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Original Article

Clinical Course, Management, and the Role of MEFV Mutations in PFAPA Syndrome: A Single-center Experience

PFAPA Sendromunda Klinik Seyir, Yönetim ve MEFV Mutasyonlarının Rolü: Tek Merkez Deneyimi

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ABSTRACT

Objective: Periodic fever, aphthous stomatitis, pharyngitis, and cervical adenitis (PFAPA) syndrome is a periodic fever syndrome that onsets in early childhood. The precise roles of medical treatments in symptom control have not yet been clarified. This study aimed to evaluate the clinical characteristics, treatment responses, and genetic findings of children diagnosed with PFAPA.

Method: Patients who were followed with a diagnosis of PFAPA between January 2021 and January 2025 were included in the study. Demographic data, clinical and laboratory findings, results of genetic analyses, and responses to corticosteroids, colchicine, and tonsillectomy were retrospectively evaluated.

Results: A total of 22 patients with a mean age of 77.6 months (male cases: 50%) were included in the study. The median duration of attacks was 4 days [interquartile range (IQR): 3-6], and the median interval between attacks was 30 days (IQR: 25-41.3). Mediterranean fever (MEFV) gene mutations were detected in 36.4% (n=8) of the patients. All patients benefited from corticosteroid therapy during attacks; however, an increase in attack frequency was observed in 45.5% of cases. A decrease in attack frequency was observed in 57.1% (4/7) of the patients using colchicine. Tonsillectomy was performed in 63.6% (n=14) of the patients, and no postoperative complications were observed, while complete recovery was achieved in all cases.

Conclusion: Our findings demonstrate that tonsillectomy is an effective treatment method for controlling febrile attacks in PFAPA.

Keywords: Colchicine, MEFV, PFAPA, tonsillectomy

ÖZ

Amaç: Periyodik ateş, aftöz stomatit, farenjit ve servikal adenit (PFAPA) sendromu, erken çocukluk döneminde başlayan bir periyodik ateş sendromudur. Semptom kontrolünde medikal tedavilerin kesin rolleri henüz net olarak aydınlatılamamıştır. Bu çalışmada, PFAPA tanısı alan çocukların klinik özelliklerinin, tedavi yanıtlarının ve genetik bulgularının değerlendirilmesi amaçlanmıştır.

Yöntem: Ocak 2021 ile Ocak 2025 tarihleri arasında PFAPA tanısıyla takip edilen hastalar çalışmaya dahil edildi. Demografik veriler, klinik ve laboratuvar bulguları, genetik analiz sonuçları ve kortikosteroid, kolşisin ve tonsillektomiye verilen yanıtlar retrospektif olarak değerlendirildi.

Bulgular: Ortalama yaşı 77,6 ay olan toplam 22 hasta (%50 erkek) çalışmaya dahil edildi. Medyan atak süresi 4 gün [çeyrekler arası aralık (IQR): 3-6], ataklar arasındaki medyan süre ise 30 gün (IQR: 25-41,3) idi. Hastaların %36,4'ünde (n=8) MEFV mutasyonları saptandı. Tüm hastalar ataklar sırasında kortikosteroid tedavisinden fayda gördü; ancak olguların %45,5'inde atak sıklığında artış gözlendi. Kolşisin kullanan hastaların ise %57,1'inde (4/7) atak sıklığında azalma görüldü. Hastaların %63,6'sına (n=14) tonsillektomi uygulandı ve postoperatif komplikasyon gözlenmezken tüm olgularda tam iyileşme sağlandı.

Sonuç: Bulgularımız, tonsillektominin PFAPA'da ateşli atakların kontrol altına alınmasında etkili bir tedavi yöntemi olduğunu göstermektedir.

Anahtar kelimeler: Kolşisin, MEFV, PFAPA, tonsillektomi

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INTRODUCTION

Periodic fever, aphthous stomatitis, pharyngitis, and cervical adenitis (PFAPA) syndrome was first described by Marshall et al.[1] in 1987. The most characteristic feature of this syndrome is the regular periodicity of febrile episodes[2]. These febrile attacks usually last 3-6 days and recur at remarkably regular intervals of 3-8 weeks[3].

