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# Presumptive myocarditis with ST-Elevation myocardial infarction presentation in young males as a new syndrome. Clinical significance and long term follow up

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## Abstract

**Background:** Acute myocarditis may mimic myocardial infarction, since affected patients complain of "typical" chest pain, the ECG changes are identical to those observed in acute coronary syndromes, and serum markers are increased. We describe a case series of presumptive myocarditis with ST segment elevation on admission ECG.

**Methods and Results:** From 1998 to 2009, 21 patients (20 males; age 17-42 years) were admitted with chest pain, persistent ST segment elevation, serum enzyme and troponine release. All but one patients had fever and flu-like symptoms prior to admission. No abnormal Q wave appeared in any ECG tracing, and angiography did not show significant coronary artery disease. Patients remained asymptomatic at long term follow-up, except 2 who experienced a late relapse, with the same clinical, electrocardiographic and serum findings as in the first clinical presentation.

**Conclusion:** Presumptive myocarditis of possible viral origin characterized by ST elevation mimicking myocardial infarction, good short term prognosis and some risk for recurrence is relatively frequent in young males and appears as a distinct clinical condition.

## Background

Myocarditis may occasionally mimic acute myocardial infarction, with a similar clinical presentation characterized by chest pain, ECG changes consistent with acute coronary syndromes, and serum markers increment [1-3]. We have previously reported, in a cohort of 11 young male patients, a clinical condition consistent with myocarditis and characterized by ST segment elevation, serum markers release and good short term outcome [4]. In the present study we describe our updated experience with a larger case series (21 patients) and an extended follow up.

## Methods

From January 1<sup>st</sup>, 1998 to December 31<sup>st</sup> 2009, 21 patients with the following clinical/ECG pattern were admitted to the Coronary Care Unit of a Southern Italian small town (Galatina). All patients were young; all but one was male; the coronary risk profile was low: 11 were light smokers (less than 10 cigarettes/day) and no one suffered from hypertension or diabetes. Hospital admission was needed for prolonged chest pain with ECG changes (ST elevation > 1 mm in at least two leads) and serum markers increment.

In all patients ECG, cardiac enzymes assay and rest echocardiogram was obtained daily. In 8 patients, RNA-enterovirus search was performed by PCR-method on stool and saliva specimens. Coronary angiography was performed in all patients during the acute phase (in 3 cases at hospital admission). In 5 patients in whom the

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admission diagnosis was STEMI, thrombolysis with r-TPA was performed; in these, fibrinogen and D-dimer levels were evaluated before and after treatment. The remaining patients received only aspirin, associated with heparin in 9.

After discharge, all patients were followed-up for  $65.6 \pm 49.1$  months (range 1-130), with clinical evaluation, ECG, echocardiogram and exercise stress-test. No medication was indicated at hospital discharge.

The study was approved by our institutional review committee. All patients gave informed consent for inclusion in the study.

### Results

Figure 1 shows a characteristic pattern of presentation in our population. The typical sample case is represented by a young man presenting with typical chest pain, normal global LV function, and ECG modification consistent with acute myocardial ischemia, normal coronary arteries and abnormal levels of serum markers of

myocardial damage. The main clinical, laboratory and electrocardiographic findings are listed in table 1. All patients were young (mean age  $27.9 \pm 7.02$  years, range 17-42), 20 were males, no one was a heavy smoker but 11 were light smokers. All patients but one had a recent history of flu-like episode, with fever and diarrhoea. The only young female showed a hairy chest.

All patients were admitted for acute chest pain that had started 50-425 minutes before admission. The characteristics of chest pain were always typical for acute coronary syndrome: midsternal constrictive pain, often radiating to the left arm and/or to the neck. Physical examination was unremarkable; in particular, no pericardial friction rub was heard and no signs of heart failure were evident. The admission ECG showed upward concave ST segment elevation in all cases (inferior in 5, lateral in 5, infero-lateral in 10, anterior in 1), followed, in the subsequent days, by T wave inversion; no abnormal Q waves, however, appeared in any patient. Figure 2 reports a typical example of ECG evolution (case 4).

