Can Clinical Tests Detect Early Signs of Monohemispheric Brain Tumors?

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Background and Purpose: Prior to modern neuroimaging, neurological treatment decisions were based on findings obtained from patient history and clinical examination. Despite the availability of sophisticated neuroimaging methods, to identify intracranial tumors the clinical recognition of associated subtle motor deficits is important for practice. Precise clinical tests are particularly advantageous, as some tumors may remain unnoticed for many. The purpose of this study was to determine the sensitivity and specificity of 13 clinical tests for detection of subtle motor deficits in patients with unilateral brain tumors.

Methods: Sixty patients with unilateral brain tumors without obvious focal signs and 30 controls with normal magnetic resonance imaging were examined. Thirteen clinical maneuvers described to detect motor deficits were performed and their sensitivity, specificity, and positive and negative predictive values were estimated.

Results: The test with greatest sensitivity and specificity (with 95% confidence interval) was the Digit Quinti Sign: 0.51 (0.41-0.61) and 0.70 (0.61-0.79), respectively. The agreement measurement among the 3 most sensitive signs (Digit Quinti Sign, Pronator Drifting Test, and Finger Rolling Test) was 21%. The Kappa index for these 3 tests indicated no significant concordance.

Conclusions: The Digit Quinti Sign, the Pronator Drifting Test, and the Finger Rolling Test are simple yet very useful maneuvers that clinicians can perform at bedside. Even without apparent motor deficits, when present, these signs suggest that comprehensive investigation for intracranial neoplams should be undertaken.

Key words: *brain tumor*, *intracranial neoplasm*, *pyramidal tract lesion*, *subtle motor sign*

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INTRODUCTION

Before the modern neuroimaging era, treatment decisions in neurology were based on findings obtained almost solely from the history and clinical examination of the patient. In spite of the development of computed tomography, magnetic resonance imaging (MRI) scans, and other sophisticated neuroimaging methods, the clinical recognition of signs that may be associated with intracranial neoplasms (brain tumor) is of importance to practice. Simple, precise, and practical clinical tests are particularly advantageous, as some tumors may remain unnoticed for many years.[1] Considering that early detection and resection of brain tumors may be curative or may significantly improve prognosis, clinicians must be alert to promptly recognize subtle motor deficits that often accompany these tumors.[1]

Recognition of subtle motor deficits, minimal reductions in strength that may not be perceived by the patient but that manifest as slight difficulty in routine activities,[2] can alert the clinician to the need to proceed to the appropriate diagnostic evaluation. The present study sought to determine the sensitivity,[3] specificity,[3] and positive and negative predictive values[3] of 13 tests used to detect subtle motor deficits as early indicators of monohemispheric brain lesions. To the best of our knowledge, such battery of tests has not been studied simultaneously in the same patients with unilateral intracranial tumors.

METHODS

Subjects

This study was performed at the outpatient clinic, neurosurgery department, at the National Cancer Institute in Rio de Janeiro, Brazil. The study was approved by the National Cancer Institute Ethics Committee (# 007/06), and all participants signed an informed consent. Sixty patients with identified monohemispheric cerebral tumors (mean age = 46 ± 28 years; range = 18-74 years) were evaluated. Thirty-two (53%) were female and 58 (97%) were right handed. All had a history of at least 1 month of headaches and/or seizures, while none complained of weaknesses. Thirty-nine (65%) had a right hemisphere cerebral tumor and 21 (35%) had a left hemisphere cerebral tumor. Histological diagnosis and tumor locations for the 60 patients are given in Table 1. A control group consisting of 30 individuals (mean age = 53.5 ± 21.5 years; range = 32-75 years) referred with complaints of vertigo, migraine, or seizures, but in whom no tumor had been identified was also evaluated. Twenty (67%) were female and 26 (87%) were right handed.

All participants from both groups underwent brain MRI. The inclusion criteria were unilateral cerebral tumor confirmed

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Table 1. Histological Diagnosis and Tumor Locations (n = 60)

	Tumor Location								
	Frontal		Temporal		Parietal		Occipital		
Histological Diagnosis	Right	Left	Right	Left	Right	Left	Right	Left	Total
Pilocytic astrocytoma	7	1	1	1	0	0	0	0	10
Anaplasic astrocytoma	2	2	2	4	1	0	0	0	11
Multiforme gliobastoma	1	0	0	1	3	0	0	0	5
Oligoastrocytoma	0	1	0	1	2	0	0	0	4
Meningioma	6	1	3	1	3	2	0	0	16
Metastasis	0	0	0	0	1	2	0	0	3
Ependymoma	0	0	1	1	0	0	0	0	2
Hemangyoma	0	0	1	0	0	0	0	0	1
Neurocytoma	0	0	0	0	0	1	0	0	1
Ganglioglioma	0	0	1	0	0	0	0	0	1
Undetermined	1	0	1	2	2	0	0	0	6