PFAPA symptoms most often become manifest before the age of 5 years, and the annual incidence in children under 5 years has been reported as 2.3-2.6 per 10,000[4]. Although the pathogenesis of the syndrome has not been fully elucidated, the involvement of palatine tonsils is thought to play a central role[3].

The main goal in the management of PFAPA is to control acute febrile episodes, prevent recurrences, or at least reduce the severity and frequency of attacks[5]. Non-steroidal anti-inflammatory drugs and corticosteroids are the main symptomatic pharmaceutical treatment options, while colchicine and cimetidine are the principal prophylactic medical alternatives[2,5]. However, the precise role of these treatments in symptom control remains uncertain and further research is needed.

The beneficial effect of tonsillectomy on the clinical course of PFAPA was first demonstrated by Abramson et al.[6]. During the following years, several studies reported varying complete clinical remission rates after tonsillectomy[5]. In a long-term follow-up study, Lantto et al.[7] reported that tonsillectomy resulted in complete resolution of febrile episodes in most children with PFAPA. Moberg et al.[3] noted that although tonsillectomy had relieved febrile episodes in the majority of children, some patients continued to experience febrile attacks or other PFAPA-related symptoms.

In this retrospective study, we have aimed to evaluate the clinical characteristics, treatment approaches, and genetic features of children diagnosed with PFAPA who were followed at a tertiary pediatric hospital in Türkiye. In addition, we sought to clarify the efficacy of tonsillectomy and the potential effects of Mediterranean fever (MEFV) gene mutations on the disease phenotype.

MATERIALS and METHODS

This retrospective, cross-sectional study was conducted at University of Health Sciences Türkiye, Dr. Behçet Uz Pediatric Diseases and Surgery Training and Research Hospital. All consecutive patients younger than 18 years of age who were diagnosed with PFAPA syndrome and followed in our clinic between January 2021 and January 2025 were screened in terms of eligibility criteria for inclusion in the study. The diagnosis of PFAPA was based on the modified Marshall criteria proposed by Thomas et al.[8]. Patients were included if they fulfilled these diagnostic criteria and had attained regular follow-up visits in our clinic. Patients with incomplete medical records or with an alternative diagnosis that could explain recurrent febrile episodes (such as infectious, autoimmune, or other autoinflammatory diseases) were excluded. The inclusion of consecutive patients during the study period was intended to reduce potential selection bias.

Ethical approval was obtained from the Local Ethics Committee of University of Health Sciences Türkiye, Dr. Behçet Uz Pediatric Diseases and Surgery Training and Research Hospital (decision no: 2025/10-04, date: 29.05.2025). Written informed consent was obtained from the parents of all patients. Data collected from medical records included the demographic characteristics, age at symptom onset, and at the time of diagnosis of PFAPA was made, comorbidities, clinical features during attacks, duration of attacks, and attack intervals. Remarkable laboratory findings detected during attacks [white blood cell (WBC) count, C-reactive protein (CRP), erythrocyte sedimentation rate (ESR)] were also recorded.

Treatment-related data were collected, concerning the use of corticosteroids during attacks, prophylactic colchicine therapy, and surgical interventions (tonsillectomy with or without adenoidectomy) performed. In addition, the type of tonsillectomy, age at surgery, time interval between diagnosis and surgery, duration of postoperative follow-up, complications, and outcomes were documented. Parental satisfaction with treatment outcomes was also noted.

Results of *MEFV* gene analysis were recorded for patients who underwent testing. According to the results, patients were divided into heterozygous mutation-positive and mutation-negative groups. Clinical findings, laboratory parameters, treatment responses, and surgical outcomes were compared according to genetic mutation status.

Statistical Analysis

Statistical analyses were performed using SPSS version 25.0 software program (IBM Corp., Armonk, NY, USA). Continuous variables were presented as mean ± standard deviation or median values and interquartile range (IQR), depending on their distribution patterns. Categorical variables were expressed as numbers and percentages. Comparisons of categorical variables were performed

using the chi-square test, while non-normally distributed continuous variables were compared using the Mann-Whitney U test. A two-sided p-value<0.05 was considered statistically significant.

