

# FMF patient with Muscle Pain

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# Introduction

- FMF – Familial Mediterranean Fever

-Auto inflammatory disease caused by mutations in **MEFV** gene .

-Autosomal recessive

-Fever attacks accompanied by

abdominal pain (95%)

joint pain(75%)

Chest pain(40%)

erysipelas like rash(5%)

Scrotal attacks - inflammation of the tunica vaginalis (5%)

Muscle pain attacks with fever ,fibromyalgia

# FMF Distribution



# FMF treatment

- ✓ Colchicine
- ✓ interleukin 1 inhibitors (Anakinra)

- **Amyloidosis up to 60%**
- Proteinuria – Renal failure – Dialysis

# Case Presentation

- 61 years old female , FMF since childhood, treated with colchicine 2 mg per day
- **Past Medical History:**
  - Behçet's disease
  - MTHFR heterozygous mutation (methylene tetra hydrofolate reductase)
  - Epilepsy

## **History of present illness :**

**11** days prior to admission- Gastroscopy (abdominal pain )-erosive gastritis and H pylori infection was suspected and empirical therapy was initiated with Amoxicillin ,clarithromycin and omeprazole

**10** days prior to her admission -abdominal pain ,watery diarrhea ,no fever or vomiting

**1** day prior to her admission- developed diffuse muscle pain and non specific chest pain.

-colonoscopy was done 3 months prior to her admission that was normal

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- Physical examination :
  - diffuse muscle tenderness
- Vital signs :
  - Fever : 36.6 c
  - Pulse : 84 bpm
  - BP : 150/88
  - O2 saturation : 96% Room air .



# Lab Results

Test	Result	Test	Result
ALT (IU/l)	89 ↑ (7-45)	CBC (K/microL)	3.6 ↓ (4-10.8)
Alkaline Phos. (IU/l)	127 ↑ (45-115)	Neutrophils	70%
Bilirubin (mg/dl)	0.9 (0.1-1.1)	Platelets (K/microL)	130 (130-440)
LDH(IU/l)	254 (100-260)	Na+ (meq/l)	137 ↓ (136-148)
CRP (mg/l)	1.3 (<0.08-5)	K+ (meq/l)	3.2 (3.5-5.2)
Troponin (micg/l)	negative	Creatinine (mg/dl)	0.7 (0.6-0.9)
Urine dipstick	Normal	Phosphorus (mg/dl)	2.2 (2-4)
		CPK (IU/l)	400 ↑ (0-170)
Blood gases	---	AST (IU/l)	81 ↑ (7-40)

# Diagnosis?



**Diagnosis :**

**Clarithromycin induced colchicine toxicity**

Manifested with :

Abdominal pain

Diarrhea

Muscle pain (Rhabdomyolysis )

Leukopenia

Abnormal liver function tests

FMF severity according to ADAMs score	Symptoms of colchicine toxicity	Reason of receiving Clarithromycin	Colchicine dose	Age	Gender
Mild	Diarrhea, abdominal pain and myalgia	H PYLORI infection	2 mg	61	Female
Moderate	Myalgia , vomiting and diarrhea	H PYLORI infection	1.5 mg	36	Female
Moderate	Diarrhea and muscle pain	H PYLORI infection	1.5 mg	71	Female
Severe	Diarrhea and muscle pain	H PYLORI infection	2.5 mg	41	Female
Severe	Vomiting diarrhea and general weakness	H PYLORI infection	2.5 mg	24	Female

## ❖ Past medical History

- Behçet's disease (3)
- Hypothyroidism (2)
- Hypertension (2)
- MGUS –monoclonal gammopathy of undetermined significance (1)

# Lab results

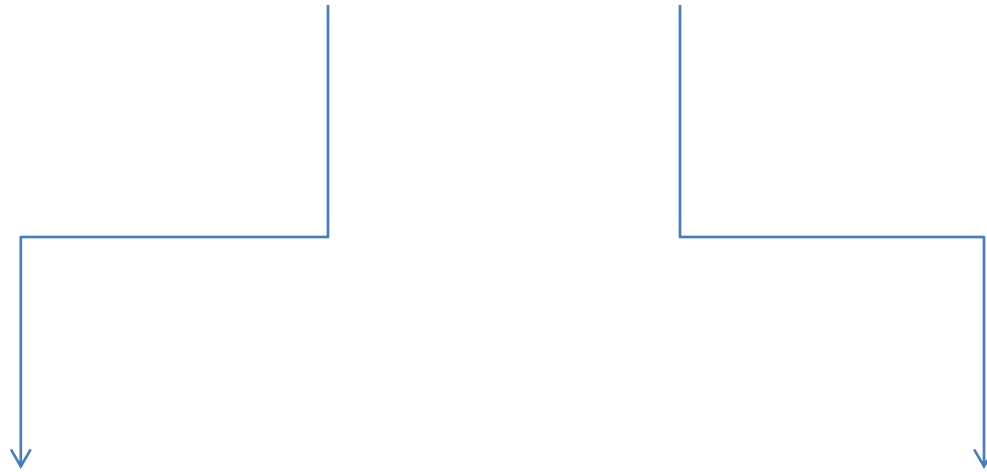
Patient Number	Blood Gases	CBC	CPK	LFT (LDH GOT)	KFT electrolytes
1	normal	normal	<b>400- elevated</b>	elevated	Hypokalemia
2	normal	normal	<b>3624- markdly elevated</b>	elevated	normal
3	normal	<b>Mild leukopenia</b>	<b>1036 Markdly elevated</b>	elevated	Hypokalemia
4	normal	normal	<b>elevated</b>	elevated	normal
5	normal	normal	<b>elevated</b>	elevated	normal
6	normal	<b>leukopenia</b>	<b>6277 Markdly elevated</b>	elevated	Hypokalemia ,Hyponatremia