by MRI, no obvious motor deficits, and Mini-Mental State Examination (MMSE)[4] with score greater than 25 points. Patients were excluded if they had nonneurological disorders that hindered neurological assessment, aphasia, movement disorders, a marked midline shift associated with a focal brain tumor, consciousness or cognitive impairments that could have affected their cooperation with the neurological examination, or brainstem, cerebellar, or bilateral cerebral tumors. Initially, 94 patients were prospectively enrolled. Four did not meet the inclusion criteria; of these, 2 presented with bihemispheric brain tumors noticed only when the MRI scans were reviewed, 1 declined to sign the informed consent, and 1 did not attain the required 25 points for the MMSE.[4]

Experimental Protocol and Data Collection

Patients and controls underwent a comprehensive neurological examination and referral to a physical therapist (E.T.M.) who performed MMSE[4] and 13 clinical tests. The physical therapist was blinded to which subjects had brain tumors and was blind to any clinical or imaging data. A list of the 13 clinical tests, the eliciting maneuvers, and the associated sign indicating a positive test are given in Table 2. For each test, we determined the sensitivity (the true positive rate), defined as the ability of the test to elicit a positive sign when the target condition is really present. We also determined the specificity, defined as the probability of an incorrect positive result in those who do not have the target condition. We determined the positive and negative predictive values that estimate the likelihood that a person who tests positively actually has the disease or is actually disease free, respectively. The Digit Quinti Rolling Sign was not performed in all patients because it was developed during the testing phase of the study. Finally, the Kappa index was used to assess concordance among measures.

RESULTS

The histopathologic diagnosis and affected lobules of the tumors identified in the 60 patients are given in Table 1. Sensitivity, specificity, and positive and negative predictive values (with 95% confidence intervals [CI]) are given in Table 3. The most sensitive tests (and 95% CI) were the Digit Quinti Sign (DQS), 0.51 (0.41-0.61); the Pronator Drifting Test (PDT), 0.41 (0.31-0.51); the Finger Rolling Test (FiRT), 0.41 (0.31-0.51); the Souques Interosseous Sign (SIS), 0.23 (0.14-0.32); and the Foot Tapping Test (FTT), 0.23 (0.14-0.32). The tests with greatest specificity were DQS, 0.70 (0.61-0.79); PDT, 0.96 (0.92-0.99); the Forearm Rolling Test (FRT), 0.93 (0.88-0.98); SIS, 0.80 (0.72-0.88); and FTT, 0.93 (0.88-0.98). The agreement measurement among the 3 most sensitive signs was 21%. The Kappa index for the 3 most sensitive tests indicated no significant concordance.

DISCUSSION

When motor system dysfunction is present, muscular weakness is the most common manifestation of this dysfunction. Several authors have described tests to detect mild arm dysfunctions indicative of brain lesions,[8,9,10] but only a few have assessed the sensitivity and specificity of these tests.[2,8] The aim of our study was to identify the most useful of 13 clinical tests for detection of monohemispheric cerebral lesion. The DQS, PDT, and FiRT were the most sensitive tests, while the DQS, PDT, and FRT had the greatest specificity.

The DQS, described by Alter in 1973,[10] showed the highest sensitivity among the 13 tests we evaluated; a positive sign was present in 31 (52%) of our patients. Alter[10] himself questioned whether the DQS was just an expression or the "phénomène des interosseux" described more than a century ago by the French neurologist Souques.[12] In our study, the SIS was present in 14 (23%) of our patients and was contralateral to the tumor in 8 of these. In all but one, the SIS was concordant with the DQS. In spite of this concordance, we cannot consider the DQS as an isolated sign, more sensitive than the SIS, or related to it.

The PDT described by Babinski[13] in 1907 is considered one of the most sensitive signs in identifying subtle motor deficits in the upper extremities. Weaver[2] studied 50 patients with subtle brachial monoparesis (not taking into account the origin of the disease or chronicity of the disease) and found that the PDT was present in 76% of the cases. Sawyer et al[8] studied 62 individuals who also had subtle upper extremity motor deficits, most of them being poststroke patients and 6 having cerebral tumors, and they found that the PDT was present in 79% of patients. On the other hand, Anderson et al[20] evaluated 46 individuals without obvious motor deficit, with cerebral lesion from different etiologies. They observed the PDT in only 22% of the patients and observed none in the 19 control subjects without cerebral lesion. In the earlier mentioned studies, patients had focal cerebral lesions coming from different origins, the majority having had cerebral infarct. Among our subjects, the PDT was present in 25 (42%), and only 1 (3.3%) individual from the control group showed an asymmetric response.

