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Movement symptoms in European Moyamoya angiopathy — First systematic questionnaire study

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ABSTRACT

Objective: Movement disorders are a rare manifestation of Moyamoya angiopathy (MMA). Data on prevalence and clinical presentation are warranted. Possible involuntary movements include focal motor seizures, tremor, limb-shaking transient ischemic attacks, choreiform and spastic or dystonic movement disorders.

Patients and methods: We developed a questionnaire to systematically assess movement disorders in MMA. Patients' history of involuntary movements and their clinical presentation were assessed systematically by interview. Additionally, demographic data were assessed as well as localization of movements, possible trigger factors and the presence of other symptoms.

Results: The questionnaire was administered to 63 European patients with MMA. The response rate was high with 93.6% participating patients. Twenty-eight patients (47.4%) reported involuntary movement disorders including periodic tremor, irregular jerks, involuntary movements with loopy or pranced character, stiffness and muscle cramps. From those patients, 16 (57.1%) individuals had the symptoms prior to the diagnosis of MMA.

The most common involuntary movements were irregular jerks witnessed by 17 (60.7%) patients, followed by stiffness and muscle cramps in 10 (35.7%). Eight (28.6%) Patients suffered from unintended loopy and pranced character, while 4 individuals (14.3%) remembered periodic tremor.

Of the 28 patients who witnessed movement disorders, 23 had undergone revascularization surgery (82.1%). From the latter subgroup, movement disorders were reversed in 7 out of 12 patients (58.3%) with irregular jerks and 4 out of 7 patients (57.1%) with unintended loopy and pranced character.

Conclusions: Our study elucidates the high incidence of movement disorders in an unselected consecutively recruited cohort of European MMA patients.

1. Introduction

Moyamoya Angiopathy (MMA) is a rare vasculopathy characterized by progressive stenosis and eventual occlusion of the distal internal carotid arteries (ICA) and the proximal cerebral arteries (anterior and medial) of the circle of Willis [1,2]. The prevalence in Asia seems to be the highest worldwide, especially in Japan and Korea [3]. The disease usually manifests with transient ischemic attacks (TIA), strokes or intracranial hemorrhages [2]. Treatment options include different revascularization techniques such as extracranial-intracranial bypass operations, but also conservative strategies using antiplatelet therapy [4]. Since revascularization surgery is known to be highly effective in preventing new strokes and consecutive morbidities [4], awareness for presenting symptoms and early diagnosis is highly beneficial [5]. Due to the rarity of the disease, it is still unclear which symptoms are early manifestation signs of MMA and which could be considered pathognomonic [5,2]. Reported series from countries with a rela-

Abbreviations: MMA, Moyamoya angiopathy; TIA, transient ischemic attack; EC-IC bypass, extracranial-intracranial bypass.

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Table 1
Characteristics of patients with and without movement symptoms.

	With movement symptom N = 28	Without movement symptom N = 31	P Chi Square
Female predominance	19 (19/28 = 68%)	26 (26/31 = 84%)	0.2 (X^2 2.084)
Age at time of question	37.86 (SE 12.88)	43.5 (SE 11.84)	
Bilateral MMA	27 (27/28 = 96%)	21 (21/31 = 68%)	0.025 (X^2 6.2025)
Stroke or TIA history	24 (24/28 = 86%)	26 (26/31 = 84%)	0.025 (X^2 6.352)
Bypass surgery	23 (23/28 = 82%)	12 (12/30 = 40%)	0.005 (X^2 9.059)
Thyreoid dysfunction	7 (7/27 = 26%)	6 (6/29 = 21%)	0.7 (X^2 0.215)
smoking	7 (7/2 = 26%)	6 (6/31 = 19%)	0.6 (X^2 0.358)
Regular alcohol intake	1 (1/28 = 4%)	2 (2/31 = 6%)	0.7 (X^2 0.253)
Prior psychiatric treatment	10 (10/28 = 36%)	7 (7/31 = 23%)	0.3 (X^2 1.237)

tive high prevalence of MMA seem to underestimate movement disorders as manifestation of the disease [6].

