

# „Mitochondrial DNA mutation *m.3243A>G*“ – a phenotypic chameleon independent of age and gender

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## Introduction:

A mitochondrial disorder is diagnosed on the basis of symptom combinations and confirmed by genetic findings. Patients with the *m.3243A>G* mutation in the mitochondrial tRNA leucine 1 (MT-TL1) do not always meet all the proposed criteria for the most frequently encountered mitochondrial syndrome “MELAS”, an acronym for mitochondrial myopathy, encephalopathy, lactic acidosis and at least one stroke-like episode.

## Cases:

We here present various phenotypic characteristics of the mitochondrial mutation *m.3243A>G* with particular focus on cardiac manifestations.

We compared their symptoms (Table 1) and biochemical findings (Table 2) as well as their outcome.

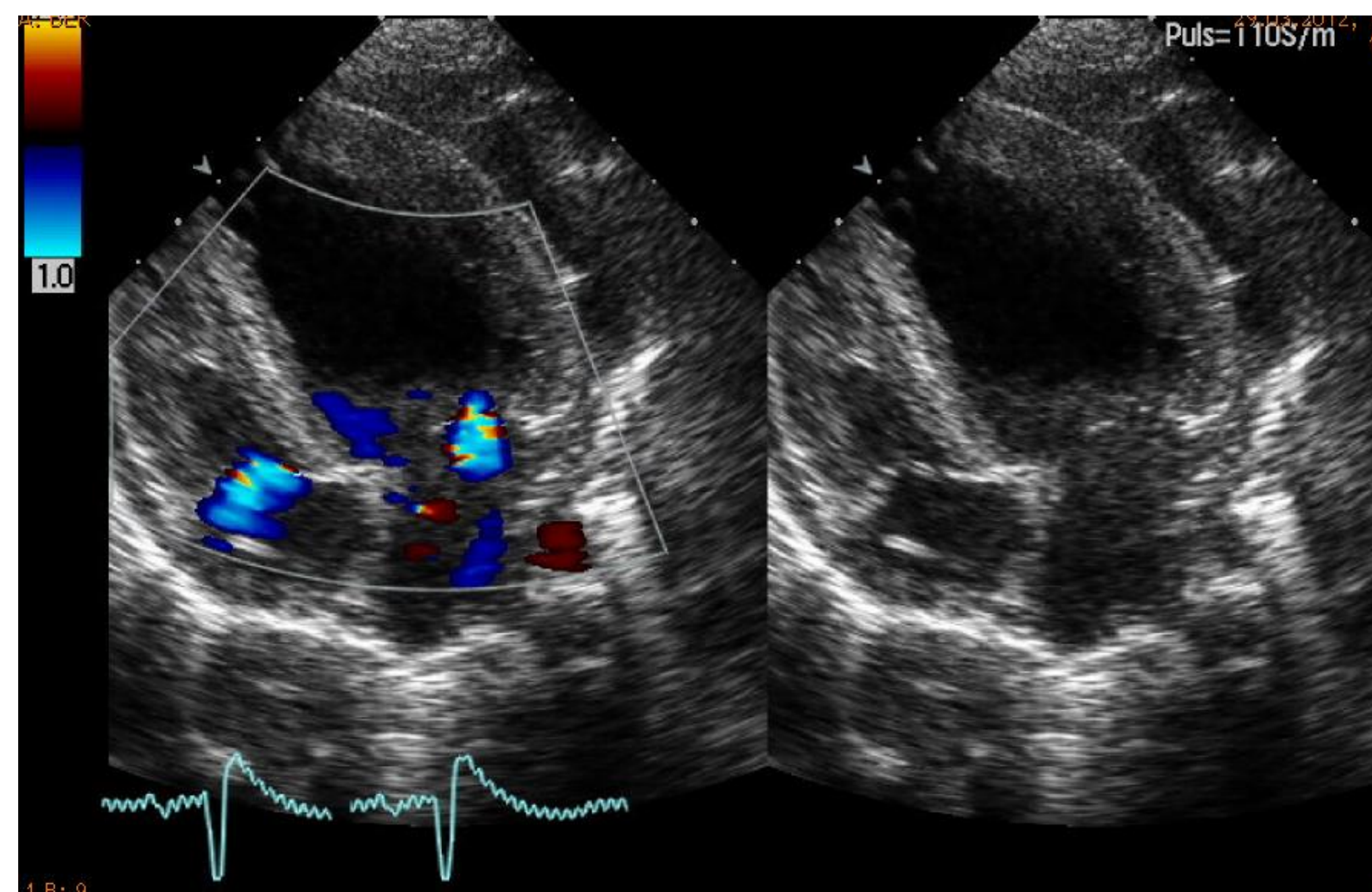


Figure 1: Echocardiography of patient 2 (♀; 14 years) at age 13 showing hypertrophic cardiomyopathy and regurgitation of tricuspid and mitral valves as well as pericardial effusions.

