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Gait analysis in children treated by surgery followed by adjuvant therapy for posterior fossa tumors

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Abstract

Children affected by posterior fossa tumors show signs and symptoms of neurological dysfunction, associated both to cancer itself and to cancer therapies. Abnormal gait and coordination difficulties are frequent presenting features.

Radiation therapy represents the main adjuvant treatment for these patients. However it can produce significant neurologic injury, also manifested as gait disturbance months after treatment.

We have analyzed temporo-spatial parameters of gait in sixteen children treated for posterior fossa tumors, mainly medulloblastomas.

In all children we found a typical gait pattern of cerebellar ataxia. There were no significant differences between data obtained in children affected by severe neurological impairment and those having slight or even hardly recognizable physical signs.

Although the number of patients studied is not large enough to allow definitive conclusions and gait analyses were performed after treatment, our results suggest that most children treated for posterior fossa tumors have gait disturbances and in some of them these are subclinical. Standard gait analysis laboratory methods can thus be a valuable tool for the careful assessment and follow-up of these patients.

Key words: Gait analysis; ataxia; posterior fossa tumors; radiotherapy; chemotherapy.

Introduction

Infratentorial CNS tumors in children are characterized by initial insidious features including clumsiness, difficulty with running and slow or halting speech. Subsequent gait and balance problems are due to dysfunction of the somatosensory system (1). As a rule, these patients show typical clinical features of the ataxic gait including widened base, unsteadiness, irregularity of steps, veering to one side (2). Standard gait analysis laboratory methods reveal that cadence and step length are significantly lower, whilst step width, stance phase and outward rotation of feet are significantly increased in cerebellar patients compared to normal subjects. Because of the reduction in step length and cadence a diminution of gait velocity is also observed (3, 4).

The mainstay of adjuvant therapy for these tumors is radiation therapy in association with chemotherapy. However, significant neurologic injury may accompany therapeutic irradiation leading to worsening of pre-existing deficits, including gait abnormalities and balance disturbance (5). Moreover, in these patients, postural control can also be affected by drugs that interact with neural and musculoskeletal systems. Namely, cisplatin and vincristine can cause peripheral neuropathy (5, 6) and corticosteroids can induce myopathy with ensuing muscle weakness (7).

The aim of the present study was to assess the gait performance status of children who had been treated for posterior fossa tumors. Data collected from children showing heavy neurological disturbances such as cranial nerve deficits, nystagmus and ataxia have been compared to those collected from patients showing only signs of gait abnormality and to data from patients without evident neurological impairment on physical examination.

Patients and methods

Children treated for posterior fossa tumors by surgery followed by adjuvant radiotherapy and/or chemotherapy were eligible for the study. Eligibility criteria also included achievement of complete remission, a stable or improving neurological status, a Karnofsky performance status of at least 60%, the absence of tumor recurrence documented by recent pre gait analysis MRI, the informed consent given by the parents.

Table 1

Patient characteristics

Patient	Age at diagnosis (yrs/mths)	Diagnosis	MRI tumor localisation	Surgery	Neurologic exam. pre-GA	ICARS score (gait and posture disturbances)	gait speed walking capacities	MRI pre-GA
1. boy	5/3	MB	vermis	partial	NEG	1	0	NEG
2. boy	12/11	MB	vermis	gross tot.	VI,ATX,NGM	2	2	NEG
3. girl	9/10	MB	vermis	gross tot.	ATX	1	1	NEG
4. boy	5/0	MB	paravermal dx	gross tot.	ATX	2	1	NEG
5. girl	8/0	MB	vermis	gross tot.	VI,VII,III,NGM,ATX	2	1	NEG
6. girl	10/9	MB	vermis	gross tot.	lll,ATX	1	1	NEG
7. girl	4/11	MB	vermis+LC dx	gross tot.	VI,ATX	1	1	NEG
8. boy	7/4	MB	vermis+LC dx+sx	gross tot.	NEG	1	0	NEG
9. girl	6/3	MB	vermis+LC dx	gross tot.	ATX	2	1	NEG
10. girl	9/6	MB	vermis	partial	VI,IX,ATX	1	1	NEG
11. girl	9/4	MB	vermis	gross tot.	VI,ATX	2	1	NEG
12. boy	3/8	EPM	LC dx	gross tot.	ATX	1	1	NEG
13. girl	1/4	EPM	vermis	gross tot.	NEG	0	0	NEG
14. boy	7/2	MB	vermis	gross tot.	ATX	1	1	NEG
15. girl	2/8	EPM	vermis	gross tot.	NEG	1	0	NEG
16. boy	8/0	LGG	LC sx	gross tot.	NEG	1	0	NEG

GA: Gait analysis; MB: Medulloblastoma; EPM: Ependymoma; LGG: Low grade glioma; NGM: Nystagmus; ATX: Ataxia; LC: Lateral cerebellum.

