risk PF tumors. **© 1999 Elsevier Science Inc.**

Ependymoma, Medulloblastoma, Irradiation, Intelligence quotient, Neuropsychological sequelae.

INTRODUCTION

The oncologist's prime objective of curing disease when treating children with malignant brain tumors is in conflict with another important goal, namely the preservation of the patient's quality of life. With encouraging long-term remission rates attaining at least 50% at 5 years in multiple studies in children with posterior fossa medulloblastoma (MB) and ependymoma (EP) (1–4), attention has recently been directed to the long-term effects of these tumors and their treatment. The reasons for sequelae in these patients are complex and not fully understood.

Cranial irradiation required for disease control has been incriminated as one of the major causes of long-term cognitive impairment. For the moment, it is difficult not to deliver irradiation, at least to the posterior fossa in these patients; however, most of the groups have decided to dispense with craniospinal irradiation (CSI) in children with localized ependymoma, because most relapses are exclusively local (4, 5). With the progress achieved in surgery and chemotherapy, many attempts have been made to lower the radiation dose for prophylaxis against metastasis in children with standard-risk medulloblastoma (1, 6, 7) or to replace it with high-dose chemotherapy (8). However, limited data have been provided by these studies on intellectual outcome. Hyperfractionation of radiotherapy is also under study (9); however, the benefits in terms of neuropsychological outcome have not yet been assessed. Updated reports on trials, in which decreased CSI doses were delivered to standard-risk patients, have shown that treatment failures are not necessarily increased when 25 Gy is used instead of 35 Gy (1, 6). However, studies on late effects do not confirm that the higher risk of disease failure and death is counter-

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balanced by a significantly improved intellectual outcome. Recently, a pilot study of reduced CSI (18 Gy) combined with 9 months of multiagent conventional chemotherapy suggested that intellectual function could be noticeably preserved in standard-risk MB patients (10). In a previous study, we confirmed the influence of the radiation volume on the intellectual outcome of children with posterior fossa tumors (11). As there is no valuable comparison to date concerning neuropsychological outcome in children with PF tumors according to the dose of CSI, we decided to evaluate the benefits gained with reduced doses of craniospinal prophylactic radiotherapy in survivors of PF tumors in terms of attenuated neuropsychological sequelae, by comparing three subgroups of patients who had undergone either PF radiotherapy alone, 25 Gy CSI with a boost to the PF (CSI low + PF) or 35 Gy CSI with a boost to the PF(CSI high + PF).

PATIENTS AND METHODS

Patients

All children treated with radiotherapy at the Institut Gustave Roussy (IGR), Villejuif, France, for PF tumors were eligible for the study. Age at evaluation was between 5 and 15.5 years, to permit valid comparisons of the results, as similar items were used in the neuropsychological evaluation. Patients were all disease-free and off therapy for at least 1 year. Study patients included those with MB or EP.

Over a 1-year period, 31 children (24 boys and 7 girls) entered the study. Only 3 children fulfilling inclusion criteria could not enter the study because they had been lost to follow-up ($n = 2$) or because of the parent's refusal ($n = 1$). The histological diagnosis was medulloblastoma (MB) in 19 patients and ependymoma (EP) in 12. The mean ages were 5.5 years (SD = 2.8) when the first symptoms occurred, 5.7 years (SD = 2.8) at diagnosis, 6.1 years (SD = 2.7) during radiotherapy, and 11.4 years (SD = 2.4) at the time of the neuropsychological evaluation. The mean interval between radiotherapy and the neuropsychological evaluation was 5.3 years (SD = 3.3).

Treatment

Surgery. All but 1 child had undergone an attempt at complete surgical removal of the tumor. Surgery had been complete in 18 children and subtotal or partial in 13.