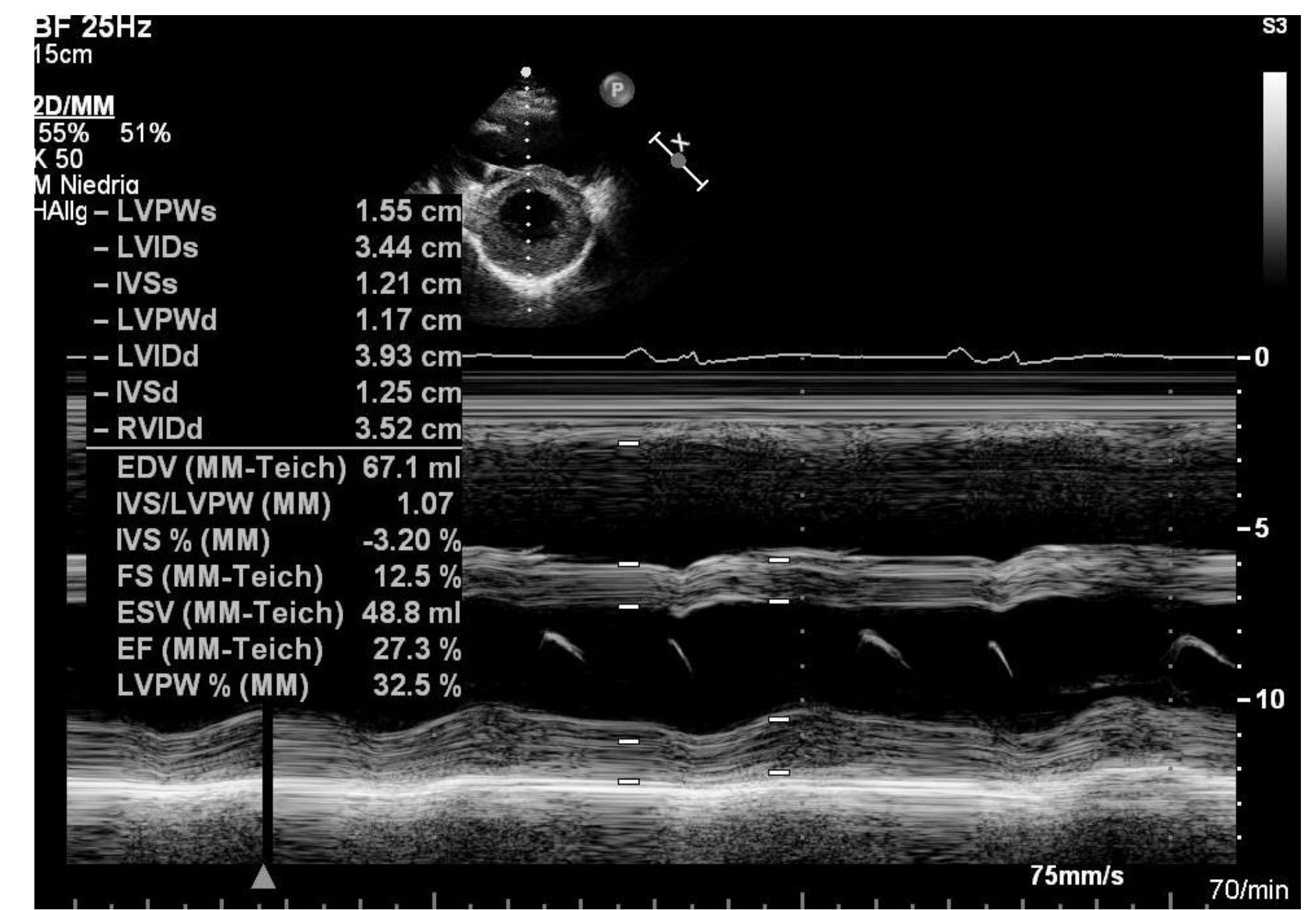


Figure 2: Echocardiography of patient 5 (♀; 42 years) at age 39 showing hypertrophic cardiomyopathy with restricted systolic left ventricular function and abnormal diastolic relaxation.

