Pediatric Rheumatology

REVIEW

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Protracted febrile myalgia syndrome in children with familial Mediterranean fever – systematic review and a case report

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Abstract

Introduction Protracted febrile myalgia syndrome (PFMS) is a rare manifestation of familial Mediterranean fever (FMF), characterized by myalgia, fever and elevated inflammatory markers lasting several weeks. As the hallmark of FMF are short episodes of disease symptoms, the long duration of PFMS may lead to a delayed diagnosis and treatment.

Objectives 1. To perform a review of literature and rheumatology textbooks focused on clinical features and treatment of PFMS in children. 2. To present our own case.

Methods All articles in Pub Med generated using the keywords "protracted febrile myalgia" and information on PFMS in seven rheumatology textbooks were collected. The systematic review was supplemented with our own case presentation.

Results In total, 18 articles with 78 pediatric patients (including our own) were retrieved. More than half of the patients presented with PFMS as the first manifestation of FMF. All complained of myalgia, 65% of abdominal pain and 26% had a rash. Corticosteroids (CS) were effective in 77%. In all CS-refractory cases, anakinra was shown efficient. MRI was used in 5 patients and showed myositis in all of them.

The scrutiny of seven rheumatology textbooks showed that PFMS presenting with myalgia was mentioned in six. Possible accompanying symptoms were described only once, the long duration of symptoms twice, the efficacy of corticosteroids three times and anakinra only once.

The presented 6 year old patient manifested with fever, myalgia, abdominal pain and petechial rash lasting 6 weeks. She had undergone multiple diagnostic procedures before her parents mentioned a positive family history for FMF. The subsequent genetic testing confirmed a homozygosity for M694V pathogenic variant in the MEFV gene.

Conclusion The long duration of PFMS may be misleading to clinicians especially if PFMS occurs at manifestation of FMF. The fact that more than half of the reported patients experienced PFMS as the presenting symptom of FMF is one of the key findings of our study. Our case presentation demonstrates the importance of genetic testing early in suspected autoinflammatory diseases. Furthermore, MRI may be an important diagnostic tool showing myositis in PFMS.

Keywords Protracted febrile myalgia syndrome, Clinical features, Treatment, Diagnostic role of MRI

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Introduction

Protracted febrile myalgia syndrome (PFMS) was first described by Langevitz [17] as part of the clinical spectrum of familial Mediterranean fever (FMF). It is a rare manifestation of FMF, affecting about 1% of patients with FMF [8]. The clinical symptoms are severe, with disabling muscle pain, fever, abdominal pain, diarrhea lasting up to several weeks, often accompanied by a rash mimicking IgA vasculitis. Inflammatory parameters are elevated [15, 19, 27]. As the typical duration of FMF symptoms does not exceed 72 h, the long duration of PFMS may be misleading to clinicians. They tend to focus on alternative diagnoses such as polyarteritis nodosa, inflammatory bowel disease, IgA vasculitis, infections etc. Hence, the diagnosis may be delayed, especially in countries with low incidence of FMF where the clinicians are not acquainted with the whole spectrum of its clinical manifestations. Thus, patients presenting with PFMS as the primary manifestation of FMF [1] may be exposed to unnecessary diagnostic procedures and to prolonged suffering without prompt adequate treatment.

While colchicine is neither sufficient in preventing nor treating these symptoms it has been shown that corticosteroids (CS) lead to a quick resolution of pain and fever [17, 24, 28]. In CS-refractory adult and paediatric patients Interleukin-1 blockade with anakinra was reported to be effective [5, 7, 9, 12, 16, 21, 30].

The aim of this study was to raise awareness of PFMS using a systematic review of literature with focus on clinical features and treatment of paediatric PFMS and our own experience with a patient whose diagnosis was delayed. Another aim was to scrutinize how standard textbooks of rheumatology deal with the topic of PFMS.

The discussion of rare disease manifestations in general might be of growing importance in times of global migration.