Chemotherapy. Children with medulloblastoma and over 3 years of age had been treated according to two consecutive protocols, the SIOP II protocol (1) and the MSFOP protocol (7), and to a sandwich chemotherapy protocol in one unpublished pilot study. The latter protocol consisted of a sandwich regimen combining two courses of etoposide-carboplatin with two courses of etoposide-cyclophosphamide, followed by CSI at a dose of 25 Gy for patients with standard-risk tumors. In this pilot study, children with high-risk tumors had received the same sandwich chemotherapy followed by CSI at a dose of 35 Gy and maintenance chemotherapy with the same combination as in the sandwich chemotherapy regimen. Children younger than 3 years had been treated with chemotherapy alone, and their outcome will be reported elsewhere. Ependymomas had also been deemed eligible for this pilot study.

Chemotherapy had been administered to 17 of 19 patients with MB and 4 of 12 patients with EP. Five patients had received the pilot study chemotherapy regimen, 8 children received the SIOP II chemotherapy regimen, and 8 children received the MSFOP chemotherapy regimen. None of the children had received intrathecal chemotherapy.

Irradiation. Children with ependymoma had not received prophylactic CSI, but limited irradiation to the whole PF based on our previous experience (4). Only one child had received 35 Gy of CSI for ependymoma, in violation of the protocol.

High-risk medulloblastoma patients (metastatic disease or incomplete surgery) had received CSI at 35 Gy, whereas standard-risk medulloblastoma patients had received 25 or 35 Gy of CSI as prophylaxis against metastasis, according to a randomized protocol (1). After 1989, all children with standard-risk medulloblastoma received 25 Gy of CSI.

Radiotherapy had been delivered according to a standard procedure (12). A dose of 25 or 35 Gy was delivered to the brain and the spine at a rate of 1.66 Gy per fraction, followed by an additional boost up to 55 Gy to the entire posterior fossa, at a rate of 2 Gy per fraction. The brain and posterior fossa were treated with a 6-MeV photon beam and the spine was treated with electrons.

Neuropsychological evaluation

The neuropsychological evaluation protocol included a uniform request for evaluation of intellectual ability using the Wechsler scales (WPPSI-R for children less than 7-years-old, $n = 2$ children; WISC-III for children over 7-years-old, $n = 29$ children) (13), laterality (14), memory (15), visuo-spatial function-shape recognition with the Kaufman-ABC scale, verbal fluency, vocabulary, written language, fine motor speed, and dexterity (Purdue Pegboard and Kaufman-ABC scales). The evaluations were performed by two neuropsychologists unaware of the patient's treatment. The duration of the tests was timed, and the entire evaluation was to be completed in 3 h.

Information on psychomotor development and school achievement both before disease onset and at the time of the neuropsychological evaluation was also collected through interviews with parents and teachers on developmental milestones and achievement at school. School achievement was considered impaired if children were at least 2 years behind compared to their peers.

Factors evaluated for impact on intellectual outcome

Socioeconomic status was defined as a high or lower standard of living based on the father's occupation (16). Tumor (T) and metastasis (M) stages were described according to Chang criteria (17). The analysis of disease presentation, defined as simple or complicated, was based on the absence or presence of complications at diagnosis

