Clinical and Experimental Health Sciences

Pseudotumor Cerebri with Familial Mediterranean Fever in an Adult Patient

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Received: 23.02.2023 **Accepted:** 03.06.2024

ABSTRACT

Familial Mediterranean fever is an autosomal recessive disease characterized by recurrent episodes of fever, peritonitis, pleuritis and arthritis. Neurological involvement in FMF is rare but serious. Headache, seizures, demyelinating lesions, stroke, posterior reversible leukoencephalopathy syndrome, aseptic meningitis and cranial neuropathy have been reported in the literature. In this paper, we present a combination of FMF and pseudotumor cerebri in an adult patient.

Keywords: Familial Mediterranean Fever, pseudotumor cerebri, headache

1. INTRODUCTION

Pseudotumor cerebri (PTC) is characterized by the presence of intracranial hypertensive symptoms despite the absence of any detectable mass lesion on radiological imaging. Headache, nausea, and vomiting are frequently encountered as the primary symptoms of the disease. Patients with PTC may also experience diplopia, blurred vision, and pulsatile tinnitus (1). Neurological manifestations commonly observed in PTC include bilateral and symmetric papilledema and unilateral or bilateral partial or complete sixth nerve palsy. Partial or complete loss of vision is frequently observed in the advanced stages of the disease. According to the updated criteria for PTC by Friedman et al., the disease is categorized into two groups: primary (idiopathic) and secondary. The primary form refers to cases where no identifiable underlying cause is found, while the secondary form encompasses cases where PTC is attributed to various causes, ranging from medication-induced factors to cerebral venous sinus thrombosis. Friedman et al. prefer the term “pseudotumor cerebri syndrome” (PTCS) to “benign intracranial hypertension” or “idiopathic intracranial hypertension” (2). Familial Mediterranean Fever (FMF) is an autoinflammatory disease characterized by recurrent fever and polyserositis, including peritonitis, pleuritis, and synovitis. It is inherited in an autosomal recessive manner. Although neurological manifestations in FMF are infrequent, they may manifest as seizures, recurrent episodes of aseptic meningitis, cranial nerve involvement, pseudotumor cerebri (PTC), ischemic stroke, vasculitis, and demyelinating lesions (3,4).

There are only few case reports on the relationship between FMF and PTC in adults (5,6). This paper presented an adult patient with FMF and PTC.

2. CASE PRESENTATION

A 30-year-old male patient presented to our outpatient department with complaints of headaches in both frontal regions and blurred vision that began approximately one month ago. He experienced a dull and intense headache that did not show any improvement with the use of painkillers. He also reported experiencing what is commonly known as pulsatile tinnitus. He has been on colchicine (60 mg/day) as he has had FMF for ten years. During the examination, the patient exhibited hypertension, while the rest of the vital signs were within the normal range. Both his eyes had grade 3 papilledema (Figure 1). His right visual field was narrowed. Visual acuity was bilateral (0.3). No abnormalities were detected during the neurological and physical examination. His brain magnetic resonance investigation and magnetic resonance venography were normal (Figure2). We performed lumbar puncture (LP). The cerebrospinal fluid (CSF) pressure was 270 mm H2O. CSF protein was high (40.7 mg/dl). Otherwise, his CSF biochemistry and cell count were normal. We performed a second LP to drain the CSF. The opening pressure dropped to 190 mm H2O. His complaints of headache and blurred vision showed significant improvement.