RESULTS

A total of 22 cases comprising 11 (50.0%) female and 11 (50.0%). Male patients diagnosed with PFAPA syndrome were included in the study. The mean age of the patients at the time of evaluation was 77.6±27.4 months. The median age at symptom onset was 21.0 months (IQR: 13.5-36.0), while the mean age at diagnosis was 46.8±22.0 months. A comorbid condition was observed in only one patient (4.5%), who had chronic urticaria. Heterozygous MEFV gene mutations were identified in 8 (36.4%) patients. The distribution of mutations was as follows: M694V in 3 (13.6%), E148Q in 3 (13.6%), R202Q in 1 (4.5%), and V726A in 1 (4.5%) patient, respectively. The demographic and clinical characteristics of the patients are summarized in Table 1.

During attacks, all patients presented with fever. The most frequent accompanying findings were tonsillar exudate in 20 (90.9%), pharyngitis in 15 (68.2%), oral aphthae in 8 (36.4%), and cervical lymphadenopathy in 17 (77.3%) patients. Abdominal pain was reported for 5 (22.7%) and arthralgia for 3 (13.6%) patients, while none of them experienced arthritis or headache. The median duration of attacks was 4 days (IQR: 3-6), and the median interval between attacks was 30.0 days (IQR: 25.0-41.3). Laboratory investigations performed during attacks revealed a mean WBC count of 8461.4±2924.9/mm^3, a mean CRP level of 58.0±26.5 mg/L, and a median ESR of 22.5 mm/h (IQR: 13.8-34.0).

All patients received corticosteroid treatment during attacks, and improvement in clinical findings was observed in all cases. However, despite this acute response, 10 (45.5%) patients experienced an increased frequency of subsequent attacks after corticosteroid treatment, which led to repeated corticosteroid use during recurrent attacks. Colchicine was used by 7 (31.8%) patients of whom 4 (57.1%) showed a reduction in attack frequency. None of the patients experienced colchicine-related adverse effects. Tonsillectomy was performed in 14 (63.6%) patients with a median age of 51.5 months (IQR: 46.5-60.8) at surgery and a median interval between diagnosis and surgery was 4.0 months (IQR: 2.0-8.5). Among these, 13 (92.9%) patients underwent total tonsillectomy, while 1 (7.1%) had partial tonsillectomy. Concurrent adenoidectomy was performed in 6 (42.9%) patients. No postoperative complications were observed, and all patients achieved complete recovery following tonsillectomy. An overview of the therapeutic interventions and clinical responses of the patients is provided in Table 2.

The clinical and genetic characteristics of the patients undergoing tonsillectomy are detailed in Table 3. Among these 14 patients, MEFV gene mutations were identified in 5 cases, including heterozygous M694V (n=2), R202Q (n=1), V726A (n=1), and E148Q (n=1) mutations. Regardless of age at tonsillectomy, gender, type of tonsillectomy, concurrent adenoidectomy, or *MEFV* status, complete recovery was achieved in all patients following surgery. During the postoperative follow-up period, which ranged from 6 to 40 months, none of the patients required corticosteroid therapy, and no attacks were observed within the last 6 months. Moreover, all parents reported a reduction in school or daycare

Table 1. Demographic and clinical characteristics of the patients

Characteristics	
Gender, female, n (%)	11 (50.0)
Age (months), mean ± SD	77.6±27.4
Age at symptom onset (months), median (IQR)	21.0 (13.5-36.0)
Age at diagnosis (months), mean ± SD	46.8±22.0
Clinical findings, and symptoms detected during attacks, n (%)	
Febrile episodes	22 (100.0)
Tonsillar exudate	20 (90.9)
Cervical lymphadenopathy	17 (77.3)
Pharyngitis	15 (68.2)
Oral aphthae	8 (36.4)
Abdominal pain	5 (22.7)
Arthralgia	3 (13.6)
Arthritis	0 (0.0)
Headache	0 (0.0)
Duration of attacks (days), median (IQR)	4 (3-6)
Intervals between attacks (days), median (IQR)	30.0 (25.0-41.3)
Abnormal laboratory findings noted during attacks	
WBC (/mm^3), mean ± SD	8461.4±2924.9
CRP (mg/L), mean ± SD	58.0±26.5
ESR (mm/h), median (IQR)	22.5 (13.8-34.0)
Comorbidities, n (%)	1 (4.5)
Heterozygous MEFV gene mutation, n (%)	8 (36.4)