There is a broad spectrum of movement disorders, which infrequently appear in MMA patients. The differentiation and interpretation of this spectrum is a challenge [7], since epidemiological data are missing. Involuntary movements in MMA include focal motor seizures, tremor, limb-shaking TIAs, choreatic movements, dyskinesia, dystonia and spasticity, stiffening and painful cramps [7–16]. The exact characterization of symptoms is essential as they reflect different pathophysiological mechanisms and require different treatment strategies. Some involuntary movements such as periodic muscle jitter in focal motor seizures, epilepsia partialis continua or tremor as well as unintended stiffening, cramps and spasticity are mainly caused by cerebral gliosis after stroke. However, irregular jerks as in limb-shaking TIAs and unintended movements with loopy or pranced character in hemichorea or dyskinesia are possible red-flags for critical hemodynamic compromised hemispheres [8,10,14,16]. The most common factors known to trigger movement disorders resulting from hemodynamic insufficiency are hyperventilation by crying, singing or excitement [11,17,18], and pregnancy (chorea gravidarum or estrogen-induced chorea)[19–21]. Treatment recommendations include antipsychotic medications [22], but more often movement symptoms are reported to recover after a direct or indirect bypass operation [8,10,23].

This study aimed to systematically evaluate the frequency and characteristics of movement disorders in MMA.

2. Patient and methods

Adult patients with bilateral MMA or a unilateral variant of MMA listed in the database of the Moyamoya outpatient clinic at the Alfried-Krupp Hospital in Essen, Germany were considered for the present study. Exclusion criteria were any other diseases known to cause movement disorders like Parkinson's disease, multiple sclerosis or Huntington's disease (HD). Moreover, medication with side effects such as movement disorders like neuroleptics or levodopa were not given. We developed a standardized questionnaire which was sent to 63 European adult patients (for details see Supplementary material). The questionnaire included 29 multiple choice questions, which covered a wide spectrum of symptoms and factors that could affect the symptomatology, concentrating however on movement disorders. The questionnaire was designed to be completed within 10 min. If patients acknowledged to have experienced movement disorders, they were asked to choose between the items "periodic tremor", "involuntary muscle stiffness or cramps", "involuntary jerks", "irregular and unintended movements with loopy or pranced character". These descriptions were intended to represent focal motor seizures, epilepsia partialis continua or tremor (=periodic tremor, German *regelmässiges Zittern*), spasticity or dystonia (=involuntary muscle stiffness or cramps, German *unwillkürliche Verkrampfungen*), limb-shaking TIAs (=involuntary jerks, German *unwillkürliche Zuckungen*) and chorea or ballism (irregular and involuntary movements with loopy or pranced character, German *unwillkürliche Bewegungen mit tänzelndem, fliessenden, choreatischen Bewegungen).* Moreover, detailed characterization like localization, duration, frequency, triggering factors, other symptoms and recovery was assessed using a multiple choice format. The study has been approved by the local ethics-committee and written informed consent was obtained by all patients. Statistical comparisons were made using Mann-Whitney U Test (Wilcoxon test). Statistical analysis was completed with SPSS 20 (IBM, Armonk, NY). p values < 0.05 were considered significant.

3. Results

3.1. Demographics

The response rate was extremely high with 59 out of 63 (93.6%) patients contacted to complete the questionnaire. Among these, 13 were male and 46 female, corresponding to a male to female ratio of approximately 3.54:1. MMA manifestation was bilateral in 48 (81.3%) patients, while 11 (18.6%) suffered from a unilateral variant of MMA. No patient had a former history of rheumatic fever, all learned to walk within a normal time range as toddlers and nobody had a family history for movement disorders. The majority of the patient already underwent bypass surgery. The characteristics of the 28 patients who acknowledged a history of movement disorders compared to the 31 who did not, are shown in Table 1.

3.1.1. Characterization of movement symptoms

Four (6.8%) patients acknowledged a history of "periodic tremor" and 17 (28.8%) reported "irregular jerks". Moreover, 10 (16.9%) chose the multiple choice description of "involuntary stiffness and cramps" and 8 (13.5%) reported to have suffered from "involuntary movements with loopy or pranced character".

Patients who reported to have suffered from movement disorders were asked to characterize these using multiple choice questions regarding frequency, duration and triggering factors. The results are summarized in Table 2.

3.1.2. Symptom recovery after bypass surgery

The majority of the patients (14/20 = 70%) who underwent bypass surgery and answered this specific question reported complete recovery of movement symptoms after surgery. Symptom recovery after bypass surgery was reported in 2 of 3 (66.6%) patients with "periodic tremor", 8 of 11 patients (72.7%) with "irregular jerks", 4 of 7 (57.1%) with "involuntary movements with loopy or pranced character" and only 1 patient of those 6 patients (16.7%) who reported "involuntary stiffness and cramps".