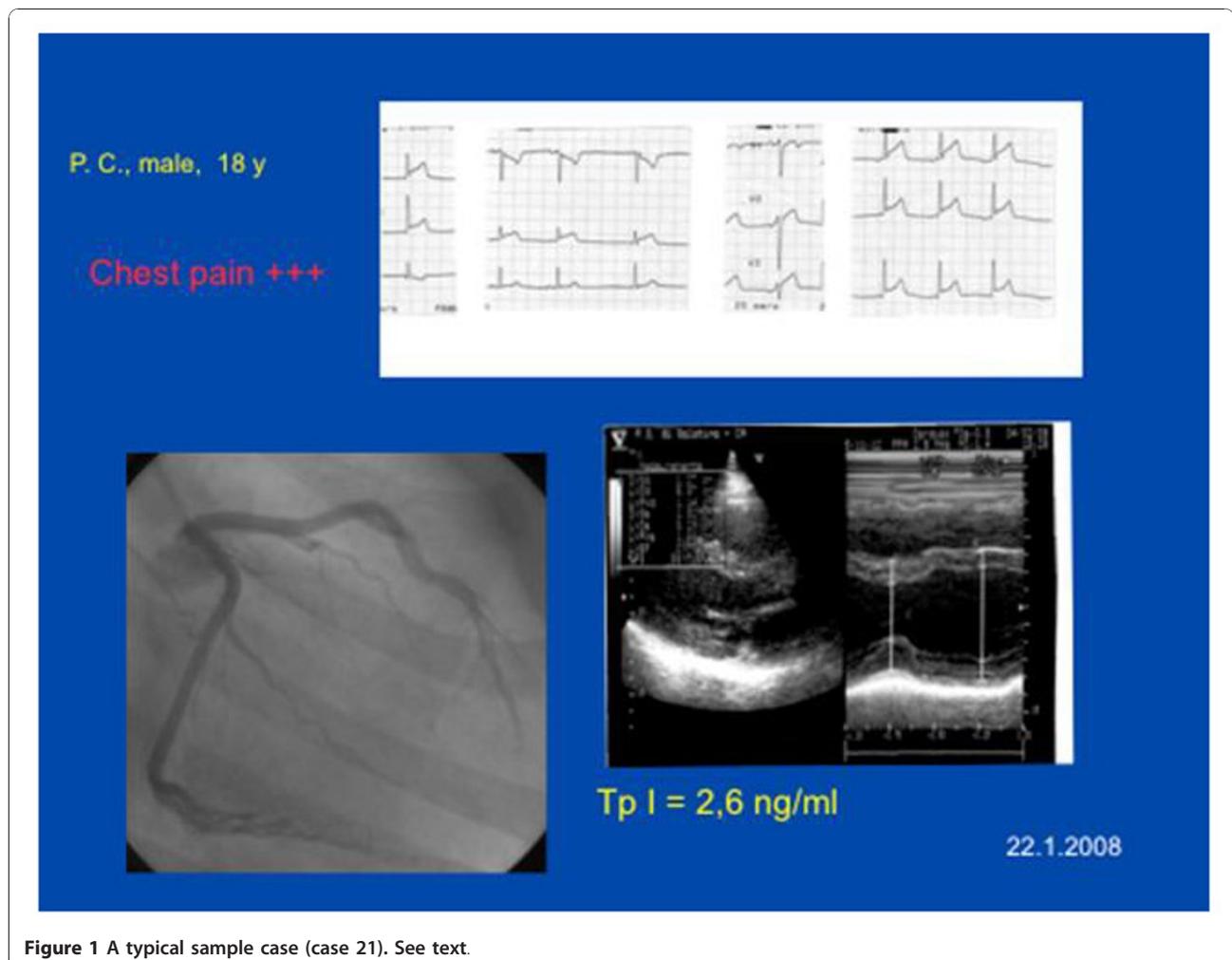


Figure 1 A typical sample case (case 21). See text.