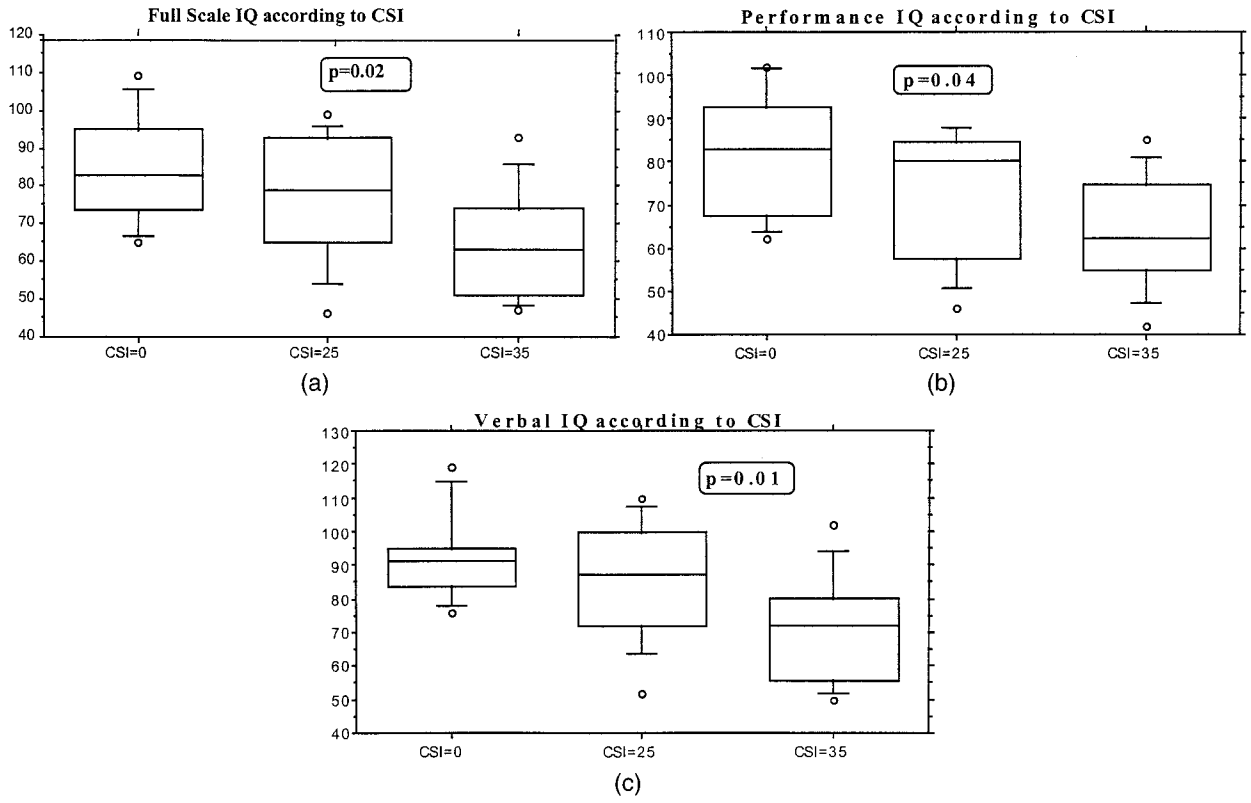

Fig. 1. Central boxes represent 50% of the distribution of the values. Central horizontal line represents the median. The extremities of the bars represent 90% of the distribution. The small circles represent the extreme values. *p*-value is given for the comparison of means. CSI = craniospinal radiation therapy in Gy.

(e.g., acute cranial hypertension with signs of herniation or obtundation). The extent of resection was determined from the early postoperative CT scan and based on the surgeon's impression at completion of surgery, according to SIOP policies (18). The postoperative course was considered as complicated if prolonged postoperative obtundation and life-threatening complications occurred that led to further surgery or a prolonged stay in the Neurosurgical Intensive Care Unit (intracranial hemorrhage, meningitis, ventriculitis, placement of a ventriculo-peritoneal shunt after surgery). All of the histological slides were centrally reviewed and divided into two groups (medulloblastomas and ependymomas) for statistical analysis. The impact of chemotherapy was analyzed according to the following two subgroups: no chemotherapy (group I), and chemotherapy, whatever the schedule (group II).

The impact of radiotherapy was analyzed according to the dose of CSI. Patients were divided into three groups for this analysis: patients who had received posterior fossa irradiation only ("PF alone" group), patients who had received CSI at a dose of 25 Gy with an additional boost up to 55 Gy to the whole PF ("CSI low + PF" group), and patients who had received CSI at a dose of 35 Gy ("CSI high + PF" group).

Statistical analysis

Statistical analysis was performed using SAS software (19). The FREQ procedure was used to test possible correlations between categorical variables. The *t*-test was used to compare means, and the CORR procedure to identify correlation between continuous variables. In addition, the General Linear Model (GLM) procedure was used for analysis of variance and to test whether the effect of RT doses on the IQ score persisted after adjustment on possible confounding variables.