Methods

We searched PubMed using the keywords "protracted febrile myalgia". The Last search was March, 24st, 2024 (Fig. 1). Neither the Cochrane library nor Embase database contained any additional relevant articles.

A review of seven standard textbooks of rheumatology was performed including: Petty et al. Textbook of Pediatric Rheumatology, Elsevier, 8th ed 2021; Hochberg et al. Rheumatology, Elsevier, 7th ed, 2019; Martini et al. PRES Textbook on Paediatric Rheumatology, BMJ 2018; Bijlsma et al. EULAR Textbook on Rheumatic Diseases 3rd ed, BMJ 2018; Wagner et al. German Textbook on Pediatric Rheumatology (Pädiatrische Rheumatologie) 3rd ed Springer 2022; Hashkes et al. Textbook of Autoinflammation, Springer 2019; Ben-Chetrit et al. UpToDate. Updated Feb 01, 2024. Last access 25.3.24. Up to date was also considered to be a standard textbook of rheumatology as the specific chapters are written by renowned experts.

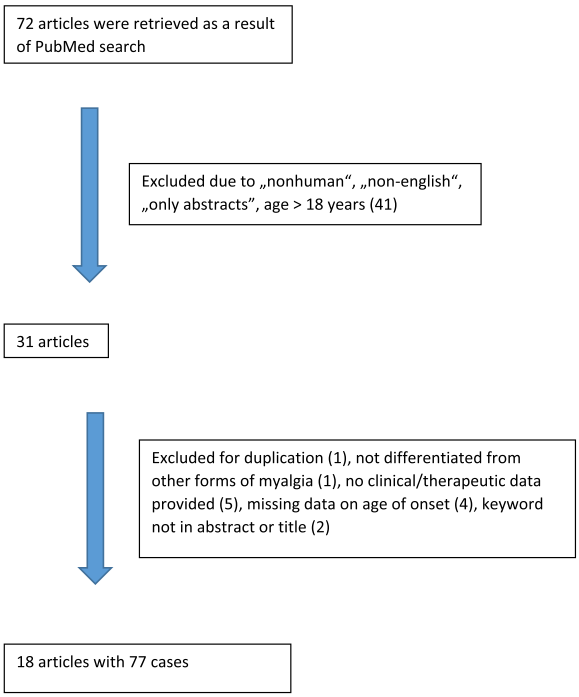

Fig. 1 Schematic overview of the included articles after search in PubMed

In addition, a free artificial intelligence system, Chat GPT (generative pre-trained transformer, artificial intelligence system), was tested on knowledge on PFMS using the keywords "fever" and "myalgia".

Finally, the clinical course and diagnostic procedures of the reported patient were retrospectively reviewed and are presented here. An informed consent was obtained from the parents.

Results

Systematic review of published pediatric cases

Our PubMed analysis revealed 18 articles published between 2000 and 2023 with a total of 78 paediatric patients (including our own report). The numbers of the reported cases in the series are low, ranging from 1 to 14. The authors´ background is mostly from areas with high incidence of FMF.

More than half of the patients (41/78, 54%) presented with PFMS as the first manifestation of FMF. Of note, 8 (10%) were afebrile. Myalgia was reported in 100% of the patients, abdominal pain in 65% and rash in 26%. CS were reported to be effective in 59 out of 77 patients (77%), in CS-refractory cases anakinra was successfully given in 5 out of 5 patients Table 1. Data on efficacy of

Table 1 Published case reports and series of pediatric patients with protracted febrile myalgia syndrome