DOI: 10.33808/clinexphealthsci.1252588

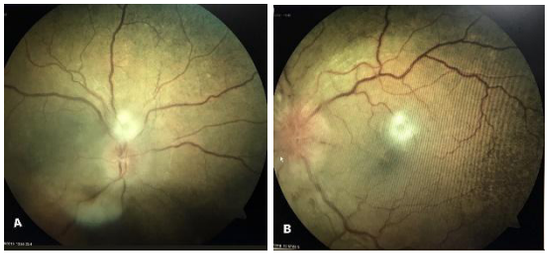

Figure 1. *The papillae borders are obscure in both fundi of the case.*

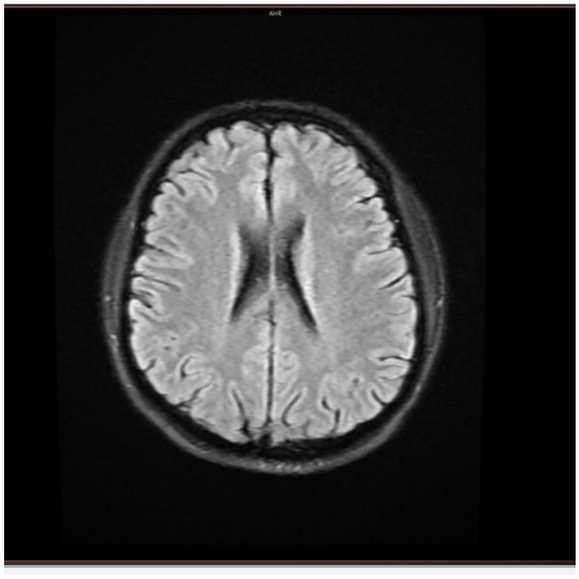

Figure 2. *MRI scan of the case was normal.*

The protein/creatinine ratio in his spot urine was high, with +++ proteinuria (9.74 mg/dl). We conducted a renal ultrasonography. Grade 1 growth was present in his kidneys. Both serum amyloid A (15.4 mg/dl) and protein C (189 mg/dl) were positive. We performed a kidney biopsy. The diagnosis was secondary amyloidosis due to FMF. Hyperlipidemia (total cholesterol: 271 mg/dl, LDL: 190 mg/dl), proteinuria (+++), and hypoalbuminuria (2.4 mg/dl) were present with FMF-related amyloidosis. Due to the presence of nephrotic syndrome, the patient was started on an angiotensin 2-type 1 receptor antagonist. He was also started on 500 mg/day acetazolamide. The treatment was effective. At the second LP, the opening pressure dropped to 190 mm H2O. He experienced a significant improvement in his complaints of headache and blurred vision and remained symptom-free throughout the two-year follow-up period.

3. DISCUSSION

Familial Mediterranean fever is a genetic disorder that is commonly observed among individuals of Armenian, Arab, Jewish, and Turkish descent. Referred to as MEFV, the gene responsible for FMF is located on chromosome 16p13.3. Its product is called pyrin, a protein including 781 amino acids (7,8). Research shows that pyrin plays a vital role in the innate immune response (9,10). Although FMF involves many organs, it rarely affects the central nervous system (3,8,11-13). From a neurological point of view, headache is the most common symptom. The majority of neurological manifestations in FMF can be attributed to the disease itself. However, neurological involvements in FMF can also arise from amyloidosis, which is the most significant and potentially fatal complication of the disorder, or as an adverse effect of treatment (4, 14).A recent review explores the relationship between increased intracranial pressure and nephrotic syndrome (NS). The researchers highlight the notable occurrence of cerebral venous thrombosis in a majority of patients presenting with both conditions. They also report hyperaldosterinism as a possible etiological factor. A nephrotic syndrome due to amyloidosis is known to develop during the course of FMF. However, as mentioned in the review, the available data and evidence are currently insufficient to establish NS as a definitive secondary cause of PTC (15). In the case of our patient, cerebral venous thrombosis was ruled out as a normal MR venography did not reveal any abnormalities. The patient was admitted to our clinic exhibiting classic symptoms and signs of PTC, including headache, blurred vision, pulsatile tinnitus, visual loss, and disc edema. We performed investigations for differential diagnosis but did not identify any pathological conditions that could account for the observed increase in intracranial pressure. He had a CSF pressure of 270 mm H_2O. Based on the presented clinical criteria, we diagnosed him with PTC.

Currently there is no consensus regarding the underlying pathophysiology of PTC associated with FMF. Etiological factors considered in relation to PTC associated with FMF include increased cerebrospinal fluid (CSF) production, venous outflow obstruction, defective CSF resorption, parenchymal edema, and expanded cerebral blood volume. As pointed out in a recent review (15) and observed in our case, it is possible that nephrotic syndrome, which can occur in individuals with FMF, might have contributed to the development of PTC. The classical treatment guidelines for pseudotumor cerebri (PTC) typically involve weight loss strategies, along with medical interventions, such as acetazolamide intake. Additionally, topiramate can be used as monotherapy or as an add-on therapy for managing the condition. Surgery (optic nerve sheath fenestration, venous sinus stenting, ventriculoperitoneal and lumboperitoneal shunt, etc.) is an option for patients unresponsive to medical treatment or with fulminant course.

4. CONCLUSION

PTC is a rare neurological manifestation of FMF. Given the potential for irreversible permanent visual loss and significant disability associated with PTC, early diagnosis and regular multidisciplinary follow-up are of utmost importance. We believe that our case will emphasize the need to consider FMF as a possible underlying condition in patients presenting with PTC, thereby expanding the list of secondary causes associated with PTC.