Between April 2006 and April 2007 we have evaluated the gait performance of 14 children. Patient characteristics are shown on table 1. Briefly, twelve patients were affected by medulloblastoma, two by cerebellar ependymoma. We also evaluated further two patients who had not received radiation therapy but only post surgical adjuvant chemotherapy, including cisplatin and vincristine; one was affected by ependymoma and the other by low grade glioma, both arising in posterior fossa. In eight out of twelve medulloblastoma patients the tumor was localized in the cerebellar vermis; in the remaining four the tumor was found in the paravermal zone (case 4) or widespread from the vermis into the lateral cerebellum. Moreover, two out of three ependymomas were located in the vermis and one in the right lateral hemisphere. At the time of evaluation all but one child were in continuous complete remission from 4 to 72 months after diagnosis (median 16 months); one (patient 9) was in second complete remission, 36 months from second induction. Four patients (cases 2,3,4,16) were tested three-time, one patient twice (case 15), at least three months apart between the evaluations. All patients affected by medulloblastoma had received craniospinal irradiation (54 Gy tumor/36 Gy neuraxis), two children affected by ependymoma have been treated by localized radiotherapy for a prescribed dose of 59.4 Gy . At the time of radiation 10 children were between 5 and 10 years of age, 2 over 10 years; both patients affected by ependymoma were 3 year and 9 month old.

Cerebellar symptomatology, as it regards posture and gait disturbances, has been evaluated and scored according to the International Cooperative Ataxia Rating Scale (ICARS) (8). The first subscore, concerning walking capacities, gives eight possible values, from normal (score 0) or almost normal naturally walking (score 1) to impossible walking (score 8). The second subscore, concerning gait speed, provides four values, from normal (score 0) or slightly reduced gait speed (score 1) to extremely low speed (score 3) or impossible walking with autonomous support (score 4). Therefore a total score from 0 to 12 was awaited for our patients. All children evaluated as negative at physical examination, when scored according to ICARS, were given a score 0 or 1; it means that at most they showed a slightly reduced gait speed or an almost normal walking capacity naturally but inability to walk with feet in tandem position. All children described as with overt gait disturbance at physical examination received a score 2 or more indicating that they suffered from both the above described gait disturbances or that they showed a clearly abnormal and irregular gait and/or a markedly reduced gait speed.

Gait analysis was performed using a motion analyzer (ELITE 2002 system, BTS, Milan, Italy) equipped with eight video cameras recording at 100 Hz (9). The acquisition protocol has been already described (10). Twenty reflective markers, representing key anatomical landmarks, were placed directly on the skin of each patient. Temporal-spatial

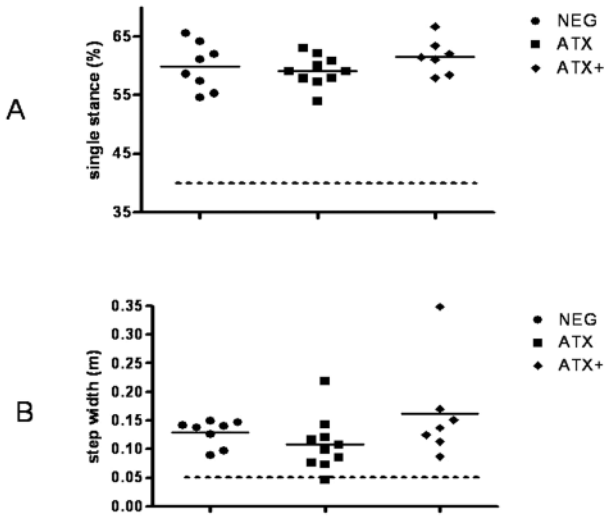

FIG. 1. — Data of single stance (A) and step width (B) of group 1 (ATX+), 2 (ATX) and 3 (NEG) patients. All figures in A and all but one in B are above the mean normative. No significant differences between groups are found.

parameters were computed from the initial and terminal contact of each foot on the ground. Children walked several times on a 6 meters walkway at their self-selected speed; at least six trials were collected for each patient. The calculated data were averaged from all trials, compared to the corresponding mean normative for age (11) and analyzed.