Author	Year	Journal	Authors from	Number of patients	Primary manifestation	Afebrile course	Myalgia	Abdominal pain	Rash	Corticosteroids effective	Anakinra effecitve
Majeed et al	2000	Semin Arthritis Rheum	Jordan	7	3	0	7	4	1	3	-
Tekin et al	2000	Acta Paediatr	Turkey	9	0	0	9	6	8	8	-
Ertekin et al	2005	Rheum Int	Turkey	2	2	0	2	1	0	2	-
Soylu et al	2006	J Clin Rheumatol	Turkey	6	5	0	6	5	2	6	-
Bircan et al	2008	J Clin Rheumatol	Turkey	6	1	0	6	5	0	6	-
Soylu et al	2008	Semin Arthritis Rheum	Turkey	1	1	0	1	0	0	1	-
Duru et al	2010	Ped international	Turkey	2	0	0	2	1	1	2	-
Senel et al	2010	Mod Rheumatol	Turkey	1	0	0	1	0	1	1	-
Bircan et al	2010	Semin Arthritis Rheum	Turkey	1	0	0	1	0	1	0	-
Demir et al	2012	Pediatr diab	Turkey	1	0	1	1	1	0	1	-
Oguz et al	2016	Indian J Pediatr	Turkey	1	1	1	1	0	0	1	-
Rom et al	2017	Semin Arthritis Rheum	Israel	8	4	0	8	8	0	8	-
Yildirim et al	2019	Rheum Int	Turkey	5	1	0	5	5	3	2	2
Cakan et al	2020	North Clin Istanb	Turkey	1	1	0	1	1	0	0	1
Ling et al	2021	J Clin Rheumatol	Israel	1	0	1	1	0	0	1	-
Öztürk et al	2021	Rheum Int	Turkey	6	6	2	6	2	1	4	-
Aviran et al	2022	Orphanet J Rare Dis	Israel	5	5	0	5	2	0	2	-
Aydin	2023	Mod Rheumato	Turkey	14	11	3	14	9	1	11	2
Hospach (present case)	2024		Germany	1	1	0	1	1	1	-	-
Sum (%)				78	42 (54)	8 (10)	78 (100)	51 (65)	20 (26)	59/77 (77)	5/5 (100)

Abbreviation: *NSAID* nonsteroidal anti-inflammatory drugs

nonsteroidal anti-inflammatory drugs (NSAIDs) were mostly not given; in 5 patients they were reported to be effective whereas in 8 patients not (data not shown). Out of the 77 patients (excluding our own case), 5 were examined with MRI, all showing T2-signal enhancement in the muscles indicating myositis [2].

Table 2 Duration of fever and myalgias in published patients

Author	Year	Duration of fever in days (range)	Duration of myalgia in days (range)
Majeed et al	2000	35[a] (28–42)	35[a] (28–42)
Tekin et al	2000	n.a	n.a
Ertekin et al	2005	15	15
Soylu et al	2006	31,5[a] (21–42)	31,5[a] (21–42)
Bircan et al	2008	n.a	28
Soylu et al	2008	14	14
Duru et al	2010	14	14
Senel et al	2010	n.a	n.a
Bircan et al	2010	12	12
Demir et al	2012	0	1
Oguz et al	2016	0	10
Rom et al	2017	n.a	15,5 (1–45)
Yildirim et al	2019	n.a	17,5 (7-/21)
Cakan et al	2020	14	14
Ling et al	2021	n.a	n.a
Öztürk et al	2021	17[a] (12–28)	21 (12–28)
Aviran et al	2022	10[a] (10–42)	10 (10–42)
Aydin	2023	5[a] (5–28)	15 (5–28)
Hospach (present case)	2024	42	42
All cases		14[a] (3–42)	15[a] (1–45)

[a] median of published cohorts

The median duration of fever and myalgia was 14 and 15 days (range 3–42 and 1–45 days), respectively (Table 2).

Review of "Rheumatology" Textbooks

The review of seven standard textbooks of rheumatology showed that severe myalgia was mentioned in six, abdominal pain, diarrhoea and rash only in one. The possible extreme duration of symptoms over weeks was clearly described only in 2 books. Effective treatment with corticosteroids was addressed in three books, anakinra only in one [3, 4, 13, 14, 20, 23, 29] (see Table 3). A digital search using Chat GPT with the terms „fever and myalgia "generated inflammatory conditions including various autoimmune diseases and vasculitides but PFMS was not offered (online last search May 27th, 2024).