During the 1990s, 2 tests were described to detect mild upper extremity paresis. Sawyer et al[8] observed the FRT in 62 patients with unilateral acute and chronic brain lesions and in none of the 20 controls with normal imaging tests. Anderson et al[20] found the FRT to be positive in 24% of 46 patients with

Table 2. Clinical Tests[a]

Clinical Test	Eliciting Maneuver	Positive Sign
Spasticity of Conjugate Gaze[5]	The examiner pulls the patient's eyelid, while the patient is instructed to exert a small amount of resistance.	Deviation of the eyes to the side opposite the lesion.
Platysma Sign[6,7]	The patient is asked to retract the mouth's angle and stretch the neck skin.	Asymmetric platysma muscle contraction.
Forearm Rolling Test (FRT)[8]	The patient is instructed to make a fist with both hands, hold the forearms horizontally so that the fists and forearms overlap, and then rotate the hands around each other in front of the torso, with an overlap of approximately 15 cm. The movement is performed for 5 to 10 seconds in each direction of rotation, and the examiner observes the movement of the forearms relative to each other. Usually the forearms rotate around each other symmetrically.	One forearm tends to orbit the other (involved side moves less).
Finger Rolling Test (FiRT)[9]	The patient is instructed to extend both index fingers and point them toward each other in front of the torso, about 1 finger-length apart, with each tip near the opposite metacarpophalangeal joint while the other fingers are flexed. The index fingers roll around each other.	One finger orbits around the other (involved side moves less, similarly to the FRT).
Digit Quinti Sign (DQS)[10]	The patient is instructed to horizontally extend the arms and fingers forward with palms down.	The fifth finger adducts on the positive side (if the fifth digits are symmetrically abducted, there is no clinical significance).
Souques Interosseous Sign[11,12]	The patient is asked to raise both upper limbs to a position 180° of shoulder flexion.	The fingers extend and abduct on the involved side.
Pronator Drifting Test (PDT)[11,13,14]	The patient is asked to hold the upper extremities outstretched in front with 90° of shoulder flexion, palms up, and elbows and wrists extended.	Inability to maintain this position for at least 20 to 30 seconds, and asymmetric pronation or downward drifting of one arm.
Mayer Sign[15]	The examiner performs a firm passive flexion at the metacarpophalangeal joints of third, fourth, and fifth fingers—especially the 4th finger. The normal response is thumb opposition and adduction combined with flexion at the metacarpophalangeal joint and extension at the interphalangeal joint.	Unilateral absence of the normal response.
Finger Tapping Sign (FiTS)[8,14]	The patient is asked to touch the tip of the index finger to the interphalangeal joint of the thumb repetitively and as quickly as possible for 10 seconds.	Discrepancy of more than 5 repetitions between the left and right index fingers. The movements will be slower at the involved side.
Digit Quinti Rolling Sign (DQRS)[16]	The position is similar to that of the FiRT, except that the digit quinti is extended while the other fingers are flexed, and the patient rolls the fifth fingers around each other.	One finger orbits around the other (involved side moves less, similarly to the FiRT).
Foot Tapping Test[8,14,17]	The patient sits with knees and ankles at 90° and taps the forefoot on the floor for 10 seconds while maintaining the heels stationary.	Discrepancy of more than 5 taps between the left and right feet.
Babinski Sign (BS)[18]	The examiner stimulates the lateral plantar surface of the patient's foot with a blunt instrument (e.g., the handle of a reflex hammer), beginning near the heel and progressing up the side of the foot.	Extension of the great toe.
Chaddock Sign[19]	Similar to the BS, the examiner stimulates the lateral aspect of the patient's foot, beginning below the lateral malleolus near the junction of the dorsal and plantar skin and drawing the stimulus from the heel forward to the small toe.	Dorsiflexion of the great toe.

[a]To preclude visual compensation, the DQS and PDT were done with eyes closed.

subtle motor deficits and unilateral cerebral lesion. In our study, the FRT was asymmetric in 17% of our patients and none of the controls. It is noteworthy that all controls were right-hand dominant and showed symmetry on this maneuver, suggesting that dominance and manual skills do not seem to influence the responses. Two years after the original description of the FRT, Yamamoto[9] compared the FiRT with the FRT in 28 patients with unilateral cerebral lesion and found it to be present in 61% of the subjects although the FRT was present in only 21%. Our results confirmed Yamamoto's finding as we observed the FRT in 17% and the FiRT in 41% of the patients.

