from healthy donors. Cloning of the mutated gene in a vector for further functional studies.

Results: WES analysis revealed the de novo heterozygous missense variation c.C1132A (p.H378N) in *PIM1* gene. This variation was never described in on-line database and was predicted as damaging by various bioinformatic tools. Preliminary functional investigations in fibroblasts showed normal expression of Pim1, but higher phosphorylation of BAD protein was measured in cells from the patient. Moreover, PBMC from the patient displayed a lower sensitivity to the PIM inhibitor PIM447. RNAseq showed an altered expression profile in genes involved in the extracellular matrix organization.

Conclusion: PIM1 is an oncogene that encodes a protein kinase and, indeed, somatic gain of function mutations can be found in cancers. Preliminary data obtained from our patient suggest a gain of function effect of the p.H378N variant. The lymphoproliferative disorder may be sustained by the anti-apoptotic action of phosphorylated BAD. Recent data correlated hyperactive PIM1 in tumors with high degree of inflammatory infiltration accompanied by NFAT and mTOR activation and IL6 expression. A role of this cytokine also in our patient was coherent with a good clinical response to a treatment with tocilizumab, targeting IL-6.

Although these results are supportive of a role of mutated PIM1 in the observed phenotype, we cannot still claim that this is causative of a novel syndrome. The detection of further cases and functional studies on cells transfected with mutated PIM1 will help shedding more light on this inflammatory and lymphoproliferative disorder.

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AB1106

PREVALENCE AND EPIDEMIOLOGY OF FAMILIAL MEDITERRANEAN FEVER AND TUMOR NECROSIS FACTOR RECEPTOR-ASSOCIATED PERIODIC SYNDROME: RESULTS FROM AN ITALIAN CENTER

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Background: Familial Mediterranean fever (FMF) and tumor necrosis factor (TNF) receptor-associated periodic syndrome (TRAPS) represent two forms of periodic monogenic autoinflammatory diseases, characterized by recurrent and auto-limiting attacks of fever and systemic inflammation. Both the diseases are due to the aberrant activation of inflammasome platforms. Several variants in the *Mediterranean Fever (MEFV)* gene and *TNF Receptor Superfamily Member 1A (TNFRSF1A)* gene are respectively at the basis of FMF and TRAPS.

Objectives: The aim of this study is to report the genotype and phenotype prevalence of a cohort of patients referring to our laboratory with a suspicious diagnosis of FMF or TRAPS.

Methods: We retrospectively collected genetic and demographic data of patients undergoing *MEFV* (NM_000243) and *TNFRSF1A* (NM_001065) genetic test at our laboratory. Both genes were analysed by direct sequencing on both strands. Data were statistically analysed for descriptive and inferential purposes.

Results: A total of 168 cases were collected, most of which were Caucasian subjects (88.0%). The most common clinical manifestation was periodic fever, occurring in 121 cases, with musculoskeletal, intestinal and cutaneous symptoms, polyserositis and lymphadenopathy occurring at variable rates. Demographic and clinical characteristics are resumed in *tab.1*. *MEFV* genotyping, performed in 159 patients, identified 8 different pathogenic variants (p.Phe479Leu, p.Met680Ile, p.Met694Val, p.Met694Ile, p.Lys695Arg, p.Val726Ala, p.Ala744Ser, p. Arg761His), associated with different geographic provenience and symptoms (*tab.2, 4*).

Analysis of *TNFRSF1A* gene in 80 subjects revealed the presence of the pathogenic variant p.Cys102Tyr in 3 patients (3.75%); *tab.3, 5*. According to Eurofever scoring system, the *MEFV* variant p.Ala744Ser was significantly associated to the likelihood of having FMF and to the severity of the disease. A higher prevalence of *MEFV* pathogenic variants was observed in Egyptians and patients living in Southern Italy.

Patients n. 168	
Age, years (mean±SD)	39.9 ± 18.0
Age at disease onset, years (mean±SD)	25.8 ± 16.3
Gender [females/males; n.(%)]	94(56.0%)/74(44.0%)
Periodic fever, n.(%)	121 (72.0%)
Musculoskeletal symptoms, n.(%)	72 (42.9%)
Cutaneous rash, n.(%)	14 (8.3%)
Eye involvement, n.(%)	4 (2.4%)
Oral aphthosis, n.(%)	19 (11.3%)
Spleen enlargement, n.(%)	4 (2.4%)
Hepatomegaly, n.(%)	6 (3.6%)
Lymphadenopathy, n.(%)	34 (20.2%)
Intestinal symptoms, n.(%)	77 (45.8%)
Pericarditis, n.(%)	39 (23.2%)
Peritonitis, n.(%)	10 (6.0%)
Pleuritis, n.(%)	22 (13.1%)
Pharyngodynia, n.(%)	23 (13.7%)
Familial history, n.(%)	22 (13.1%)
NSAIDs, n.(%)	27 (16.1%)
Steroids, n.(%)	36 (21.4%)
Colchicine, n.(%)	35 (20.8%)
Immunosuppressants, n.(%)	12 (7.1%)

Table 1. Demographic characteristics of the whole cohort of patients examined.