Case report

A 6 year old girl was referred from another hospital with fever up to 39 degrees Celsius lasting for three weeks. Her main complaints were disabling bilateral thigh pain so that no weight bearing was possible. Furthermore, she suffered from a very severe abdominal pain and a petechial rash was observed on the dorsal sides of her feet. The parents were consanguineous of Syrian origin and they initially denied any diseases of close family members.

Due to microhematuria and leukocyturia—with insignificant bacteriuria—the patient was treated with antibiotics. The patient was known to have had suffered from recurrent pyelonephritides due to vesicoureteral reflux (VUR). The VUR had already been operated two years prior the present illness. Before referral to our hospital, the patient had undergone a lumbar puncture with normal cerebrospinal fluid findings with no bacterial growth.

Table 3 Review of seven textbooks of rheumatology

	Frequency	Statement "severe disease"	Myalgia	Abdominal pain	Diarrhea	Rash	Duration	Corticosteroids effective	Anakinra effective
Petty et al. 8th ed 2021 [23]	Un-common	+	+	-	-	-	-	+	-
Hochberg et al. 7th ed 2019 [14]	rare	+	debilitating	-	-	-	-	-	-
Martini et al. 2018 [20]	-	-	-	-	-	-	-	-	-
Hash(Hashkes R 2019)kes et al. 2019 [13]	-	+	disabling	-	-	-	> 5 days	+	-
Bijlsma et al. 3rded 2018 [4]	rare	+	debilitating	-	-	-	Several weeks	-	+
Ben-Chetrit et al. Feb 01, 2024 [3]	-	-	bouts	-	-	-	Up to 8 weeks	+	-
Wagner et al. 3rd, ed 2022 [29]	-	-	paralysing	+	+	+	long	(+)	-

On admission, the physical examination revealed a tender abdomen, a splenomegaly and a mild petechial rash on the lower extremities. Her blood count showed a leucocytosis 25.000 (normal range: 4 500 – 13 000), 80% neutrophils, hemoglobin 8,7 g/dl (11.8 – 15), MCV 56 fl (69 – 93), MCH 17,3 pg (22—34); MCHC 20 g/dl (32 – 40) and a thrombocytosis 731 000/µl (150 000 – 410 000). The CRP was raised to 153 mg/l (< 5), the creatine kinase was normal. Proteinase 3 and myeloperoxidase antibodies were negative. The urinalysis showed again a mild microhematuria and leukocyturia with growth of Proteus mirabilis making a urinary tract infection probable (number of colonies not available).

The differential diagnosis included bacterial Infection (recurrent pyelonephritis, enteritis), intraabdominal abscess, inflammatory bowel disease (abdominal pain, fever), IgA vasculitis (petechiae, abdominal pain) and polyarteritis nodosa (fever, vasculitic rash, abdominal and muscular pain, hematuria). FMF was initially not considered due to the long fever duration.

Apart from the bacteriuria the microbiological workup was negative for bacteria. It revealed PCR positivity for enterovirus and adenovirus in stool, explaining neither the prolonged symptoms nor the very high inflammatory parameters. Due to microhematuria, leukocyturia and growth of Proteus mirabilis in urine culture, antibiotic treatment with Cefpodoxim was commenced without any effect. At disease onset, an abdominal MRI with contrast enhancement in the referring hospital had been unremarkable, but did not include T2 weighted images with fat suppression. We repeated the examination 3 weeks later, including STIR images. The MRI was initially interpreted as unremarkable. Subtle pathological hyperintense foci in the muscles of the abdominal wall as well as at the insertion sites of the gluteus muscles to the iliac bones were detected only retrospectively (Fig. 2). In a whole body MRI with STIR sequences 1 week later, these findings were no longer present.