Gender current age	Patient 1 ♂ 1 month	Patient 2 ♀ 14 years	Patient 3 ♀ 23 years	Patient 4 ♂ 24 years	Patient 5 ♀ 42 years	Patient 6 ♂ 43 years	Patient 7 ♂ 45 years	Patient 8 ♀ 61 years	Patient 9 ♂ 68 years
Onset of symptoms	postpartum	8 years	10 years	5 years	36 years	21 years	37 years	41 years	52 years
Height [cm]	~ 46	130	137.3	~ 160	160	161	174	156	165
Current weight [kg]	2.9	15.7	34.5	51.7	50.5	68	70	48	68
Diabetes mellitus	-	-	-	-	+	+	+	+	+
Sensorineural hearing loss	-	+	+	-	+	+	+	+	+
Eyes	Ptosis	blindness	strabismus	-	Venous thrombosis	Oculo-motor apraxia	cataracta senilis	-	Fundus hyper-tonicus I°
Activity	↓↓	↓↓↓	↓↓↓	↔	↔ (b.t.)	↔	↔	↓	↓↓
Power	↓↓	↓↓↓	↓↓	↓↓↓	↔ (b.t.)	↔	↔	↓	↓↓
Cardiomyopathy	+	+	+	-	+	+	+	+	+
Valve regurgitation	TR I°, MR I°	TR III°, MR III°	TR II-III°, MR I°	MR I°	TR I°, MR II°, AR I° (b.t.)	MR I°	PR I°	TR I°, PR I°	TR I°, MR I°
Effusions	-	pericardial, pleural	-	-	- (b.t.)	-	-	pericardial	pericardial
Electrocardiography pathology	WPW syndrome	short PR	WPW syndrome	-	- (b.t.)	-	sick-sinus-syndrome, AV I	-	-
Stroke-like episodes	-	3	-	3	-	1 (?)	-	-	-

Table 1: Comparison of symptoms of nine patients with *m.3243A>G* mutation

## Conclusion:

Cardiac manifestation can encompass hypertrophic or dilated cardiomyopathy, as well as preexcitation syndromes or conduction delay. In general, the clinical presentation to meet the “MELAS” criteria varies due to heteroplasmy. Thus, cardiologists should screen patients with unexplained cardiac features in the context of deafness, short stature and learning disabilities for mtDNA mutations, especially the *m.3243A>G* mutation. A clear diagnosis is essential as a basis for prognostic advice concerning the disease course and clinical impact on family testing.

Gender current age	Patient 1 ♂ 1 month	Patient 2 ♀ 14 years	Patient 3 ♀ 23 years	Patient 4 ♂ 24 years	Patient 5 ♀ 42 years	Patient 6 ♂ 43 years	Patient 7 ♂ 45 years	Patient 8 ♀ 61 years	Patient 9 ♂ 68 years
L-lactate [mmol/L]	8.66 ↑	3.69 ↑	4.20 ↑	10.32 ↑	2.31 ↑	3.30 ↑	nd	nd	nd
Pyruvate [μmol/L]	106.4 ↑	nd	28 ↓	166.5 ↑	nd	nd	nd	nd	nd
Lactate-pyruvate ratio	49 ↑	nd	15	62 ↑	nd	nd	nd	nd	nd
Triglyceride [mmol/L]	1.39	1.67 ↑	nd	nd	2.35 ↑	3.08 ↑	1.91 ↑	nd	2.73 ↑
Urea [mmol/L]	17.86 ↑	19.14 ↑	6.50	5.71	29.20 ↑	31.42 ↑	18.07 ↑	16.96 ↑	21.53 ↑
Creatinine [μmol/L]	35.36 ↓	30.06 ↓	55.93	37.13 ↓	152.05 ↑	132.60 ↑	88.40	76.91	90.71 ↑
NT-proBNP [ng/L]	nd	2346 ↑	nd	nd	3006 ↑ (b.t.); 753 ↑ (a.t.)	813 ↑	944 ↑	429 ↑	1989 ↑
Troponin T [ng/L]	nd	35.4 ↑	nd	nd	51.1 ↑ (b.t.); 12.2 (a.t.)	77.9 ↑	35.5 ↑	241.7 ↑	41.7 ↑
GOT [U/L]	61 ↑	48 ↑	30	45 ↑	21	50 ↑	51 ↑	19	25
GPT [U/L]	10	111 ↑	24	19	10	59 ↑	84 ↑	13	28
γ-GT [U/L]	60 ↑	224 ↑	20	43 ↑	13	278 ↑	298 ↑	16	23
Alanine [μmol/L]	1024.2 ↑	374.4 ↑	nd	700 ↑	466.5 ↑	491.9 ↑	nd	nd	nd
Alanine-lysine ratio	5.9 ↑	3.6 ↑	nd	nd	3.4 ↑	3.1 ↑	nd	nd	nd

Table 2: Kidney-, heart or liver-parameter can be elevated due to involvement.