Analyzed parameters included: a) cadence, as the number of steps per minute (mean normative: 146.64 in the 3-4 year olds, 138.14 in the 5-6, 126.9 in the 7-8 and 120.23 in the 9+ year olds), b) step length, as the y-axis displacement between the lateral malleolus target positions of the two feet between heel strike and the subsequent controlateral heel strike (mean normative: 0.5 meters in all age groups), c) step width, as the x-axis displacement between the lateral malleolus target positions of the two feet between heel strike and the subsequent controlateral heel strike (mean normative: 0.05 m across all age groups), d) the percentage of stance phase in the gait cycle (mean normative: 40% across all age groups), and d) the average gait velocity, as the stride length divided by the stride time (mean normative: 0.89 m/s in the 3-4 year olds, 0.96 in the 5-6, 1.09 in the 7-8, 1.10 in the 9+ year olds).

Statistical analysis

Data were collected in three groups: 1) data obtained in patients with severe neurological impairment including cranial nerve deficits, nistagmus and cerebellar ataxia, 2) data obtained in patients with overt gait disturbance at physical examination (score 2-4), 3) patients without clearly recognizable symptoms and signs of gait abnormality or lack of coordination (score 0-1). In order to test for significant group differences ($P < 0.05$) the one way ANOVA's analysis of variance with Barlett's test for equal variances were used.

Results

All children, in all trials, showed a gait disturbance regarding three or more temporo-spatial parameters, corresponding to the typical pattern of ataxic gait. All estimated data of stance phase were found higher than the mean normative in childhood; the minimum registered value of this temporo-spatial parameter was 54% (in the group scored 2 or more) and the maximum value was 66.5% (in the group scored 2 or more plus other signs of neurological injury), versus a mean normative value of 40%. Moreover, all but one estimated data of step width were also found over the mean normative in childhood (0.05 m) with a minimum pathological value of 0.07 m in the group of patients scored 2 or more and a maximum value of 0.34 in the group of patients with ataxia and other neurological signs. All but nine determinations of step length were found under the mean normative of 0.5 m, with a maximum pathological value of 0.47 and a minimum one of 0.28. Sixteen out of twenty-five data of cadence were under the minimum normative of 120.23 (9+ yrs age group) and twelve data of gait velocity were also found under the minimum normative of 0.89 m/s (3-4 yrs age group). Finally, for all calculated temporo-spatial parameters, no significant differences were observed between groups of patients (Table 2).

Discussion

A recently published meta-analysis of the presenting signs and symptoms in pediatric CNS tumors (12) emphasizes that abnormalities of gait and coordination are among the more frequent ones. Gait disorders are evident at presentation in about 80% of brain stem tumors, 60% of posterior fossa tumors, 40% of spinal cord tumors and even 10% of supratentorial tumors. This implies that, in a large majority of cases, gait abnormalities are evident from the beginning of the disease and independent of subsequent surgical or other therapeutic procedures.

Moreover, it is well known that important neurological dysfunctions are associated with cancer therapies, in particular radiation therapy and chemotherapy (13). The former can produce significant

Table 2

Gait temporal-spatial parameters assessed in patients showing ataxia (score 2 or more) and other signs of neurological injury, (B) only ataxia (score 2 or more) and (C) without evident neurological impairment or showing minimal signs of ataxia (score 0-1)

	A (mean)	B (mean)	C (mean)	MEAN NORMATIVE	p from ANOVA's
Cadence (steps/mm)	109.6	116.0	123.2	min 120.23 (9+yrs) max 146.64 (3-4yrs)	0.1683
Gait velocity (m/s)	0.89	0.87	0.89	min 0.89 (3-4yrs) max 1.10 (9+yrs)	0.9112
Single stance (%)	61.7	59.3	60.0	40.0 (all age groups)	0.3146
Step length (m)	0.50	0.45	0.44	0.50 (all age groups)	0.3104
Step width (m)	0.16	0.10	0.12	0.05 (all age groups)	0.1837