Variant	Amino acid Change	rs Code	Exon	Clinical Significance	Wild Type Patients, n. (%)	Heterozygous Carriers, n. (%)	Homozygous Carriers, n. (%)	Missing Subjects, n. (%)
c.306T>C	p.Asp102>	rs224225*	2	Benign	52 (33.1%)	49 (31.2%)	25 (15.9%)	31 (19.7%)
c.414A>G or T	p.Gly138>	rs224224*	2	Benign	53 (33.8%)	48 (30.6%)	25 (15.9%)	31 (19.7%)
c.440G>C	p.Glu148Gln	rs3743930	2	Uncertain	147 (93.6%)	10 (6.4%)	0 (0%)	0 (0%)
c.495C>A	p.Ala165>	rs224223*	2	Benign	49 (31.2%)	52 (33.1%)	25 (15.9%)	31 (19.7%)
c.605G>	p.Arg202Gln	rs224222*	2	Benign	82 (52.2%)	38 (24.2%)	7 (4.5%)	30 (18.1%)
c.804A>G	p.Asn270Asp	/	2	Other	155 (98.7%)	2 (1.3%)	0 (0%)	0 (0%)
c.866C>T	p.Ala289Val	rs104895132	2	Uncertain significance	156 (99.4%)	1 (0.6%)	0 (0%)	0 (0%)
c.942C>T	p.Arg314>	rs224211*	3	Benign	81 (51.7%)	61 (38.9%)	34 (21.7%)	31 (19.7%)
c.1105C>T	p.Pro369Ser	rs11466023	3	Other	156 (99.4%)	1 (0.6%)	0 (0%)	0 (0%)
c.1322G>A	p.Arg441Gln	/	4	/	156 (99.4%)	1 (0.6%)	0 (0%)	0 (0%)
c.1422G>A	p.Glu474>	rs224208*	5	Benign	34 (21.7%)	55 (35.0%)	37 (23.6%)	31 (19.7%)
c.1428A>G	p.Gln476>	rs224207*	5	Benign	34 (21.7%)	55 (35.0%)	37 (23.6%)	31 (19.7%)
c.1437 C>G or A	p.Phe479Leu	rs104895083	5	Pathogenic	150 (95.5%)	2 (1.3%)	0 (0%)	0 (0%)
c.1503C>T	p.Arg501>	rs76464258	5	Benign	156 (99.4%)	1 (0.6%)	0 (0%)	0 (0%)
c.1518 C>T	p.Ile506>	rs104895099	5	Likely benign	156 (99.4%)	1 (0.6%)	0 (0%)	0 (0%)
c.1530T>C	p.Asp510>	rs224206*	5	Benign	36 (22.9%)	54 (34.4%)	36 (22.9%)	31 (19.7%)
c.1764G>A	p.Pro588>	rs1231122*	9	Benign	40 (25.5%)	58 (36.9%)	29 (18.5%)	30 (18.1%)
c.1772T>C	p.Ile591Thr	rs11466045	9	Other	154 (98.1%)	1 (1.9%)	0 (0%)	0 (0%)
c.1818C>G or T	p.Trp606>	rs10489521	10	Unstested	156 (99.4%)	1 (0.6%)	0 (0%)	0 (0%)
c.2040G>A	p.Met680Ile	rs28940580	10	Pathogenic	149 (94.9%)	7 (4.5%)	1 (0.6%)	0 (0%)
c.2080A>G	p.Met694Val	rs61752717	10	Pathogenic	149 (94.9%)	8 (5.1%)	0 (0%)	0 (0%)
c.2085G>A	p.Met684Ile	rs28940578	10	Pathogenic	151 (96.2%)	6 (3.8%)	0 (0%)	0 (0%)
c.2084A>G	p.Lys695Arg	rs104895094	10	Pathogenic	154 (98.1%)	3 (1.9%)	0 (0%)	0 (0%)
c.2118G>A	p.Pro706>	rs2234939	10	Likely benign	155 (98.7%)	2 (1.3%)	0 (0%)	0 (0%)
c.2377T>C	p.Val726Ala	rs28940579	10	Pathogenic	150 (95.5%)	7 (4.5%)	0 (0%)	0 (0%)
c.2390G>T	p.Ala744Ser	rs61732474	10	Pathogenic	154 (98.1%)	3 (1.9%)	0 (0%)	0 (0%)
c.2282G>A	p.Arg761His	rs104895097	10	Pathogenic	155 (98.7%)	2 (1.3%)	0 (0%)	0 (0%)

Table 2. Variants identified in *MEFV* gene (NM_000243).