**Table 1 Clinical, laboratory and electrocardiographic findings**

Patient, sex, age (years)	Admission month	Recent Fever	CK-MB, U/L admission/peak (Troponine I, ng/ml)	Coronary risk factors (smoke)	ECG leads with ST elevation on admission ECG	Abnormal T waves on discharge ECG	Follow up (months)	Relapse
16) 1 SW, M, 19	March	+	71/73 (NA)	0	I, aVL, V4-V6	Diphasic V4-V6	130	no
2 TG, M, 24	November	+	39/83 (NA)	0	I, aVL, V6	Negative I, II, aVL, V5,V6	122	yes
3 CE, M, 32	December	-	76/77 (NA)	0	I, II, V4-V6	Negative V4-V6	121	no
4 AA, M, 38	February	+	67/120 (NA)	1 (smoke)	II, III, aVF, V5, V6	Diphasic III, aVF	119	no
5 CM, M, 30	April	+	91/130 (NA)	1 (smoke)	II, III, aVF	Negative III,V6	105	no
6 BM, M, 17	January	+	60/60 (NA)	0	I, II, aVF, V4-V6	Negative II, III, aVF, V4-V6	96	no
7 CR, M, 32	August	+	24/43 (17)	1 (smoke)	II, III, aVF,V4-V6	None	77	no
8 CG, M, 39	October	+	17/30 (16)	1 (smoke)	I, aVL	Negative I, aVL, V6	63	no
9 SS, M, 28	December	+	23/23 (10.5)	1 (smoke)	II, III, aVF, V5-V6	None	61	no
10 CR, M, 21	April	+	34/34 (5.4)	1 (smoke)	II, III, aVF, V6	None	57	no
11 CR, M, 28	April	+	17/17 (3.6)	0	I, aVL	Flat I, aVL	57	no
12 SM, M, 26	July	+	8/14 (4.3)	0	II, III, aVF	Negative II, III, aVF	54	yes
13 CA, M, 19	April	+	21/21 (16.1)	0	II, V6	None	45	no
14 LF, M, 42	October	+	10/12 (5.3)	0	I, II, III, aVF, V6	Negative III, V6	38	no
15 AG, M, 20	April	+	55/55 (29)	1 (smoke)	I, aVL, V2-V6	Negative V4-V6	38	no
16 DA, M, 33	March	+	7/16 (2)	1 (smoke)	II, III, aVF, V5-V6	Flat II	34	no
17 DM, F, 31	April	+	19/19 (9.4)	1 (smoke)	II, III, aVF	Negative III	33	no
18 IA, M, 25	February	+	30/30 (3.4)	0	II, III, aVF	Negative II, III, aVF	23	no
19 FR, M, 35	December	+	14/14 (1.9)	1 (smoke)	II, III,, aVF	None	13	no
20 AM, M, 27	January	+	19/24 (2,3)	0	II, III, aVF	Negative II,III, aVF	1	no
21 PF, M, 18	January	+	23/28 (3,56)	1 (smoke)	I, aVL, V2-V6	Negative I, II, aVL, V2-V6	1	no

NA = not available.