As polyarteritis nodosa or other rare types of vasculitides were considered in the differential diagnoses, an MR angiography as well as a conventional angiography were performed showing no aneurysms of intraabdominal arteries. Furthermore, a gastroscopy and a colonoscopy excluded inflammatory bowel disease and a bone marrow aspiration excluded leukemia. The treatment with Ibuprofen did not lead to complete pain relief or fever resolution. After six weeks the fever spontaneously subsided and the pain terminated. A repeated thorough family history revealed that the parents 'cousins suffered from FMF. Hence, a targeted genetic analysis was indicated in our patient and it confirmed a homozygosity for the M694V pathogenic variant in the MEFV gene.

Discussion

PFMS is a rare but severe FMF manifestation requiring a quick diagnosis and commencement of adequate treatment in order to relieve pain and avoid unnecessary diagnostic and therapeutic procedures. The diagnostic challenge that PFMS may pose was illustrated by the presented case. Our report may help raise awareness of PFMS especially among clinicians from FMF low-incidence countries. In fact, this is the first report from this geographical region.

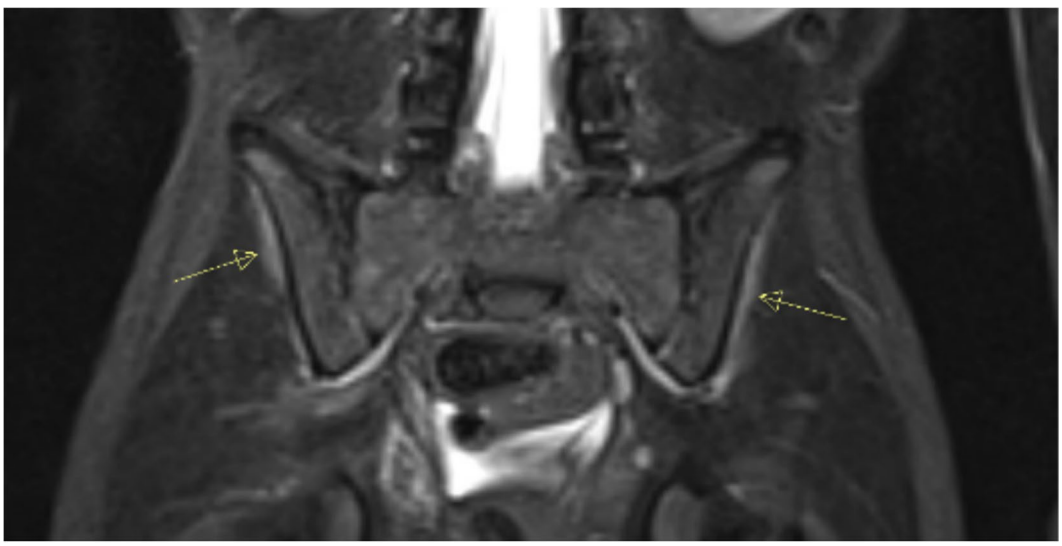

Fig. 2 MRI T2 STIR coronal showing signals bilaterally at the insertion sites of the mm glutei to the ossa ilii

Our review further illustrates the rarity of this disease entity as only 78 paediatric patients have been reported so far in case reports or small case series with a maximum number of 14 patients [1].

The most important finding of our review is the fact that more than half of the patients (42/78, 54%) presented with PFMS as the first manifestation of FMF. These patients are particularly challenging to clinicians who are mostly acquainted with the typical course of FMF characterized by short fever episodes of maximum 72 h. In contrast, in PFMS, symptoms may last from days to over six weeks as shown in Table 3. With the long duration and the plethora of symptoms like fever, myalgia, abdominal pain and vasculitic rash other systemic diseases such as polyarteritis nodosa (PAN) may more likely be considered [6]. This was also the case in our patient who underwent multiple MRI scans as well as an angiography and a gastrointestinal tract endoscopy with a biopsy.