RESULTS

The mean full scale intellectual quotient (FSIQ), the verbal IQ (VIQ), and the performance IQ (PIQ) were 76 (SD = 17), 83 (SD = 18), and 73 (SD = 16), respectively. The VIQ scores of most children were usually above their PIQ scores, with a mean difference of 10 points (SD = 11). The mean results of the WISC III performance subtests were constantly below 7 (mean value in normal children = 10), with a marked drop for coding and picture arrangement. Among the WISC III factors, the mean scores for perceptive organization and speed were below 80. Reading had also deteriorated, with mean scores for comprehension attaining 76.1 (SD = 19.4).

Risk factors for impaired intellectual outcome

Table 1 lists the factors evaluated for their impact on the patient's IQ, and their significance in univariate and multivariate analysis.

Table 1. Risk factors for impaired intellectual outcome

Risk factor	*n*	mean FSIQ (SD)	*p* univariate	adjusted *p*
SES			0.10	0.26
High standard of living	12	82.1 (16.7)		
Lower standard of living	19	71.8 (16.5)		
Age at RT			0.44	0.99
>6 years	16	73.4 (17.0)		
<6 years	15	78.3 (17.5)		
Interval			0.65	0.40
>5 y	15	74.4 (17.0)		
<5 y	16	77.3 (17.7)		
Presentation			0.93	0.74
Complicated	8	75.6 (17.2)		
Uncomplicated	23	76.3 (18.1)		
Surgery			0.65	0.75
Complicated	17	77.4 (16.8)		
Uncomplicated	14	74.5 (17.8)		
Histology			0.01	ND
Medulloblastoma	19	69.8 (16.7)		
Ependymoma	12	85.3 (13.6)		
Metastasis or tumor residue			0.03	ND
Absence	22	79.9 (16.4)		
Presence	9	65.6 (15.1)		
Chemotherapy			0.12	0.40
Yes	21	72.4 (15.4)		
No	10	82.8 (19.2)		
Radiation				
PF alone	11	84.5 (14.0)		
CSI low + PF	11	76.9 (16.6)	0.02	0.03
CSI high + PF	9	63.7 (15.4)		

SES = socio-economic status; RT = radiotherapy; CSI = craniospinal irradiation; PF = posterior fossa; SD = standard deviation; ND = not done.

Multivariate analysis was done with adjustment on all risk factors except for histology and the presence of a metastasis or a tumor residue (high-risk patients). These latter two factors were associated with radiation policies, and adjustment was not possible.

We used the median as the cut-off value for age at irradiation and interval to determine the two classes.

Table 2 describes the distribution of the factors evaluated for their impact on intellectual outcome (IQ) in the three radiation groups.

No correlation was found between the main neuropsychological scores and age at radiotherapy, the interval between radiotherapy and testing, disease presentation, and postoperative complications. The correlation between the FSIQ and the socioeconomic status (SES) was just short of significance; the mean FSIQ was 71.8 (SD = 16.5) when parents were less affluent, versus 82.1 (SD = 16.7) when they were wealthier. The tumor type and presence of metastasis or incomplete resection strongly correlated with the radiation dose, as stipulated in the treatment policies, and were therefore associated with a poorer intellectual outcome (*p*-values 0.01 and 0.03, respectively).

Radiation doses correlated with lower scores for the FSIQ ($p = 0.02$), VIQ ($p = 0.01$), PIQ ($p = 0.04$), information ($p = 0.04$), arithmetic ($p = 0.002$), vocabulary ($p = 0.04$), the cubes and squares test ($p = 0.02$), comprehension of reading ($p = 0.02$), delayed recall of a list of words ($p = 0.005$), and the Purdue Pegboard for the dominant hand ($p = 0.04$).

When the three radiation groups were analyzed together, the difference between the mean FSIQ scores of the CSI high + PF and PF alone groups was significant (Scheffe's test). When the analysis was restricted to patients with medulloblastoma, all of whom had been treated with CSI, the difference between the mean FSIQ scores of the CSI high + PF and CSI low + PF—was significant (see Table 3, *t*-test, $p = 0.02$).