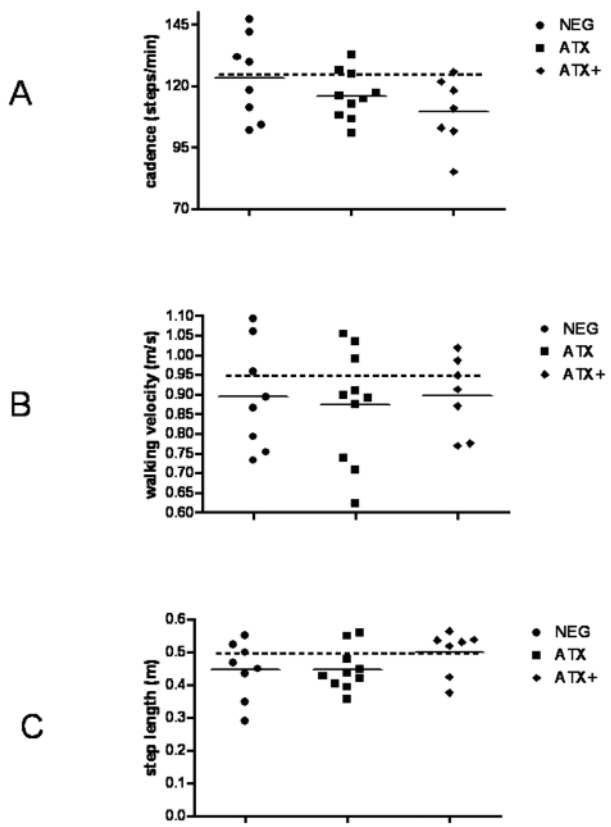

FIG. 2. — Data of cadence (A), walking velocity (B) and step length (C). Means of all groups are under the corresponding mean normative (dotted lines) and significant differences between groups are not found.

neurological damage, usually recognizable at MRI, and clinically expressed as gait disturbances even months after the end of treatment (14, 15). As a matter of fact, on pre-gait analysis MRI there was no evidence of radiation toxicity in our patients. The long delay between administration of drugs and gait analyses was such that the observed gait disturbances are unlikely due to a drug effect.

Because of the multiple cerebellar pathways involved in the control of voluntary movements, cerebellar ataxia turns out to be a complex dysfunction, that is difficult to describe and to quantify. The medial, fastigial zone of the cerebellum contributes to the modulatory control of the flexor and extensor locomotor pattern. A lesion in this zone will produce imbalance and impairment of postural tone. The main function of the paravermal zone is to control limb movements including timing, elevation and trajectory of limb elevation and descent; damage to this region leads to gait ataxia but not to overt impairment in balance. The lateral cerebellum is particularly involved in walking activities where precise limb placement is necessary; damage to this zone will produce limb ataxia and locomotion problems. The complexity of these different mechanisms leading to cerebellar ataxia explains why descriptions of ataxic gait based on clinical observation are generally inadequate to quantify the dysfunction, to compare patients between each other or to follow-up the distrubances over the time in a given patient.

Formerly, the severity of cerebellar ataxia was evaluated using the International Cooperative Ataxia Rating Scale (ICARS) that divides it in four subcategories, namely posture and gait, limb kinetics, speech and oculomotor deficits (8). When scored by this method our patients showed different degrees of ataxia, ranging from score 0 to score 4.

At present, computerized gait analysis can be a better tool for the evaluation of patients with cerebellar damage. It separately analyzes single temporo-spatial parameters of the gait cycle, such as cadence, velocity, percent of cycle spent in single stance, step length, and step width. During uninterrupted walking, balance deficits resulting from damage to the medial and intermediate zone more

strongly contribute to ataxic gait than does injury to the lateral region that mainly modulates visual guided motor activities. As a matter of fact, by the above methodology all patients in this study (most of them with damage to the vermal and paravermal regions) disclosed the typical pattern of ataxic gait. In particular, data on stance phase and step width were markedly impaired, regardless of the clinical signs and of the ICARS score. This indicates that these two parameters are particularly sensitive measures in ataxic patients. It is of notice that we did not find any significant difference in temporal-spatial parameters between the different groups of patients. Therefore, although computerized gait analysis seems highly sensitive to detect subtle signs and symptoms , its ability to score the severity of cerebellar ataxia turns out to be low. Dividing patients in different "clinical" groups may thus be arbitrary and results from the inaccuracy of the clinical examination. Standard laboratory gait analysis was in our hands a valuable tool for a more careful assessment of gait performance.

The number of patients studied is not large enough to allow definitive conclusions and the recordings were performed only after treatment. Nonetheless, our study suggests that the presence of a mass lesion in the posterior fossa and the ensuing surgical treatment followed by adjuvant treatments nearly always produce gait abnormalities. Provided that a careful method of evaluation is used, gait imbalance can be recognized and measured in almost all patients, even in those without overt neurological abnormalities. One could argue that cerebellar ataxia at presentation of posterior fossa tumors could have been underestimated by the clinician in some cases. We think, therefore, that computerized gait analysis ought to be included in the initial evaluation of patients with posterior fossa tumors as well as in their follow-up.

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