Furthermore, the literature search revealed that while fever was absent in 10%, all patients complained of myalgias, 65% of abdominal pain and 26% had rashes (Table 1). This illustrates that the diagnosis of PFMS requires a high degree of awareness as it is based on a combination of clinical symptoms that overlap with other systemic diseases such as vasculitides, inflammatory bowel disease or infections. No single pathognomonic test for PFMS is available up to now—CK is usually normal, even muscle biopsies did not show any pathological findings [18]. The diagnostic criteria of PFMS proposed by Kaplan et al. include severe disabling myalgia of at least 5 days in a young patient with FMF, associated with fever, elevated levels of inflammatory markers and the presence of at least one M694V mutation [15]. Hence, the diagnosis of PFMS may be readily established in patients with a known, genetically confirmed FMF. On the other hand, patients, who present with PFMS as the first manifestation of FMF, remain challenging. Even if the diagnosis is considered, the required genetic confirmation may last from days to weeks depending on resources. Therefore, genetic testing should be performed as early as possible in all suspected cases. And availability of fast targeted genetic testing should be supported. A more extensive genetic testing based on genetic panels or whole exome sequencing (WES) might more likely be considered in similar patients, especially in cases where the clinical and laboratory constellation does not suggest a specific diagnosis. Nevertheless, the analysis may last even longer. Based on the family history and the clinical symptoms in this particular patient we decided for a targeted genetic testing focused on FMF.

It has been shown that PFMS is more common in patients with homozygous mutations in the 10th exon (e.g. M694V) of the MEFV gene [25].

Regarding MRI imaging as a diagnostic tool only few patients have been reported so far showing various findings. While Aviran et al. reported high T2-signal enhancement in muscles of all 5 examined patients indicating myositis [2, 11], a report from an adult Japanese patient described thickening of the fasciae [11].

Our own case showed a hyperintense signal at the insertion sites of the gluteus muscles at the ilium bone as well as small hyperintense foci in other muscles, highlighting the importance of T2 weighted images with fat suppression (STIR, TIRM, T2 SPAIR, T2 Dixon, etc.).

Generally, alternative imaging methods such as ^{18}F-FDG-PET/CT may be considered in children with fever of unknown origin (FUO). The ^{18}F-FDG-PET/CT has been shown to be superior to MRI for example in early phases of spondylodiscitis [26]. However, considering the radiation exposure, the long duration of symptoms and the high sensitivity of MRI in detecting muscular inflammation, the ^{18}F-FDG-PET/CT was not thought to be indicated in our case.

Another challenge is raised when patients present with afebrile myalgia as seen in 10% of the reviewed cases (Table 1). In this constellation per definitionem other (than PFMS) types of myalgia have to be considered. In the report by Majeed et al. 8% of children with FMF had spontaneous myalgias and 81% exercise induced myalgias [19].

Regarding treatment, in PFMS CS were reported to be highly effective [6, 10, 24]. On the other hand there were also CS—refractory patients who responded completely to Il-1 blockade with anakinra [30]. NSAIDs were mostly not effective.

In addition, our literature review shows that the vast majority of the authors come from FMF—high incidence countries and the publishing journals might probably not reach a broader audience of rheumatologists, especially in FMF—low incidence countries. Although PFMS is described in specific publications including EULAR recommendations on management of FMF [22], it is not sufficiently addressed in standard textbooks of rheumatology, not mentioning fever duration of several weeks and mostly not describing further symptoms such as abdominal pain, diarrhoea and petechial rash (Table 3). Although these clinical features may not be present in all cases of PFMS, they should be addressed in standard textbooks as their presence usually indicates an alternative diagnosis than FMF and may thus mislead the clinicians. Using the artifical intelligence tool, Chat GPT, with the terms „fever and myalgia “did not prove helpful as it did not yield the diagnosis of PFMS.