# Management

- Admission
- Hydration
- Discontinuation of colchicine and clarithromycin
- following discharge colchicine was continued gradually till reaching the targeted dose.



# Colchicine toxicity



Overdose

Drug to drug interaction

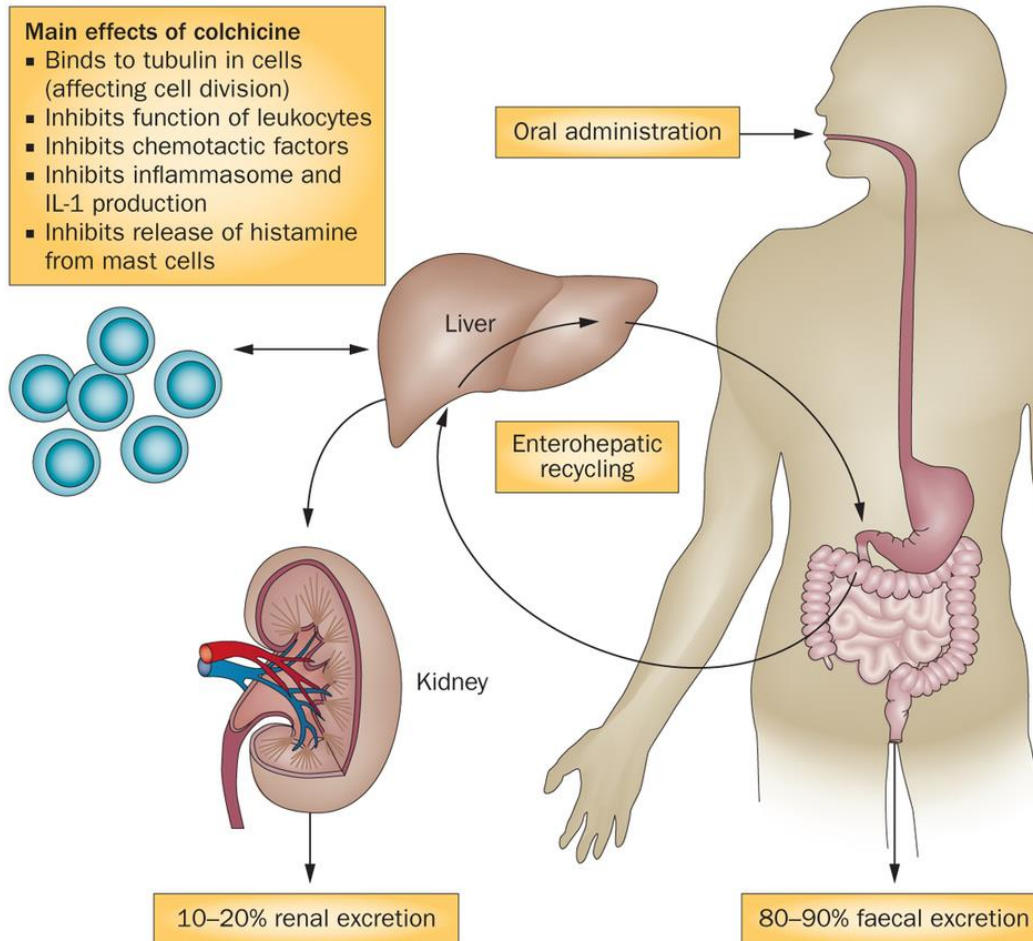


# Overdose toxicity of colchicine

- ❖ Symptoms started from 3-5 hours after ingestion
  - burning sensation in the mouth and throat
  - Fever
  - Abdominal pain
  - Vomiting and diarrhea
  - ☐ Dehydration → electrolyte imbalance → acute renal failure → hepatic failure → rhabdomyolysis → multi organ failure → Death!
  
- ❖ No antidote for colchicine
  
- ❖ No available blood test to check colchicine levels.
  