Acknowledgement: *None*
Funding: *None*
Conflicts of interest: *None*
Ethics Committee Approval: *Consent form included*
Peer-review: *Externally peer-reviewed.*
Author Contributions:
Research idea: DY
Design of the study: EY
Acquisition of data for the study: EY, RS
Analysis of data for the study: EY, RS, FE
Interpretation of data for the study: DY, EY, RS, FE
Drafting the manuscript: DY, EY
Revising it critically for important intellectual content: DY
Final approval of the version to be published: DY, EY, RS, FE

REFERENCES

[1] Rangwala LM, Liu GT. Pediatric idiopathic intracranial hypertension. Surv Ophthalmol. 2007; 52(6):597-617. DOI: 10.1016/j.survophthal.2007.08.018

[2] Friedman DI, Liu G, Digre KB. Revised diagnostic criteria for the pseudotumor cerebri syndrome. Neurology 2013; 81(13):1159-1165. DOI: 10.1212/WNL.0b013e3182a55f17

[3] Kalyoncu U, Eker A, Oguz KK, Kurne A, Kalan I, Topcuoglu AM, et al. Familial Mediterranean fever and central nervous system involvement: A case series. Medicine (Baltimore) 2010; 89(2):75-84. DOI: 10.1097/MD.0b013e3181d5dca7.

[4] Feld O, Yahalom G, Livneh A. Neurologic and other systemic manifestations in FMF: Published and own experience. Best Pract Res Clin Rheumatol 2012; 26(1):119-133. DOI: 10.1016/j.berh.2012.01.004.

[5] Gökalp HZ, Başkaya MK, Aydin V. Pseudotumor cerebri with familial Mediterranean fever. Clin Neurol Neurosurg 1992; 94(3):261-263. DOI: 10.1016/0303-8467(92)90101-8.

[6] Kumar S. Bilateral disc edema in familial Mediterranean fever. J Clin Diagn Res 2007; 1(6): 521-524.

[7] French FMF Consortium. A candidate gene for familial Mediterranean fever. Nat Genet 1997; 17(1): 25-31. DOI: 10.1038/ng0997-25.

[8] Akman-Demir G, Gül A, Gürol E, Özdoğan H, Bahar S, Öge AE, vd. Ailesel Akdeniz ateşinde (FMF) inflamatuar / demiyelinizan santral sinir sistemi tutulumu: tesadüf mü yoksa birliktelik mi? J. Neurol 2006; 253: 928-934.

[9] Manukyan G, Aminov R. Update on pyrin functions and mechanisms of familial Mediterranean fever. Front Microbiol. 2016; 7(34): 456. DOI: 10.3389/fmicb.2016.00456.

[10] Kiyoshi Migita, Tomoyuki Asano, Shuzo Sato, Tomohiro Koga, Yuya Fujita & Atsushi Kawakami. Familial Mediterranean fever: overview of pathogenesis, clinical features and management. Immunological Medicine 2018; 41(2):55–61. DOI: 10.1080/13497.413.2018.1481579.

[11] Zamir S. Ailesel Akdeniz ateşinde nörolojik bulgular. Pediatr Neurol 1993; 9: 301-302. DOI: 10.5152/jarem.2015.642.

[12] Yılmaz U, Gülez N, Çubukçu D, Güzel Ö, Akıncı G, Öztürk A. Ailesel Akdeniz ateşi olan bir çocukta tekrarlayan periferik yüz felci. Pediatr Neurol 2013; 49: 289-291. DOI: 10.12956/tjpd.2013.24

[13] Ertekin V, Selimoğlu MA, Pirim I. Doğu Anadolu'da bir çocukluk çağında ailevi Akdeniz ateşi. Pediatr Int 2005; 47: 640.

[14] İncecik F, Herguner OM, Besen S, Aynaci E, Yılmaz M, Altunbaşak S. Pseudotumor cerebri in a child with Mediterranean fever. Arch Rheumatol 2015; 30(3): 256-258. DOI:10.5606/ArchRheumatol.2015.5606

[15] Piccini CD, Morillos MB, Formoso CR, Rodrigues MAC, Londero RG. Increased cerebrospinal fluid pressure and nephrotic syndrome: A case report and literature review. Clin Neurol Neurosurg 2023; 225(1):1-6. DOI: 10.1016/j.clineuro.2022.107567

How to cite this article: Yalçın D, Yılmaz E, Sürmeli R, Evliyaoğlu F. Pseudotumor Cerebri with Familial Mediterranean Fever in an Adult Patient. Clin Exp Health Sci 2024; 14: 585-587. DOI: 10.33808/clinexphealthsci.1252588