Figure 1 details the results of the IQ scores according to radiation groups. After adjustment on confounding factors, the CSI dose was still the risk factor most implicated in low FSIQ ($p = 0.03$), PIQ ($p = 0.13$), and VIQ ($p = 0.02$) scores.

As children in group A were different from children in the other two groups, especially in terms of age at radiotherapy, diagnosis, and treatment policies (no CSI), we performed a second analysis restricted to the 19 children with medulloblastoma who had all received CSI either at 25 or 35 Gy (CSI low + PF and CSI high + PF groups). In univariate analysis, the only risk factor associated with a low IQ was the irradiation dose. The CSI low + PF group had higher FSIQ (77 vs. 60, $p = 0.02$), VIQ (85 vs. 66, $p = 0.02$), and PIQ (73 vs. 61, $p = 0.07$) scores than the CSI high + PF group. After adjustment of the *p*-value on the presence of metastasis or a tumor residue, radiation doses still correlated with FSIQ, VIQ, and PIQ scores, with *p*-

Table 2. Distribution of risk factors in the 3 radiation groups

Risk factors	Radiation groups 0 Gy $n = 11$	25 Gy $n = 11$	35 Gy $n = 9$	p-value
Socio-economic status				NS
High standard of living	6	7	5	
Lower standard of living	5	4	4	
Age at first symptoms	3.7 (1.8)	7.5 (2.2)	5.9 (3.5)	0.05*
Age at radiotherapy	4.1 (1.9)	8.0 (2.4)	6.3 (3.5)	0.05*
Interval between RT and testing	6.9 (3.7)	4.7 (2.6)	4.2 (4.2)	NS
Age at testing	11.0 (2.2)	12.7 (1.9)	10.5 (2.7)	NS
Histology (MB/EP)	0/11	11/0	8/1	0.05*
Complications at presentation	2	4	2	NS
Metastasis or incomplete surgery	2	0	7	0.05†
Surgical complications	5	7	5	NS
Chemotherapy (CT)				NS
Group I (no CT)	7	1	2	
Group II (sandwich CT)	4	10	7	

MB = medulloblastoma; EP = ependymoma.
Surgery was considered incomplete when the early postoperative scan showed an enhancing lesion in the posterior fossa, whatever its size.
For chemotherapy, group I = no chemotherapy, group II = short and intensive chemotherapy.
* Difference is between group A (O Gy) and the other 2 groups.
† Difference is between group C (35 Gy) and the other 2 groups.
Numbers in parentheses represent standard deviations (SD) of the mean.

values attaining 0.04, 0.05, and 0.08, respectively. Table 2 details the main neuropsychological scores in the 2 groups of MB patients. None of the 8 children who had been treated with standard CSI had an FSIQ score above 75, whereas 6 of 11 children treated with reduced-dose CSI had an FSIQ score above 75. Figure 2 show the distribution of IQ values in the two groups of medulloblastoma patients.

Table 3. Neuropsychological scores of children with medulloblastoma according to craniospinal radiation doses

Scores mean (SD)	25 Gy $n = 11$	35 Gy $n = 8$	p-value
FSIQ	76.9 (16.6)	60.0 (11.6)	0.02
VIQ	85.3 (17.4)	66.0 (12.4)	0.02
PIQ	73.1 (15.2)	60.9 (11.2)	0.07
VIQ-PIQ	12.2 (12.5)	5.1 (7.3)	NS
Information	7.8 (2.3)	4.3 (3.5)	0.03
Similarities	7.7 (3.8)	5.3 (2.3)	0.17
Arithmetic	6.9 (2.9)	4.4 (1.4)	0.07
Vocabulary	8.0 (3.0)	4.3 (2.8)	0.03
Comprehension	7.5 (3.3)	4.5 (3.1)	0.12
Digit span	8.1 (3.9)	4.5 (2.0)	0.08
Picture completion	6.7 (3.0)	4.0 (2.4)	0.08
Picture arrangement	5.5 (3.3)	4.3 (3.3)	NS
Block design	6.7 (4.0)	3.9 (2.3)	0.10
Object assembly	5.8 (3.4)	3.8 (3.0)	NS
Chessboard/coding	4.5 (2.7)	2.5 (2.3)	0.11
Mazes	7.6 (3.8)	5.8 (2.8)	NS
Symbols	5.5 (2.7)	4.0 (2.0)	NS

