

## A Rare Case of Ibuprofen-Induced Eosinophilic Meningitis in a 13-Year-Old Girl

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**ABSTRACT:** Eosinophilic meningoencephalitis is based on clinical manifestations and microscopic identification of eosinophils present in cerebrospinal fluid (CSF). It is caused by a variety of helminthic infections with most common being angiostrongyliasis, gnathostomiasis, toxocariasis, cysticercosis, schistosomiasis, baylisascariasis, and paragonimiasis. Many case reports are there in which parasites have been found responsible, but there are rare reports of CSF eosinophilia associated with the use of drugs. We report a case of drug-induced (ibuprofen) eosinophilic meningitis in a healthy female who presented to us with severe headache and improved dramatically after drug withdrawal.

**KEYWORDS:** eosinophilic meningitis, drug-induced meningitis, ibuprofen, CSF eosinophilia

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### Introduction

Eosinophilic Meningitis (EM) is a distinct clinical entity that may have infectious and noninfectious causes. Infection with the helminthic parasite, *Angiostrongylus cantonensis*, is the most common infectious etiology worldwide including India that causes meningitis termed Meningitic Angiostrongyliasis (MA). Neurognathostomiasis (NG) is the main parasitic disease in the differential diagnosis of MA. Other causes of EM include neurocysticercosis, cerebral paragonimiasis, *Toxocara canis*, *Baylisascaris*, tuberculous meningitis, and cryptococcal meningitis.<sup>1,2</sup> However, few drugs have also been reported to be the cause of EM including ibuprofen, ciprofloxacin, amoxicillin, and trimethoprim-sulfamethoxazole.<sup>3,4</sup> Here we report a case of ibuprofen-induced EM in a 13-year-old girl who presented to us with severe headache and photophobia, which is very atypical presentation of ibuprofen as it is a very commonly used Nonsteroidal Antiinflammatory Drugs (NSAID).

### Case Report

A 13-year-old girl was brought to our OPD with complaints of headache and vomiting for three days. The headache

was predominantly in the frontal region, which was associated with projectile vomiting and photophobia. Before the onset of headache, she had fever for five to six days, which got subsided with ibuprofen and paracetamol combination advised by the local physician. On examination, her vital signs were stable with lean and thin built. Cardiovascular, respiratory, and abdominal examination was normal. Central Nervous System (CNS) examination was within normal limits with no neurological deficit except photophobia and nuchal rigidity as signs of meningeal irritation. She was hospitalized with a probable diagnosis of meningitis. Complete blood count showed eosinophilia with a Total Leucocyte Count (TLC) 8900/ $\mu$ L, and differential count showed neutrophil 63%, lymphocyte 25%, eosinophil 7% with absolute eosinophil count 623/ $\mu$ L, basophil 1%, monocyte 4%, and erythrocyte sedimentation rate (ESR) 20 mm in the first hour. Lumbar puncture was done, and on cerebrospinal fluid (CSF) examination, total cell count was 810 with 42% eosinophils and 58% lymphocytes. CSF proteins were raised (214.9 mg/dL), and sugar was low (<10 mg/dL) with simultaneous blood sugar 78 mg/dL. CSF culture showed no growth. Further



investigation was done that included Montoux test, chest X-ray, Magnetic Resonance Imaging (MRI) of brain and bone marrow, and abdomen USG, which were within which were normal. The patient was evaluated for parasitic infestation as she had eosinophilia. The stool examination for parasite and serology for parasitic infestation was negative for any infestation. Initially, she started with steroids and intravenous (IV) antibiotics, but after we reviewed the literature and there was no parasitic infestation, she was diagnosed to have drug-induced (ibuprofen) EM and IV antibiotics were stopped. Her headache was relieved within 48 hours of IV steroids, and she was discharged on day 7 without steroids and antibiotics, and without any sign of meningeal irritation. On follow-up, on day 11 repeat lumbar puncture was done, which showed cell count— $<15/\text{mm}^3$ , eosinophil—nil, proteins—15.6 mg/dL, sugar—60 mg/dL (against blood sugar of 86 mg/dL), and chloride—108 meq/L. CSF culture was sterile.

## Discussion

Drug-induced meningitis is an uncommon form of meningitis and present mainly as adverse reaction with numerous drugs. It is a diagnosis of exclusion, and the clinical features and CSF findings vary greatly including neutrophilia and rarely eosinophilia.<sup>3,5</sup> In our patient, predominant cells in the CSF were eosinophils. EM is defined by the presence of 10 or more eosinophils per cubic millimeter in the CSF or eosinophilia of at least 10% of total CSF leukocyte count.<sup>6</sup> Ibuprofen, a common NSAID, is the most frequent cause of drug-induced EM Drug Induced Eosinophilic Meningitis (DIEM). It is interesting to know that while small doses of ibuprofen can cause EM, patient can tolerate other NSAID both before and after the meningitis episode and that not all the drug in this group lead to meningitis.<sup>3,4</sup> In one series of DIEM, 32 of the 43 cases were due to ibuprofen. Among them, two patients had elevated eosinophil, 13 and 60%.<sup>4,7</sup> The incidence of ibuprofen-induced meningitis is increasingly reported mainly among patients with underlying autoimmune connective disorder. However, few cases have been reported in previously healthy patients also.<sup>7</sup> Most episodes consist of an acute meningeal syndrome with a predominance of neutrophils in 72.2% of episodes and elevated protein in the CSF, so the clinical presentation of this type of aseptic meningitis may be quite similar to that of acute bacterial meningitis.<sup>2-4</sup> In some cases, the clinical presentation is that of meningoencephalitis with neurologic focal deficits. Peripheral eosinophilia may not be present during the initial manifestations.<sup>8</sup> CSF glucose levels are usually normal, which may help to differentiate between

these two types of meningitis. Our patient fits into the diagnosis of EM, which is usually based on the following criteria—temporal relationship between the use of the drugs and subsequent onset of meningeal symptoms, CSF pleocytosis ( $>10 \text{ cell}/\text{mm}^3$ ), negative CSF culture, absence of any other explanation for the meningitis, and a resolution of symptoms on drug withdrawal.<sup>5,6</sup> However, CSF glucose was  $<10 \text{ mg}\%$  in our case, which is not reported yet.

## Lesson to Clinicians

When evaluating patients with eosinophilic pleocytosis, clinicians should consider parasitic aetiologies as well as less common drug-induced forms of aseptic meningitis because although these are rare causes, unnecessary investigation and treatment can be avoided if proper diagnosis is made.

## Author Contributions

Wrote the first draft of the manuscript: SB, DS. Contributed to the writing of the manuscript: SB. Agree with manuscript results and conclusions: SB, DS, SB. Jointly developed the structure and arguments for the paper: SB, DS, SB, MG. Made critical revisions and approved final version: MG. All authors reviewed and approved of the final manuscript.

## DISCLOSURES AND ETHICS

As a requirement of publication the authors have provided signed confirmation of their compliance with ethical and legal obligations including but not limited to compliance with ICMJE authorship and competing interests guidelines, that the article is neither under consideration for publication nor published elsewhere, of their compliance with legal and ethical guidelines concerning human and animal research participants (if applicable), and that permission has been obtained for reproduction of any copyrighted material. This article was subject to blind, independent, expert peer review. The reviewers reported no competing interests.

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