- ❖ colchicine Fab antibody solution
  
- ❖ Colchicine is not secreted throughout dialysis

# DRUG TO DRUG INTERACTION

## -CYT P450 3A4



CLARITHROMYCIN

\_Amiodarone

Atazanavir

Cyclosporine

Erythromycin

COLCHICINE

CYTOCHROME  
P450 3A4

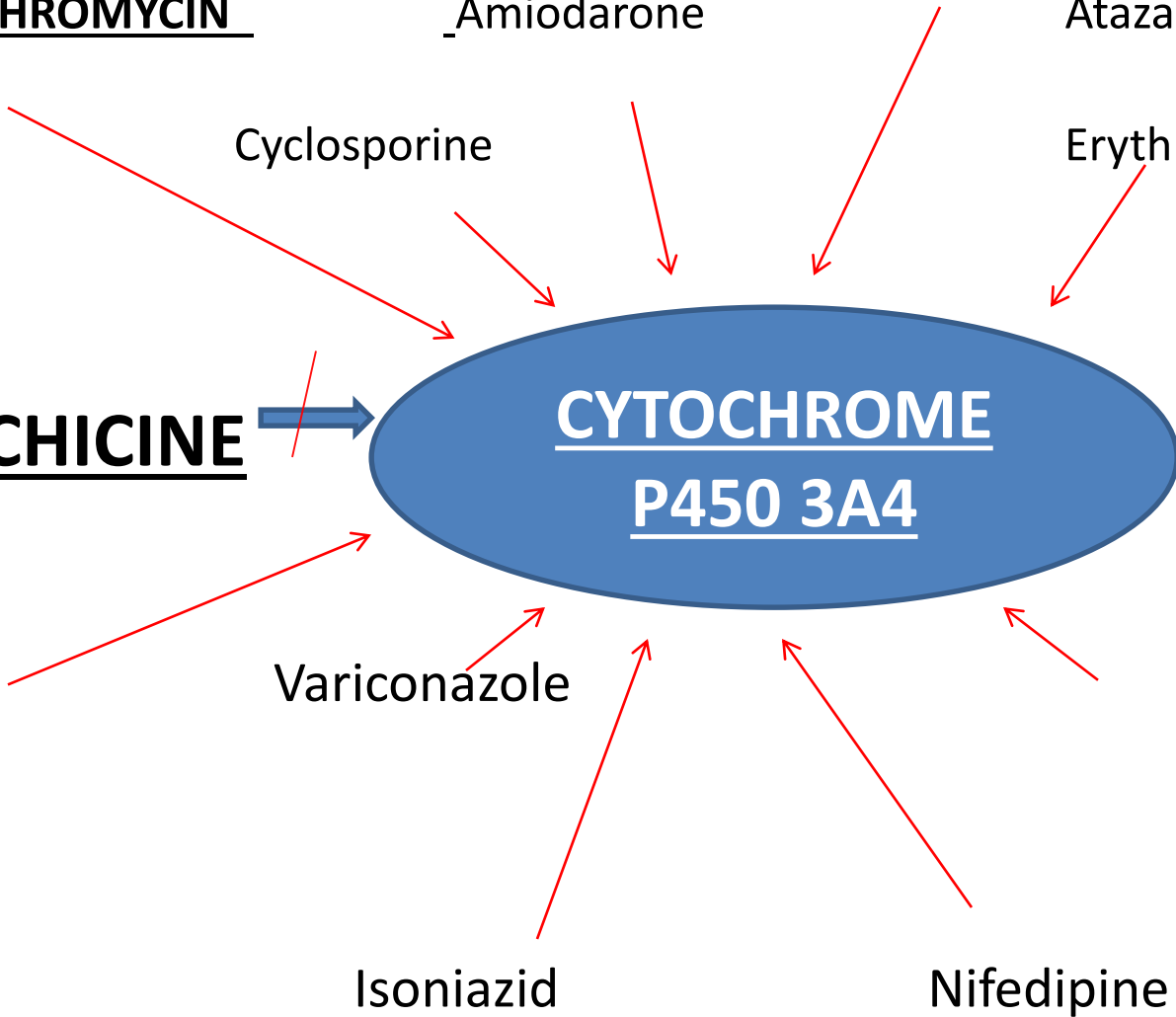
statin

Variconazole

Verapamil

Isoniazid

Nifedipine



# How to diagnose Colchicine toxicity ?

- **Clinical** : signs and symptoms of toxicity include: diarrhea, myalgia, fatigue, abdominal pain, renal failure, bone marrow suppression(leukopenia and thrombopenia ), abnormal liver enzymes, metabolic acidosis and elevated CPK.
- **Muscle biopsy**: basophilic vacuoles at the center of muscle fibers
- **EMG** : polyphasic motor unit potentials with low amplitude and short duration indicative of myopathy
- **Colchicine level at blood** - not available

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Letter to the Editor

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## Colchicine-Induced Rhabdomyolysis Caused by Interaction With Clarithromycin in a Patient With Behçet Disease

Kim, Ji-Beom MD; Kim, Sujeong MD; Yoon, Sun-young MD; Lee, Taehoon MD; Lee, Yoon Su MD; Kwon, Hyuk-Soo MD, PhD; Cho, You Sook MD, PhD; Moon, Hee-Bom MD, PhD; Kim, Yong-Gil MD, PhD; Kim, Tae-Bum MD, PhD

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# Take home message

- Colchicine toxicity – narrow therapeutic index
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- Over diagnosis of H pylori among FMF population
- high index of suspicion !
- Awareness among doctors !



## Sheba Medical Center – Tel Hashomer