Based on the knowledge that the corticospinal tract produces facilitatory postsynaptic action potentials predominantly for the control of fine, discrete movements of the fingers,[21] and that the digit quinti has less cortical representation than the forearm or index finger,[8] we developed the Digit Quinti Rolling Sign.[16] If discrete pyramidal tract lesions are associated with subtle paresis of the hand, then it is more likely to manifest deficits in the fifth digit than any other. Unfortunately, our patients presented great difficulty in correctly performing the rolling movements of only the digit quinti, showing a tendency to move the entire hand. This might have contributed

Table 3. Sensitivity, Specificity, and Predictive Values of the Tests[a]

	Focal Lesion (n = 60)		Control (n = 30)					
	Pos	Neg	Pos	Neg	Sensitivity (95% CI)	Specificity (95% CI)	PPV (95% CI)	NPV (95% CI)
DQS	31	29	9	21	0.51(0.41-0.61)	0.70(0.61-0.79)	0.77(0.68-0.86)	0.42(0.32-0.52)
PDT	25	35	1	29	0.41(0.31-0.51)	0.96(0.92-0.99)	0.96(0.92-1.00)	0.45(0.35-0.55)
FiRT	25	35	2	28	0.41(0.31-0.51)	0.93(0.88-0.98)	0.92(0.87-0.98)	0.44(0.34-0.54)
SIS	14	46	6	24	0.23(0.14-0.32)	0.80(0.72-0.88)	0.70(0.61-0.79)	0.34(0.24-0.44)
FTT	14	46	2	28	0.23(0.14-0.32)	0.93(0.88-0.98)	0.87(0.80-0.94)	0.37(0.27-0.47)
FiTT	11	49	3	27	0.18(0.10-0.26)	0.90(0.84-0.96)	0.78(0.70-0.86)	0.35(0.26-0.44)
FRT	10	50	0	30	0.16(0.08-0.24)	1	1	0.37(0.27-0.47)
BS	5	55	0	30	0.08(0.02-0.14)	1	1	0.35(0.26-0.47)
MS	4	56	4	26	0.06(0.01-0.11)	0.86(0.79-0.93)	0.50(0.40-0.60)	0.31(0.21-0.41)
DQRS[a]	2	28	1	21	0.06(0.01-0.11)	0.95(0.91-0.99)	0.66(0.56-0.76)	0.42(0.32-0.52)
CS	2	58	0	30	0.03(0.00-0.07)	1	1	0.34(0.24-0.44)
SCG	1	59	0	30	0.01(0.00-0.04)	1	1	1
PS	1	59	0	30	0.01(0.00-0.04)	1	1	1

Abbreviations: BS, Babinski Sign; CI, confidence interval; CS, Chaddock Sign; DQRS, Digit Quinti Rolling Sign; DQS, Digit Quinti Sign; FiRT, Finger Rolling Test; FiTT, Finger Tapping Test; FRT, Forearm Rolling Test; FTT, Foot Tapping Test; MS, Mayer Sign; Neg, Negative Test; NPV, negative predictive value; PDT, Pronator Drifting Test; Pos, Positive Test; PPV, positive predictive value; PS, Platysma Sign; SCG, Spasticity Conjugate Gaze; SIS, Souques Interosseous Sign.

[a]Assessed with 30 patients and 22 controls.

to the unexpected very low sensitivity of the test. We believe that more patients must be tested before reaching a definite conclusion regarding this maneuver.

Subtle motor deficits can also be measured by evaluating repetitive rapid movements and comparing the maximum frequency of uninterrupted beatings of the index finger or strikes of the forefoot while the heel remains fixed.[14] Miller and Johnson[17] performed a comparative study of the Babisnki Sign versus the FTT for diagnosis of pyramidal tract dysfunction. Despite considerable criticism for making comparisons between a reflex response and the ability to perform a voluntary motor activity,[22] the authors considered the FTT to be advantageous. In our study, the FTT was positive in only 14 (23%) of our 60 patients.

Despite the fact that positive results for the Spasticity of Conjugate Gaze,[5] Platysma Sign,[6,7] Babinski Sign,[18] Chaddock Sign,[19] and Mayer Sign[15] all indicate pyramidal tract dysfunction, they presented low indices of sensitivity (0.01, 0.01, 0.08, 0.03, and 0.06, respectively) for monohemispheric brain tumors.

Limitations

The limited number of recruited patients is a limiting factor of this study and may have contributed to the low specificity and sensitivity results for some of the tests we included. Furthermore, differences among patients in the tumor location may have contributed to the lack of positive findings in some tests. It is possible that a combination of tests may improve sensitivity and provide a more comprehensive battery of clinical tests to identify the need for imaging.

CONCLUSIONS

Our results indicate that the DQS, PDT, and FiRT are the most sensitive tests to detect the subtle motor deficits associated with monohemispheric brain tumors. Clinicians should consider using tests to identify subtle motor deficits as complementary items in their neurological examination. These tests are simple to perform and easy to interpret; their presence may indicate the need for neuroimaging for a definitive diagnosis.

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