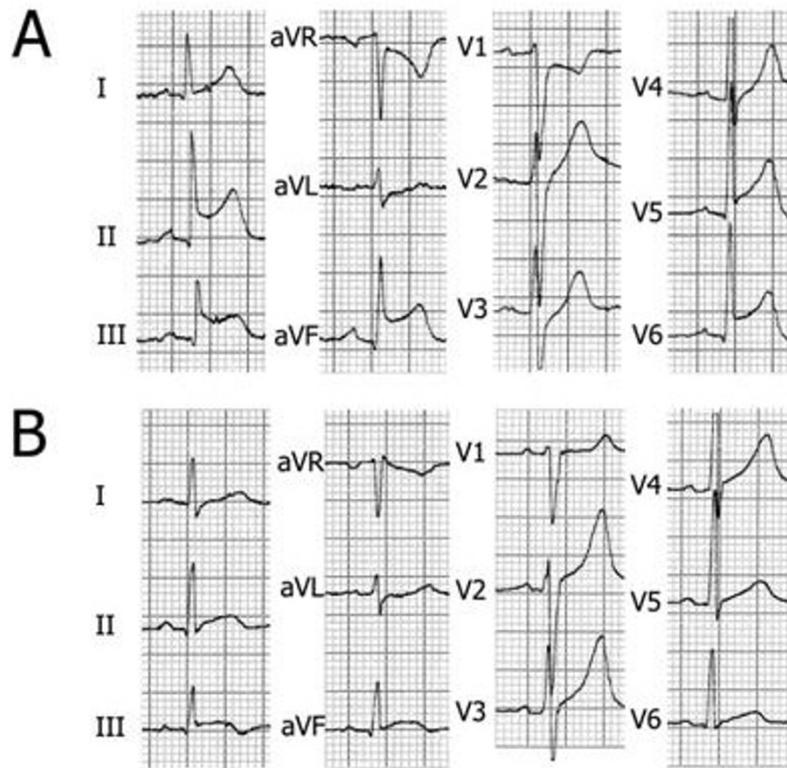
+ = present.

- = absent.

Cardiac serum enzymes, as well as troponin, were abnormal, but with an atypical pattern, being increased on admission (even when the elapsed time from chest pain onset was very short), with a relatively low peak, and late normalization (5-8 days). At echocardiography, no wall motion abnormality was detected in 17 patients, whereas a transient regional dysfunction, lasting only a few days, was observed in 4 cases, with good correspondence between the echocardiographic location of wall

motion impairment and the ECG leads showing ST segment and/or T wave abnormality. Ejection fraction (Simpson's rule) was normal in all patients (mean  $67 \pm 11\%$ ).

In 5 patients (n. 2, 4, 5, 10, 11), an initial diagnosis of STEMI prompted thrombolytic treatment with r-tPA. In 4 of these, fall of serum fibrinogen levels, not associated to any D-dimer increase, was observed. Coronary angiography showed normal coronary arteries in all cases,



**Figure 2** Electrocardiograms recorded on admission (A) and discharge (B) from patient n. 4.

including the subset ( $n = 3$ ) who underwent the exam immediately after hospital admission. Screening for enterovirus, performed in 8 patients, was positive in 5.

The clinical course was uneventful in 19 cases. A transient third sound was heard in one patient, without any other sign or symptom of heart failure. In one case, frequent asymptomatic ventricular arrhythmias (polymorphic ventricular ectopic beats and runs of non sustained ventricular tachycardia) occurred during the first 2 days. All patients were discharged in good clinical state,  $8.5 \pm 2.8$  days after admission.

At follow-up, 19/21 cases remained asymptomatic, with normal physical findings, ECG, echocardiogram, and exercise stress-test. In two cases (2 and 12), a relapse was observed, 89 and 45 months after the first episode. In both patients, the recurrence of the clinical condition was preceded by a flu-like disease, with fever and diarrhoea, with same clinical presentation and ECG and serum modifications as in the first episode. Coronary angiography was repeated in one of these patients and did not show significant abnormalities.

## Discussion

Our patients suffered from an acute non-coronary cardiac disease characterized by chest pain, ST

segment elevation, enzyme and troponin release, normal coronary angiogram, good prognosis and relative risk of late relapse (10%). This acute condition affected mostly young males. Several features are likely to exclude an ischemic origin: a) young age and low coronary risk profile; b) atypical ECG evolution, with slow ST segment normalization and no Q wave appearance; c) atypical pattern of bio-markers release, with high admission value even when hospital admission occurred within 1 hour from pain onset, myocardial involvement before symptoms appearance; d) absence of D-dimer level elevation in spite of marked fibrinogen decrease following treatment with r-TPA, an observation suggesting the likelihood that no intravascular thrombi were present; e) normal coronary angiogram.