CRP: C-reactive protein, ESR: Erythrocyte sedimentation rate, IQR: Interquartile range, MEFV: Mediterranean fever, SD: Standard deviation, WBC: White blood cell

Table 2. Treatment modalities and responses of the patients	
	n (%)
Corticosteroid therapy	22 (100.0)
Response to corticosteroid therapy	22 (100.0)
Increased attack frequency after corticosteroid use	10 (45.5)
Colchicine use	7 (31.8)
Response to colchicine	4 (57.1)
Adverse effects of colchicine	0 (0.0)
Tonsillectomy performed	14 (63.6)
Age at tonsillectomy (months), median (IQR)	51.5 (46.5-60.8)
Interval between diagnosis and surgery (months), median (IQR)	4.0 (2.0-8.5)
Type of tonsillectomy	
Partial tonsillectomy	1 (7.1)
Total tonsillectomy	13 (92.9)
Concurrent adenoidectomy	6 (42.9)
Postoperative complication	0 (0.0)
Outcome after tonsillectomy	
Complete recovery	14 (100.0)
IQR: Interquartile range	

absenteeism and expressed overall satisfaction with the surgical outcomes.

A total of 16 patients underwent *MEFV* gene analysis, of whom 8 had heterozygous mutations and 8 were mutation-negative. The age at symptom onset did not differ significantly between the heterozygous mutation-positive (22 months, IQR: 18-42) and mutation-negative (21 months, IQR: 12-39.8) groups (p>0.05). Similarly, intervals between attacks were comparable (30 days, IQR: 22.5-37.8 vs. 30 days, IQR: 25-30; p>0.05). During attacks, WBC counts (9086.3±3354.7 vs. 7272.5±2060.8/mm^3; p>0.05) and ESR levels (23.5 mm/h, IQR: 22.0-34.0 vs. 21.5 mm/h, IQR: 13.8-33.0; p>0.05) were also comparable between the groups. However, CRP levels were significantly higher in the heterozygous mutation group (76.8±19.5 vs. 47.3±25.1 mg/L; p=0.020). Although an increase in attack frequency following corticosteroid use was observed in 62.5% of heterozygous-mutation and 37.5% of mutation-negative patients, this difference was not statistically significant (p>0.05). Response to colchicine was also comparable, with improvement observed in 50.0% of heterozygous-mutation and 66.7% of mutation-negative patients (p>0.05).

DISCUSSION

Our study has focused on evaluating the clinical, laboratory, and genetic characteristics, as well as the outcomes of therapeutic approaches in patients followed up at a pediatric diseases and surgery training and research hospital with the diagnosis of PFAPA syndrome. Heterozygous MEFV mutations were detected in 36.4% of patients, and this rate increased to 50% in the subgroup who underwent genetic testing. This finding suggests that genetic factors may play a role in the susceptibility to this disease, the pathogenesis of which has not yet been fully elucidated. Corticosteroids, commonly used in the management of PFAPA syndrome were found to increase attack frequency in 45.5% of cases. In addition, tonsillectomy was performed in 63.6% of patients, with no complications reported during follow-up, and complete resolution of febrile attacks was observed.

PFAPA is an autoinflammatory syndrome of unknown etiology, with symptoms typically become manifest during the early childhood[9]. In our study, the median age at symptom onset was 21 months, consistent with the literature data[3]. The attacks exhibit a periodicity that can be easily recognized by parents; however, no standardized treatment protocol exists for their management. Corticosteroids represent the main medical option for relieving symptoms during attacks and have been reported to be effective in 85-95% of the cases[2,5]. In our cohort, all patients received corticosteroid therapy during attacks and showed a clinical response. Although this dramatic response is considered an important finding supporting the diagnosis of PFAPA, corticosteroids do not prevent the emergence of new episodes[5,10]. Furthermore, in 45.5% of our study patients an increased frequency of flare-ups was observed following corticosteroid therapy.