SD = standard deviation; CSI = craniospinal radiotherapy; FSIQ = full scale intellectual quotient; PIQ = performance IQ; VIQ = verbal IQ.
The scores analyzed here are only the subtests of the Wechsler scales. Twenty-nine children received the WISC III battery, while only 2 received the W PPSI-R battery 27.
Exact p-values are given only when below 0.20. The results of each subtest are given with the mean and standard deviation (in parentheses). Standardized mean results in normal controls are 10.0 (2.0).

Academic achievement and schooling

None of the children who entered the study had any delay in psychomotor development or academic achievement before the onset of disease, as recorded during interviews conducted by parents and teachers. Most of the children who had received reduced-dose CSI or PF radiation were able to pursue normal schooling (84% and 92%, respectively), whereas only 27% of the children who had received a higher dose of CSI were able to do so ($p = 0.001$). Among the 19 patients with medulloblastoma who had received CSI, 5 of 8 treated with standard CSI doses required adapted schooling. Such was the case for only 2 of 11 children who had been treated with reduced-dose CSI.

DISCUSSION

Reducing CSI doses in children with standard-risk medulloblastoma (total or subtotal surgery and absence of metastasis) is a potential means of limiting toxicity during the subacute and late phases. Earlier studies in children with leukemia provided convincing arguments in favor of this attitude by showing a significant improvement of IQ scores when the prophylactic craniospinal radiation dose was lowered from 24 to 18 Gy, or even avoided (20–22). As a reduced CSI dose combined with chemotherapy appears to yield cure rates similar to those achieved with standard-dose CSI in standard-risk MB patients (1, 6), this strategy is