Conclusion

PFMS is a severe and rare manifestation of FMF. As its duration may substantially exceed the typically short (max 72 h) duration of FMF symptoms, the diagnosis may be challenging and considerably delayed in countries with low incidence of FMF especially in cases with PFMS as the primary FMF manifestation. Actually, one of the key findings of our study is the fact that more than half of the paediatric patients experienced PFMS as the presenting symptom of FMF. Genetic testing for FMF should be performed in early stages of suspected PFMS and the health care systems should support genetic testing in hospital setting accordingly. In addition, MRI imaging with T2 weighted sequences with fat suppression may confirm the edema of muscles and/or fasciae and thus support the diagnosis of PFMS. Our case illustrates that lack of awareness of PFMS may lead to unnecessary and invasive procedures as well as to a delay of efficient treatment. Based on our experience, we suggest PFMS should be discussed in more detail in standard textbooks of pediatric rheumatology.

Abbreviations

PFMS	Protracted febrile myalgia syndrome
FMF	Familial mediterranean fever
CS	Corticosteroid
NSAID	Nonsteroidal anti-inflammatory drug
GPT	Generative pre-trained transformer

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Authors' contributions

Conceptualization: TH, KR, FB, AH; Collection of data and writing the first draft of the manuscript: TH; Consultation regarding imaging: TvK; Review and editing: KR, YU, TK, TvK, FB. All authors have read and approved the final manuscript.

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Availability of data and materials

The patient's data are available at the department of pediatric rheumatology, Klinikum Stuttgart.

Declarations

Ethics approval and consent to participate

Ethics approval was not required as all patients' data were de-identified.

Consent for publication

The patient's parents gave a written consent with publication.

Competing interests

None.