Variant	Amino acid Change	rs Code	Exon	Clinical Significance	Wild Type Patients, n. (%)	Heterozygous Carriers, n. (%)	Homozygous Carriers, n. (%)	Missing Subjects, n. (%)
c.36A>G	p.Pro12>	rs767455*	1	Benign	17 (20.5%)	38 (45.8%)	15 (18.1%)	13 (15.7%)
c.305 G>A	p.Cys102Tyr	/	3	Likely pathogenic	82 (98.8%)	1 (1.2%)	0 (0%)	0 (0%)
c.362G>A	p.Arg121Gln	rs14149584	4	Uncertain	81 (97.6%)	2 (2.4%)	0 (0%)	0 (0%)
c.369C>T	p.Thr123>	rs104895260	4	Uncertain	82 (98.8%)	1 (1.2%)	0 (0%)	0 (0%)

Table 3. Variants identified in *TNFRSF1A* gene (NM_001065).

Variant	Amino acid Change	rs Code	Significant associations	p
c.442G>C	p.Glu148Gln	rs3743990	Provenience from Egypt	0.006
c.808A>G	p.Asn270Asp	/	Provenience from Sicily	0.008
c.866C>T	p.Ala289Val	rs104895132	Provenience from Campania	<0.001
c.1105C>T	p.Pro365Ser	rs11466023	Provenience from Abruzzo	<0.001
c.1322G>A	p.Arg441Gln	/	Provenience from Abruzzo	<0.001
c.1437 C>G or A	p.Phe479Leu	rs104895083	Provenience from Sicily	<0.001
c.1503C>T	p.Arg501=	rs76464258	Provenience from Abruzzo	<0.001
c.1518 C>T	p.Ile506=	rs104895099	Pleural effusion	<0.001
c.1772T>C	p.Ile591Thr	rs11466045	Provenience from Lombardy	0.002
c.1818C>G or T	p.Thr606=	rs10489521	Provenience from Emilia Romagna	<0.001
c.2040G>A	p.Met680Ile	rs28940580	Provenience from Sicily	<0.001
c.2080A>G	p.Met694Val	rs61752717	Provenience from North Africa	0.02
c.2082G>A	p.Met694Ile	rs28940578	Provenience from Sicily	0.03
c.2177T>C	p.Val726Ala	rs28940579	Provenience from Sicily	<0.001
c.2230G>T	p.Ala744Ser	rs61732874	Provenience from Sicily	0.003
c.2282G>A	p.Arg761His	rs104895097	Provenience from Sicily	0.002
			Provenience from Campania	<0.001
			Provenience from Egypt	<0.001

Table 4. Significant associations between pathogenic or uncertain significance variants and geographical provenience and clinical data of *MEFV* gene-tested patients.

Variant (nucleotide)	Amino acid Change	rs Code	Clinical significance	p
c.305 G>A	p.C102Y	/	Peritoneal effusion	<0.001
c.362G>A	p.R121Q	rs4149584	Lymphadenopathy	0.01
			Provenience from Emilia Romagna	<0.001
			Provenience from Campania	<0.001
c.369C>T	p.T123=	rs104895260	Provenience from Campania	<0.001
			Buccal aphthosis	0.01

Table 5. Significant associations between pathogenic or uncertain significance variants and geographical provenience and clinical data of *TNFRSF1A* gene-tested patients.

Conclusion: Our data report *MEFV* and *TNFRSF1A* genotypes identified in a cohort of patients referring to an Italian center, affected by periodic fever and other systemic symptoms. Only the *MEFV* variant p.Ala744Ser appeared to be significantly correlated with the Eurofever classification score.

REFERENCES

- Vitale A, Rigante D, Lucherini OM, De Palma A, Orlando I, Gentileschi S, Sota J, Simpatico A, Fabiani C, Galeazzi M, Frediani B, Cantarini L. The diagnostic evaluation of patients with a suspected hereditary periodic fever syndrome: experience from a referral center in Italy. *Intern Emerg Med*. 2017;12(5):605-611.
- Federici S, Sormani MP, Ozen S, Lachmann HJ, Amarian G, Woo P, Koné-Paut I, Dewarant N, Cantarini L, Insalaco A, Uziel Y, Rigante D, Quartier P, Demirkaya E, Herlin T, Meini A, Fabio G, Kallinich T, Martino S, Butbul AY, Olivieri A, Kuemmerle-Deschner J, Neven B, Simon A, Ozdogan H, Toutou I, Frenkel J, Hofer M, Martini A, Ruperto N, Gattorno M; Paediatric Rheumatology International Trials Organisation (PRINTO) and Eurofever Project. Evidence-based provisional clinical classification criteria for autoinflammatory periodic fevers. *Ann Rheum Dis*. 2015;74(5):799-805.