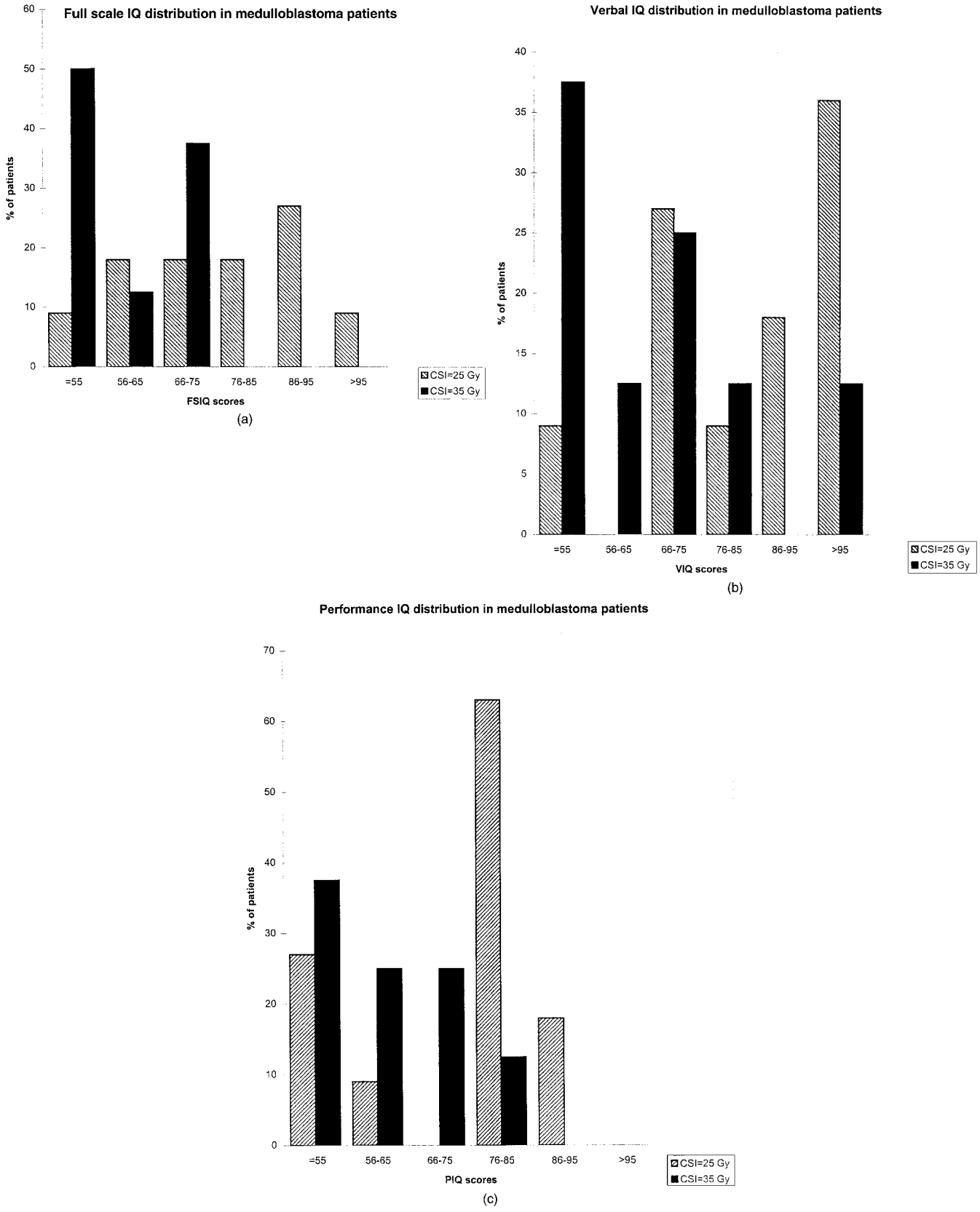

Fig. 2. CSI = craniospinal radiation therapy in Gy. Number of patients in group CSI = 25 Gy− is 11. Number of patients in group CSI= 35 Gy− is 8.

acceptable as long as survival is encouraging. Whether reduced-dose CSI substantially attenuates neuropsychological sequelae has yet to be proven.

Radiation dose and neuropsychological sequelae

Our study clearly shows that low-dose (25 Gy) CSI is associated with a major improvement in intellectual outcome compared to standard-dose (35 Gy) CSI, in an homogeneous population of children treated for PF tumors. The gain in IQ scores is similar to that reported by Silber *et al.* (23) in a mixed population of children treated with radiation doses ranging from 18 to 36 Gy for brain tumors and leukemia. The multicentric study of the Pediatric Oncology Group recently suggested that neuropsychological sequelae were lower for reduced-dose CSI in a selected group of 22 patients with medulloblastoma treated by standard (36 Gy) or reduced-dose (23.4 Gy) CSI (24). Although the IQ tests varied among these patients according to age, the authors detected a significant order effect when the radiation dose and the age of the patients were combined in 4 groups.

In our patients, the CSI dose was clearly the main risk factor for impaired intellectual outcome and schooling failures, and outweighed the usual impact of age at irradiation, or time since treatment (25, 26). Our treatment policies, which strive to preserve the youngest children from the deleterious effects of CSI, may account for these results. When irradiation is delayed until patients are over 3 years of age, age may no longer be the critical risk factor for low IQ scores, as suggested in this study. As age at radiotherapy and time since treatment were similar in all patients in our study, the correlation frequently reported in the literature between these risk factors and IQ scores did not emerge (for review, see 26). These two risk factors may have an independent impact on intellectual morbidity as shown by Dennis *et al.* (25), who found that the younger the age at diagnosis, the lower the PIQ score and the longer the interval since treatment, the lower the VIQ score.