Colchicine has been investigated as a potential prophylactic treatment option in PFAPA patients to reduce corticosteroid use and the frequency of febrile attacks[5]. In the literature, response rates to colchicine treatment have been reported to range between 45% and 95.1%[11]. In our study, a reduction in frequency of attacks was observed in 57.1% of patients receiving colchicine. The treatment was well tolerated, and no colchicine-related adverse effects were detected in our study. In contrast, Welzel et al.[12] reported adverse effects associated with colchicine therapy in PFAPA patients which had not necessitated discontinuation of therapy including mild to moderate gastrointestinal symptoms, asymptomatic mild elevations of transaminases, and leukopenia.

In the Turkish population, the prevalence of *MEFV* gene mutations is approximately 20%, whereas in our study,

Table 3. Clinical and genetic characteristics of patients undergoing tonsillectomy

Patient no.	Gender	MEFV genetic test results	Age at tonsillectomy (months)	Type of tonsillectomy	Concurrent adenoidectomy	Postoperative complications	Outcome after tonsillectomy	Follow-up duration after tonsillectomy (months)	Number of attacks after tonsillectomy (previous 6 months)
1	M	Negative	50	Partial	Yes	None	Complete recovery	12	0
2	F	Heterozygous M694V	89	Total	No	None	Complete recovery	12	0
3	F	Negative	56	Total	Yes	None	Complete recovery	24	0
4	F	Heterozygous M694V	60	Total	No	None	Complete recovery	12	0
5	F	Negative	63	Total	Yes	None	Complete recovery	12	0
6	F	Not analyzed	40	Total	No	None	Complete recovery	6	0
7	F	Negative	53	Total	Yes	None	Complete recovery	6	0
8	F	Heterozygous R202Q	49	Total	Yes	None	Complete recovery	12	0
9	M	Heterozygous V726A	97	Total	No	None	Complete recovery	6	0
10	M	Not analyzed	53	Total	No	None	Complete recovery	6	0
11	F	Not analyzed	40	Total	No	None	Complete recovery	9	0
12	M	Heterozygous E148Q	42	Total	Yes	None	Complete recovery	26	0
13	M	Not analyzed	48	Total	No	None	Complete recovery	40	0
14	F	Not analyzed	50	Total	No	None	Complete recovery	24	0

F: Female, M: Male, MEFV: Mediterranean fever

its prevalence rate (50%) among PFAPA patients who underwent genetic testing was markedly higher than observed in the general population[13]. The impact of MEFV mutations on the disease phenotype in PFAPA, particularly with regard to treatment response, has been investigated[11]. Pehlivan et al.[14] reported that PFAPA patients carrying MEFV mutations exhibited a better response to colchicine, whereas Otar Yener et al.[15] found no significant association between MEFV mutation status and treatment response. Özaslan et al.[11] suggested that M694V carriage was the only predictor of colchicine responsiveness. In our study, patients with MEFV mutations did not differ in terms of age at disease onset or attack frequency. CRP levels during attacks were significantly higher in patients with MEFV mutations; however, this finding did not translate into a distinct disease phenotype. Although an increase in attack frequency following corticosteroid use was observed more frequently in patients with heterozygous MEFV mutations relative to those without, but the difference in incidence rates was not statistically significant. Similarly, no differences were found between groups in terms of response to colchicine therapy.

Although PFAPA is considered a self-limiting disease, it has a substantial negative impact on the health status of both children and their caregivers[5]. Rydenman et al.[4] demonstrated that health-related quality of life deteriorates during febrile episodes and that this effect persists even during afebrile periods. In our study, the median interval between PFAPA diagnosis and tonsillectomy was 4 months, reflecting parents' desire to achieve a curative treatment as soon as

possible despite its potential surgical risks. A Cochrane review published in 2019 reported that children may benefit from tonsillectomy; however, only moderate level of evidence has favoured surgical intervention[9].