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References

1. Arslanoglu Aydin E, Baglan E, Bagrul I, Tuncez S, Ozdel S, Bulbul M. Protracted febrile myalgia as a first and challenging manifestation of familial Mediterranean fever. Mod Rheumatol. 2023;33:1030–5.
2. Aviran N, Amarilyo G, Lakovsky Y, Tal R, Garkaby J, Haviv R, Uziel Y, Spielman S, Natour HM, Herman Y, Scheuerman O, Butbul Aviel Y, Levinsky Y, Harel L. Magnetic resonance findings may aid in diagnosis of protracted febrile myalgia syndrome: a retrospective, multicenter study. Orphanet J Rare Dis. 2022;17:15.
3. Ben-Chetrit E, et al. Familial mediterrean fever. Uptodate. 2024.
4. Bijlsma J, Hachulla E, et al. EULAR textbook on rheumatic diseases. 2018.
5. Bircan Z. Steroid-resistant protracted febrile myalgia. Semin Arthritis Rheum. 2010;40:e1-2.
6. Bircan Z, Usluer H. Protracted febrile myalgia mimicking polyarteritis nodosa. J Clin Rheumatol. 2008;14:222–5.
7. Cakan M, Karadag SG, Ayaz NA. Corticosteroid-resistant anakinra-responsive protracted febrile myalgia syndrome as the first manifestation of familial Mediterranean fever. North Clin Istanb. 2020;7:78–80.
8. Demir F, Bolac GL, Merter T, Canbek S, Dogan OA, Demirkol YK, Yildiz J, Doganay HL, Sozeri B. The musculoskeletal system manifestations in children with familial Mediterranean fever. North Clin Istanb. 2020;7:438–42.
9. Deniz R, Mandaci A, Gerdan I, Ozgur DS, Karaalioglu B, Akkuzu G, Yildirim F, Bes C. A case of protracted febrile myalgia syndrome with atypical course and severe asymmetric loss of muscle strength. Mediterr J Rheumatol. 2023;34:550–4.
10. Ertekin V, Selimoğlu MA, Pirim I. Familial Mediterranean fever in a childhood population in eastern Turkey. Pediatr Int. 2005;47:640–4.
11. Fujikawa K, Migita K, Tsukada T, Kawakami A, Eguchi K. Protracted febrile myalgia syndrome in a Japanese patient with fasciitis detected on MRI. Intern Med. 2014;53:2817–9.
12 Giat E, Ben-Zvi I, Lidar M, Livneh A. The preferential use of Anakinra in various settings of FMF: a review applied to an updated treatment-related perspective of the disease. Int J Mol Sci. 2022;23:3956.
13. Hashkes R, Laxer R, et al. Textbook of autoinflammation. 2019.
14. Hochberg M, Gravallese E, et al. Rheumatology. 2019.
15. Kaplan E, Mukamel M, Barash J, Brik R, Padeh S, Berkun Y, Uziel Y, Tauber T, Amir J, Harel L. Protracted febrile myalgia in children and young adults with familial Mediterranean fever: analysis of 15 patients and suggested criteria for working diagnosis. Clin Exp Rheumatol. 2007;25:S114-7.
16. Kharouf F, Tsemach-Toren T, Ben-Chetrit E. IL-1 inhibition in familial Mediterranean fever: clinical outcomes and expectations. Clin Exp Rheumatol. 2022;40:1567–74.
17. Langevitz P, Zemer D, Livneh A, Shemer J, Pras M. Protracted febrile myalgia in patients with familial Mediterranean fever. J Rheumatol. 1994;21:1708–9.
18. Livneh A, Langevitz P, Zemer D, Padeh S, Migdal A, Sohar E, Pras M. The changing face of familial Mediterranean fever. Semin Arthritis Rheum. 1996;26:612–27.
19. Majeed HA, Al-Qudah AK, Qubain H, Shahin HM. The clinical patterns of myalgia in children with familial Mediterranean fever. Semin Arthritis Rheum. 2000;30:138–43.
20. Martini A, Hachull E, et al. EULAR textbook of paeditric rheumatology. 2018.
21. Mercan R, Turan A, Bitik B, Tufan A, Haznedaroglu S, Goker B. Rapid resolution of protracted febrile myalgia syndrome with anakinra: Report of two cases. Mod Rheumatol. 2016;26:458–9.
22. Ozen S, Demirkaya E, Erer B, Livneh A, Ben-Chetrit E, Giancane G, Ozdogan H, Abu I, Gattorno M, Hawkins PN, Yuce S, Kallinich T, Bilginer Y, Kastner D, Carmona L. EULAR recommendations for the management of familial Mediterranean fever. Ann Rheum Dis. 2016;75:644–51.
23. Petty R, Laxer R, et al. Textbook of pediatric rheumatology. 2021.
24. Rom E, Amarilyo G, Levinski Y, Bilavsky E, Goldberg O, Amir J, Harel L. Protracted febrile myalgia syndrome treated with pulse of corticosteroids. Semin Arthritis Rheum. 2018;47:897–9.

25. Sidi G, Shinar Y, Livneh A, Langevitz P, Pras M, Pras E. Protracted febrile myalgia of familial Mediterranean fever. Mutation analysis and clinical correlations. Scand J Rheumatol. 2000;29:174–6.
26. Smids C, Kouijzer IJ, Vos FJ, Sprong T, Hosman AJ, de Rooy JW, Aarntzen EH, de Geus-Oei LF, Oyen WJ, Bleeker-Rovers CP. A comparison of the diagnostic value of MRI and ^{18}F-FDG-PET/CT in suspected spondylodiscitis. Infection. 2017;45(1):41–9.
27. Soylu A, Kasap B, Turkmen M, Saylam GS, Kavukcu S. Febrile myalgia syndrome in familial Mediterranean fever. J Clin Rheumatol. 2006;12:93–6.
28. Tufan G, Demir S. Uncommon clinical pattern of FMF: protracted febrile myalgia syndrome. Rheumatol Int. 2010;30:1089–90.
29. Wagner N, Dannecker G, Kallinich T. Pädiatrische rheumatologie. 2022.
30. Yildirim DG, Bakkaloglu SA, Buyan N. Protracted febrile myalgia as a challenging manifestation of familial Mediterranean fever: case-based review. Rheumatol Int. 2019;39:147–52.

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