With respect to the three radiation groups, the drop in IQ scores was greater between the CSI low + PF and CSI high + PF groups than between the PF alone and CSI low + PF groups. Better neuropsychological outcome, in terms of FSIQ scores, were observed in our study for ependymoma patients who had only received PF irradiation compared with medulloblastoma patients who had received additional CSI is in accordance with our previous studies (11). The differences in FSIQ scores between the three radiation groups should be even more pronounced, because patients in the PF alone group were significantly younger than their counterparts in the other two groups, and the effects of the tumor and radiotherapy are known to be more pronounced in younger patients (26). Moreover, the impact of the CSI dose on intellectual outcome was demonstrated among the homogeneous subgroup of patients with medulloblastoma who had been treated with CSI.

In this study, it has been possible to measure the extent of the radiation dose and volume on the intellectual outcome of children with PF tumors, regardless of age. In our opinion, the attenuation of neuropsychological sequelae among medulloblastoma patients who had received reduced-dose CSI appears worthwhile, in spite of a possible increased risk of relapse, particularly as this risk has yet to be demonstrated. Furthermore, neuropsychological sequelae could be limited even more if irradiation could be confined to the posterior fossa. CSI can be dispensed within children with localized ependymoma without significantly increasing the risk of relapses, which are mainly local (4, 5). Our group has demonstrated that it is possible to replace CSI by high-dose chemotherapy in children with medulloblastoma under 3 years of age after a relapse while on conventional chemotherapy (8, 27). However, clinicians should realize that reducing or even dispensing with CSI in children with medulloblastoma is at the cost of increasing the weight of chemotherapy. Data on the assessment of the long-term effects of chemotherapy on neuropsychological sequelae are few and far between. In our study, chemotherapy was not associated with impaired intellectual outcome. It will be important to verify during the coming years whether it is safe to reduce radiotherapy doses by new strategies with conventional chemotherapy or high-dose chemotherapy. To date, the follow-up of these patients is still too short to allow definitive conclusions concerning this issue.

Neuropsychological profile

The neuropsychological profile was quite homogeneous in these patients, with impairment mainly in speed processing and perceptive organization abilities. PIQ and VIQ deficits were significantly worse when CSI doses were higher. Children who had been treated with the higher CSI dose also sustained significant impairment of verbal comprehension. These deficits probably account for the major schooling failures encountered by these patients (25). The CSI dose could be responsible for their failure to assimilate new verbally-based knowledge at a developmentally-appropriate rate. Rehabilitation measures should take into account the specific needs of these children.

Posterior fossa irradiation and cognitive impairment

Most of the children, however, experienced impaired intellectual function, even those treated with PF irradiation alone. There has been some speculation as to whether the cerebellum participates in even higher cognitive functions than has heretofore been appreciated (28). The damage associated with the tumor itself and its surgical treatment has already been mentioned in children with benign cerebellar astrocytoma (29). In a subsequent report, the percentage of IQ scores below 90 in children treated for cerebellar astrocytomas without irradiation were similar to those of

children treated for ependymoma with PF irradiation (11). However, these comparisons were historical, and patients were not of a similar age. We cannot assume that PF irradiation alone will not increase the risk of neuropsychological sequelae. Moreover, it should be emphasized that the PF irradiation field may encompass a substantial part of the supratentorial structures including the inferior part of the occipital and parietal lobes, the thalamus and diencephalon, and even the posterior part of the temporal lobe (12, 31). The studies of young children with medulloblastoma (29) or ependymoma (30) treated without irradiation may elucidate this question. Whether individual neuropsychological profiles may be due to the radiation dose to specific functional areas of the brain is a matter of debate, and we are addressing this issue in ongoing studies.

CONCLUSION

This study confirms that CSI, and more specifically, the dose, is mainly responsible for the poor neuropsychological outcome of children treated for posterior fossa tumors. After the analysis of neuropsychological sequelae, this preliminary report supports the use of reduced-dose CSI doses as prophylaxis against metastasis in children with standard-risk medulloblastoma. The gain in terms of intellectual outcome may be substantial in these settings. However, attention should be paid to the deleterious effects likely to occur with wide fields when irradiation is delivered to the entire PF. Some neuropsychological sequelae could eventually be attenuated with conformal radiotherapy techniques.

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