Headache and Treatment of Unruptured Intracranial Aneurysms

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Background and Purpose: The relationship between unruptured intracranial aneurysms (UIAs) and chronic headache and the impact of aneurysm treatment on headache outcome are controversial. The aim of this study was to determine clinical features of a supposedly primary headache in patients with UIA. We also assessed changes in headache characteristics after UIA treatment. *Methods:* We examined clinical and imaging data of patients in whom a UIA was diagnosed during diagnostic workup of a suspected primary headache. Medical records were reviewed and personal telephone follow-ups were performed after UIA treatment to assess changes in the frequency and intensity of the headache. *Results:* Forty-two patients (76%) reported a substantial improvement in headache frequency and intensity after UIA treatment. Forty-five patients (81%) reported a decrease in headache frequency from a median of 8 days/month before treatment to 1 day/month after treatment (95% confidence interval [CI] 81-83, $P < .001$). The average intensity in an analog pain scale was 7.7 ± 1.6 before treatment and 5.6 ± 2.4 after treatment ($P < .001$). Higher headache frequency was associated with a greater odd of improvement after treatment (odds ratio 1.12, 95% CI 1.0-1.26, $P = .03$). No associations were found between the type of headache, type of treatment (endovascular versus surgical), number, size, or localization of the aneurysms and the response to treatment. *Conclusions:* The treatment of UIA had a robust beneficial effect on previous headache. Although a "placebo" effect of aneurysm treatment cannot be ruled out, these results suggest a potential association between UIA and certain chronic headaches usually considered to be primary. **Key Words:** Headache—intracranial aneurysm—therapeutics—endovascular therapy.

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Introduction

Unruptured intracranial aneurysms (UIAs) are common in the general population. Imaging and autopsy studies have shown a prevalence ranging from .4% to 6%.[1,2] Aneurysmal subarachnoid hemorrhage has an incidence of 6-8 cases per 100,000 person/year[3] and generally occurs in patients unaware of the presence of a UIA. Chronic primary headache is not usually considered a clinical manifestation of UIAs.[2]

Certain UIAs can become symptomatic due to enlargement and compression of the second and third cranial nerves. UIAs are clinically expressed as vision loss or oculomotor abnormalities, respectively. Signs of brainstem compression, as well as cerebral ischemia as a result of emboli originating in the aneurysm, can also occur.[4,5] However, most UIAs are diagnosed in patients undergoing imaging studies during workup for long-standing uncomplicated headache. Those UIAs are usually deemed incidental and presumed asymptomatic.

Despite the fact that the nature of the association, if any, between headache and UIA is not well established, several studies have mentioned the presence of headache in subjects with UIAs, in 18%-34% of cases.[6-8] Several types of headache including cluster headache, hemicrania continua, and migraine, are present in patients with UIAs. Symptoms occasionally improve after treatment of the aneurysm.[9-15] In prior reports, aneurysm treatment was followed by improvement in severity or frequency of headache in 59%-92% of patients, regardless of the type of treatment (endovascular or surgical).[16-19] However, these studies included patients in which the aneurism had been diagnosed in the workup of various conditions other than headache. Also, information about the characteristics of the headache that may indicate the presence of a UIA and its response to treatment is scarce.

The aims of the present study were to describe headache characteristics in patients diagnosed with a UIA during workup of an otherwise primary headache, to determine clinical features that should raise suspicion of a possible underlying UIA, to assess headache changes after UIA treatment, and to find potential predictors of favorable outcome.

Methods

In this single-center study, we identified patients undergoing endovascular or surgical treatment for UIA between 2002 and 2013, and selected those in which the UIA was diagnosed during the workup of a headache determined to be primary by International Classification of Headache Disorders, 3rd edition (ICHD-III), criteria.[20] All patients were followed up at the outpatient clinic or received phone calls for verification of outcome and vital status.

Although current guidelines do not strongly recommend treatment of UIAs, the decision to treat the aneurysms was finally based on the preference of the patient and the primary physician.

Patients meeting criteria for thunderclap headache according to ICHD-III[20] were excluded from the study because this could also be a manifestation of subarachnoid hemorrhage or could represent "sentinel headache" from early bleeding of the aneurysm.[21-23]

Medical records were reviewed and demographic characteristics and comorbidities were assessed. The characteristics of the previously referred headache, including type (in some cases more than 1 type of headache were reported), localization, frequency, intensity (using a numeric rating scale for pain),[24] and response to medication, were assessed. Headache types were classified according to the ICHD-III criteria.[20] Aneurysm characteristics (i.e., number, location, and size) and type of treatment (i.e., endovascular versus surgical) were also recorded.

Personal or telephone interviews were conducted after endovascular or surgical treatment by neurologists using a standardized questionnaire. The questionnaire included questions about headache characteristics before and after aneurysm treatment, including the number of days with headache, analog pain scale rating, response to symptomatic treatment, and subjective impression of improvement, worsening, or no change after treatment. Headache was classified according to the ICHD-III criteria.[20] Also, as endovascular treatment does not result in aneurysm size change, whereas surgery produces a reduction in the size of the lesion, we compared outcomes in both groups.

Anxiety, in general,[25] and in patients with UIA diagnosis in particular, may influence symptoms and the effect of treatment.[26] We investigated changes in headache characteristics in the period between aneurysm diagnosis and treatment (type of headache, frequency, intensity, and response to symptomatic treatment) to assess potential changes in headache due to the psychological impact of harboring a UIA. Additionally, 29 migrainous patients without UIAs, previously studied with magnetic resonance angiography, were randomly selected from our clinic database, and served as controls. We investigated whether migraine in patients with UIA had clinical or demographic features distinct from those who had migraine but no UIA.

Approval from the Ethics Standards Committee was obtained to conduct the present study.

Statistics

We assessed differences between groups using the Fisher exact test, χ^2 test, or analysis of variance according to variable type. A Poisson regression model with mixed effects for individuals, adjusted by age, gender, and type of headache, was used to compare pre- and post-treatment headache episodes. Logistic and ordinal mixed effects models were used to assess changes in headache intensity and subjective improvement. Factors associated with headache improvement were studied in univariable and