To date, only two randomized controlled trials have evaluated the efficacy of tonsillectomy in PFAPA[9]. In the first study, complete resolution of postoperative febrile attacks was reported in 63% of patients (12/19), while in the second study, all 14 patients (100%) had achieved remission[16,17]. In other series, rates of complete clinical remission have been reported to range between 74% and 97%[3,14,18-20]. In our study, tonsillectomy alone was performed in 8 patients, while 6 patients underwent concurrent adenoidectomy. Regardless of the type of tonsillectomy, and concurrent adenoidectomy performed, or *MEFV* mutation status, complete recovery was achieved in all patients following surgery.

Study Limitations

The main limitations of our study are its retrospective design and its single-center design. In addition, MEFV genetic mutation analysis was not performed in all patients. The relatively rare occurrence of PFAPA limited the sample size, thereby restricting the generalizability of the findings, particularly with regard to surgical complications.

CONCLUSION

In conclusion, this study demonstrates that tonsillectomy per se or in combination with adenoidectomy, is an effective treatment for controlling febrile attacks in children with PFAPA. Nevertheless, the potential risks of surgery should be carefully communicated to families. Furthermore, the detection of a high frequency of MEFV mutations among the analyzed patients strengthens our view that advances in genetics may contribute to elucidating the pathogenesis of this syndrome.

Ethics

Ethics Committee Approval: Ethical approval was obtained from the Local Ethics Committee of University of Health Sciences Türkiye, Dr. Behçet Uz Pediatric Diseases and Surgery Training and Research Hospital (decision no: 2025/10-04, date: 29.05.2025).

Informed Consent: Written informed consent was obtained from the parents of all patients.

Declaration of AI Use: AI tools were used for language correction only.

Footnotes

Author Contributions

Concept: Ç.Ö., Design: Ç.Ö., Data Collection or Processing: Ç.Ö., Ö.A.G., Analysis or Interpretation: Ç.Ö., Ö.A.G., Literature Search: Ç.Ö., Writing: Ç.Ö., Ö.A.G.

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REFERENCES

1. Marshall GS, Edwards KM, Butler J, Lawton AR. Syndrome of periodic fever, pharyngitis, and aphthous stomatitis. J Pediatr. 1987;110(1):43-6. doi: 10.1016/s0022-3476(87)80285-8.
2. Wang A, Manthiram K, Dedeoglu F, Licameli GR. Periodic fever, aphthous stomatitis, pharyngitis, and adenitis (PFAPA) syndrome: a review. World J Otorhinolaryngol Head Neck Surg. 2021;7(3):166-73. doi: 10.1016/j.wjorl.2021.05.004.
3. Moberg T, Rydenman K, Berg S, Fasth A, Wekell P. Long-term symptoms in periodic fever, aphthous stomatitis, pharyngitis, and cervical adenitis syndrome after tonsillectomy. J Pediatr. 2025;278:114424. doi: 10.1016/j.jpeds.2024.114424.
4. Rydenman K, Sparud-Lundin C, Karlsson-Bengtsson A, Berg S, Fasth A, Wekell P. Tonsillectomy reduces the family impact of periodic fever, aphthous stomatitis, pharyngitis and cervical adenitis (PFAPA) syndrome and improves health-related quality of life in affected children. Orphanet J Rare Dis. 2023;18(1):153. doi: 10.1186/s13023-023-02773-8.
5. Anselmi F, Dusser P, Kone-Paut I. Periodic fever, aphthous stomatitis, pharyngitis, and cervical adenitis (PFAPA) syndrome in children-from pathogenesis to treatment strategies: a comprehensive review. Paediatr Drugs. 2025;27(5):575-92. doi: 10.1007/s40272-025-00699-1.
6. Abramson JS, Givner LB, Thompson JN. Possible role of tonsillectomy and adenoidectomy in children with recurrent fever and tonsillopharyngitis. Pediatr Infect Dis J. 1989;8(2):119-20.
7. Lantto U, Koivunen P, Tapiainen T, Renko M. Long-term outcome of classic and incomplete PFAPA (periodic fever, aphthous stomatitis, pharyngitis, and adenitis) syndrome after tonsillectomy. J Pediatr. 2016;179:172-7.e1. doi: 10.1016/j.jpeds.2016.08.097.
8. Thomas KT, Feder HM Jr, Lawton AR, Edwards KM. Periodic fever syndrome in children. J Pediatr. 1999;135(1):15-21. doi: 10.1016/s0022-3476(99)70321-5.
9. Burton MJ, Pollard AJ, Ramsden JD, Chong LY, Venekamp RP. Tonsillectomy for periodic fever, aphthous stomatitis, pharyngitis and cervical adenitis syndrome (PFAPA). Cochrane Database Syst Rev. 2019;30;12(12):CD008669. doi: 10.1002/14651858.CD008669.pub3.
10. Batu ED. Periodic fever, aphthous stomatitis, pharyngitis, and cervical adenitis (PFAPA) syndrome: main features and an algorithm for clinical practice. Rheumatol Int. 2019;39(6):957-70. doi: 10.1007/s00296-019-04257-0.
11. Özaslan Z, Şen A, Uçar SA, Çakan M, Sanisoğlu B, Kaya F, et al. Exploring factors for predicting colchicine responsiveness in