It is likely that the clinical condition may be of viral origin: a) all but one patients experienced fever with flu-like symptoms, often associated with diarrhoea, a few days before admission; b) the disease shows a seasonal prevalence (maximal incidence in winter and spring, with peak in April), parallel to that of flu-like viral infections in our region; c) the evidence of enterovirus infection in 5 out of the 8 cases in which PCR research was performed.

An intriguing finding is that all but one of our patients was of male gender. According to the small sample size, this could be a casual phenomenon. Alternatively, it could represent the clinical counterpart of an experimental observation pointing out that some viral strains induce myocarditis only in adult male animals [5]. Coxsackievirus B3 infection results in cardiac inflammation in male, but not in female B1.Tg.Ealpha mice [6]. In addition, although weanling male BALB/c mice show minimal cardiac injury after infection, young adult male animals develop severe myocarditis while female age-matched mice do not [7]. Moreover, female animals given testosterone demonstrate in their hearts ten times higher virus levels than female animals given estradiol [8]. Testosterone could affect susceptibility to infection by increasing virus receptor expression on endothelial cells and myocytes, and/or by influencing the immune-response [9,10]. It should be pointed out that the only young woman in our population had a hairy chest, a phenomenon that could suggest a possible role of testosterone in favouring a presumptive viral myocarditis. Interestingly enough, the disease can relapse, even after many years, with the same clinical/electrocardiographic presentation. The characteristics of the clinical relapse pose a viral etiology of the disease, with a likely immune pathogenesis [11]. Finally, a warning should be recommended to physicians before treating patients with atypical clinical presentation for myocardial infarction. There are a few features that physicians should check in order to avoid potential potential life-threatening side effects of thrombolysis: young age; male sex; low coronary risk profile; concomitant flu-like symptoms in the few days before admission; atypical electrocardiographic presentation; atypical serum markers release. In such a clinical scenario, coronary angiography is preferable to thrombolysis.

### Study Limitations

The diagnosis of presumptive myocarditis was empiric and deductive, based on a very likely (and in some cases proved) recent viral infection, clinical presentation and evolution, ECG pattern, cardiac bio-markers release, and lack of epicardial coronary artery disease. Myocardial biopsy could have resulted in unquestionable demonstration of myocarditis [12], but was not performed because not strictly appropriate in this clinical context [13].

### Conclusions

STEMI-like presumptive myocarditis occurring in young males appears as a distinct acute cardiac non-coronary illness whose origin is not unequivocally proved, although viral aetiology is suggested. The disease shares some characteristics with other conditions that mimic acute coronary syndromes but are associated with

**Table 2 Parallelism between “Galatina’s” and tako tsubo like syndromes**

Syndrome	Galatina’s	Tako-tsubo like
STEMI-like presentation	yes	yes
Usually benign	yes	yes
Occasionally recurrence	yes	yes
Gender predominance	male	female
Age (years)	< 40	> 45
Prodromal phase	Flu-like	Psychological stress
Favourite target region	inferior	apical

angiographically normal coronary arteries. In this group, tako-tsubo disease has recently become very popular, and several “variants” have been described, with more or less pronounced differences from the original report [14]. Tako-tsubo syndrome, however, is more common in females over 45 years, is often preceded by a psychological stress, and is associated with wall motion abnormalities mainly affecting the apical region [15]. The herewith discussed disease, in contrast, is characterized by male gender prevalence, young age of patients, preceding flu-like disease, and absence of any stereotyped ventricular wall motion involvement (table 2). Further studies, involving larger cohorts of patients, are necessary to define whether STEMI-like presumptive myocarditis affecting young males is indeed a syndrome deserving further attention.

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### Authors’ contributions

MC conceived of the study, and participated in its design and coordination. AA, AR, GDF, GS, AL, SC, CT, CF, RR, AM participated in the design of the study and performed the statistical analysis. GO and EP critically revised the manuscript and participated in study design. All authors read and approved the final manuscript.

### Competing interests

The authors declare that they have no competing interests.

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