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AB1107

COMPLEMENTARY AND ALTERNATIVE MEDICINE USAGE IN PATIENTS WITH FAMILIAL MEDITERRANEAN FEVER

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Background: Familial Mediterranean Fever (FMF) is the most common hereditary, chronic autoinflammatory disease. Colchicine is the mainstay of the treatment, which reduces frequency of attacks and amyloidosis risk. Complementary and alternative medicine (CAM) therapies can be a non-mainstream treatment choice in chronic diseases. Frequency of use of CAM therapies among patients with FMF is not established yet.

Objectives: In the current study we aimed to identify the prevalence of the patients using CAM therapies and the factors associated with CAM usage among the patients with FMF.

Methods: One hundred and sixty-five patients were included in the study. Data regarding demographic, social and clinical characteristics were obtained from the patients. The patients were asked whether they were using any type of CAM and if they had suffered harm and/or benefit. The treatment adherence of the patients was assessed using by Morisky Green Levine Scale (MGLS). The Beliefs About Medicines Questionnaire (BMQ-T) was used to assess patient's beliefs about medicines.

Results: Fifty-six (33.9%) patients declared to use at least one CAM. The mean age of the patients was 34.1 ±12.7 years and the mean disease duration was 16.8±10.8 years. The mean dose of colchicine was 1.4±0.4 mg/day. Patients with concomitant disease and positive history of FMF in relatives had higher rates of using of CAM (p=0.011 and p=0.014 respectively). There was no statistically significance between age, sex, marital, socioeconomic and working status, difficulty of access to the treatment center, dose of colchicine, adverse events related to colchicine, attack frequency and disease severity of the patients and frequency of CAM using (p>0.05). The most frequently chosen types of CAM modalities were massage therapy (12.1%), imagining (9.7%), relaxation techniques (9.1%), cupping (9.1%) and natural products (9.1%). It is found that 42 (75.0%) of patients reported that they have suffered benefit from CAM. The mean duration of the using of CAM was 7.9 ±6.4 years. According to the BMQ-T, there was higher rate of concern about colchicine among patients that were using CAM (p=0.035) (Table 1). There was no statistically significance between compliance with colchicine treatment and using of CAM (p=0.313).

Abstract AB1107 Table 1. Comparison of Beliefs about Medicines Questionnaire Scale of patients according to the use of CAM

Variable	CAM user (n=56)	CAM non-user (n=109)	test	p
	Median (25th–75th percentile)	Median (25th–75th percentile)		
BMQ-T-Specific Necessity	4.0 (3.6-4.6)	4.0 (3.3-4.6)	-0.410 ^a	0.682
BMQ-T-Specific Concerns	3.2 (2.6-3.8)	2.8 (2.4-3.6)	-2.110 ^a	0.035
BMQ-T-General Overuse	2.5 (2.3-3.3)	2.5 (2.0-3.1)	-0.675 ^a	0.500
BMQ-T-General Harm	2.4 (2.0-3.0)	2.3 (2.0-3.0)	-0.858 ^a	0.391

CAM complementary and alternative medicine, BMQ-T Beliefs about Medicines Questionnaire Turkish translation, a Mann-Whitney U test:

Conclusion: Colchicine is the gold standard of treatment because of the known effect of colchicine treatment on the severity and frequency of FMF attacks and the risk of development of amyloidosis. Approximately one third of patients with FMF were using at least one of the CAM modalities in the current study. Concerns about colchicine treatment may have increased the tendency to use CAM therapies. On the other hand, patients should be informed that CAM therapies should not be an alternative to colchicine.

Disclosure of Interests: None declared

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AB1108

COEXISTENCE OF SARCOIDOSIS AND CHRONIC INFLAMMATORY RHEUMATIC DISEASES

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Background: Sarcoidosis is a systemic granulomatous disease of unknown etiology, mediated by Th1 lymphocytes, characterized by bilateral hilar adenopathies, pulmonary infiltrates, ocular, articular and cutaneous involvement and histologically by noncaseating granulomas. Sarcoidosis can simulate many chronic rheumatic diseases but can also coexist with them, so there are doubts about whether there is a true association or is incidental. Likewise, the occurrence of sarcoidosis has been described as a paradoxical effect during treatment with biological drugs, especially with tumor necrosis factor antagonists possibly due to a dysregulation in the compensatory proinflammatory cascade related of TNF blockade. The association between sarcoidosis and Sjögren's syndrome, systemic lupus