children with PFAPA. Eur J Pediatr. 2024;183(10):4337-43. doi: 10.1007/s00431-024-05703-3.

12. Welzel T, Ellinghaus M, Wildermuth AL, Deschner N, Benseler SM, Kuemmerle-Deschner JB. Colchicine effectiveness and safety in periodic fever, aphthous stomatitis, pharyngitis, and adenitis. Front Pediatr. 2021;9:759664. doi: 10.3389/fped.2021.759664.
13. Celiksoy MH, Ogur G, Yaman E, Abur U, Fazla S, Sancak R, et al. Could familial Mediterranean fever gene mutations be related to PFAPA syndrome? Pediatr Allergy Immunol. 2016;27(1):78-82. doi: 10.1111/pai.12490.
14. Pehlivan E, Adrovic A, Sahin S, Barut K, Kul Cınar O, Kasapcopur O. PFAPA syndrome in a population with endemic familial Mediterranean fever. J Pediatr. 2018;192:253-5. doi: 10.1016/j.jpeds.2017.08.078.
15. Otar Yener G, Aktaş İ, Altıntaş Meşe C, Çakan M. Does having MEFV gene sequence variants affect the clinical course and colchicine response in children with PFAPA syndrome? Eur J Pediatr. 2023;182(1):411-7. doi: 10.1007/s00431-022-04709-z.
16. Renko M, Salo E, Putto-Laurila A, Saxen H, Mattila PS, Luotonen J, et al. A randomized, controlled trial of tonsillectomy in periodic fever, aphthous stomatitis, pharyngitis, and adenitis syndrome. J Pediatr. 2007;151(3):289-92. doi: 10.1016/j.jpeds.2007.03.015.
17. Garavello W, Romagnoli M, Gaini RM. Effectiveness of adenotonsillectomy in PFAPA syndrome: a randomized study. J Pediatr. 2009;155(2):250-3. doi: 10.1016/j.jpeds.2009.02.038.
18. Licameli G, Lawton M, Kenna M, Dedeoglu F. Long-term surgical outcomes of adenotonsillectomy for PFAPA syndrome. Arch Otolaryngol Head Neck Surg. 2012;138(10):902-6. doi: 10.1001/2013.jamaoto.313.
19. Lantto U, Tapiainen T, Pokka T, Koivunen P, Helminen M, Piitulainen J, et al. Tonsillotomy for periodic fever syndrome: a randomized and controlled trial. Laryngoscope. 2024;134(2):968-72. doi: 10.1002/lary.30863.
20. Gozen ED, Yildiz M, Kara S, Tevetoglu F, Haslak F, Adrovic A, et al. Long-term efficacy of tonsillectomy/adenotonsillectomy in patients with periodic fever aphthous stomatitis pharyngitis adenitis syndrome with special emphasis on co-existence of familial Mediterranean fever. Rheumatol Int. 2023;43(1):137-45. doi: 10.1007/s00296-022-05210-4.