LETTERS TO EDITOR

HEADACHE AS THE ONLY SIGN OF PHEOCHROMOCYTOMA: AN ANALYSIS

Sir,

Pheochromocytoma is an uncommon disease and headache is one of the most frequent symptoms, present in 80% of cases. Headache as the only presentation of pheochromocytoma in the absence of other symptoms is rare.

In this paper, we present the characteristics of patients in whom headache was the only presentation of pheochromocytoma in the absence of symptoms of sympathetic overactivity. The present study is based on a retrospective review of data collected (prospectively) over a 10-year period of 28 consecutive patients with pheochromocytoma admitted in the medical/ surgical endocrinology department between December 1996 and June 2005. Diagnosis of pheochromocytoma was based on 24-hour urine metanephrines/ Vanillyllmandelic acid with CT of the abdomen. Patients were included in the present study if headache was the only presentation of pheochromocytoma in the absence of features of sympathetic overactivity, and also they had normal blood pressure.

We obtained a detailed description of the features of headache, including its mode of onset, location, severity, pattern and evolution; and these were classified according to the criteria of the International Headache Society (IHS). For all patients, we recorded the past history of the headache and residual headache 2 months, 6 months after the surgery of pheochromocytoma. A visual analogue scale (VAS) was used to record pain severity (severe headache = VAS >7/10). Three modes of onset of headache were defined depending on the time between the initial pain sensation and the most severe headache:

'Thunderclap' – sudden onset of an excruciating headache (VAS more than 8/10); acute headache defined as developing in less than 24 h; progressive headache defined as headache lasting over 24 h. After 24 hours, the pain was characterized as continuous or intermittent. All patients underwent an extensive evaluation for their headache with CT of the brain and sinuses.

Of the 28 patients, 4 patients (14.3%) presented with headache as the only manifestation at the time of initial evaluation. There were 3 males and 1 female; with mean age 20 years, range 17-23 years. The mean delay between the onset and diagnosis was 54.3 days (range 36-48 days). All the patients had tumors in the adrenal region and had predominant secretion of norepinephrine.

The headache characteristics are given in Table 1.

The most frequent characteristics were migraine-like presentation in three patients (75%), unilateral location (75%) and throbbing quality (75%). There was no family history of migraine in all the three patients. There was no history of use of beta blockers and no history

Table 1: Characteristics of headache in patients with pheochromocytoma

Patient	*History of migraine*	*Onset*	*Evolution*	*Pattern*	*Severity*	*Location*	*Associated signs*
1.	No	Progressive	Continuous	Constrictive	8	Diffuse	No
2.	No	Progressive	Intermittent	Throbbing	7	Right Hemi Cranium	Nausea Vomiting Photophobia Visual aura
3.	No	Progressive	Intermittent	Throbbing	8	Left Hemi Cranium	Nausea Vomiting Photophobia Visual aura
4.	No	Progressive	Intermittent	Throbbing	10	Right Hemi Cranium	Nausea Vomiting Photophobia Visual aura

of diabetes, which would have impaired the sympathetic nervous system manifestations. All the three patients had visual aura in the form of fortification spectra. All the four patients had complete resolution of headache after surgery, further relating the headache to pheochromocytoma. The demographic characteristics, the biochemistry and the radiological features of patients with headache were no different from patients presenting with other classical features.

The clinical triad of headache, diaphoresis and palpitation is suggestive of pheochromocytoma and peculiar to the specific patient population but occurs in only 11-22% of cases.[1-4] Hypertension is also not the only factor in headache pathogenesis; and changes in catecholamines, adrenomedullin and other neuropeptides may cause some of these symptoms.[5] Our study has clearly shown that headache was the initial presenting symptom in 14% of patients in the absence of other symptoms of sympathetic overactivity. Although the incidence of headache in the absence of other symptoms of sympathetic overactivity is high in our study, we could not find any confounding factor to alter the results; and if there was variability in complaints by patients, then they should have had an elevated blood pressure along with other symptoms of sympathetic overactivity, which was not the case.

This study has highlighted that a close suspicion is required to look for sympathetic overactivity in patients with recent-onset headache with normal blood pressure at initial evaluation; because headache, particularly migraine-like headache, could be an initial presenting manifestation of pheochromocytoma. This study highlights the need for doing 24-hour urine catecholamine estimation for all patients presenting with headache.

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N. UDAYAKUMAR*, S. SIVAPRAKASH, M. CHANDRASEKARAN
Institute of Internal Medicine, *University of Cincinnati, USA; Madras Medical College, Chennai, India

Correspondence:
Dr. N. Udayakumar, Department of Internal Medicine, University of Cincinnati, USA.
E-mail: udhaykumar81@yahoo.co.in