Myasthenia gravis is an autoimmune neuromuscular disorder characterized by skeletal muscle involvement, causing muscle weakness and fatigue. The prevalence of the disease is approximately 1:7500 with a maximal prevalence during the second and third decade in women and the fifth and sixth decade in men, although it may appear at any age. The disease has a slight female preponderance, with a sex ratio of 3:2. Cardiac involvement in myasthenia gravis may take several forms, ranging from asymptomatic ECG changes to ventricular tachycardia, myocarditis, conduction disorders, heart failure and sudden death [3–5]. We hereby report two cases of patients with myasthenia gravis who developed signs and symptoms of cardiovascular involvement, requiring admission in a cardiology ward for further investigation and treatment. The particular characteristics of the first case may be summarized by the symptomatic conduction disturbances with frequent episodes of syncope in a patient with myasthenia gravis who necessitated permanent pacing and the difficulties we encountered in the establishment of conduction disturbances etiology (due to the disease or due to the treatment with acetylcholinesterase inhibitors). The second case shows a different kind of cardiac involvement in myasthenia gravis – the ECG changes (giant diffuse T waves in a patient with cardiovascular risk factors) which needed further investigation and long term surveillance.

Key words: myasthenia gravis, conduction disturbances, syncope, myocardial ischemia.

Myasthenia gravis is an autoimmune neuromuscular disorder characterized by skeletal muscle involvement, causing muscle weakness and fatigue. The prevalence of the disease is approximately 1:7500 with a maximal prevalence during the second and third decade in women and the fifth and sixth decade in men, although it may appear at any age. The disease has a slight female preponderance, with a sex ratio of 3:2 [1][2].

The physiopathological background of this disorder is represented by the decrease of the number of acetylcholine receptors at the level of the neuromuscular junction caused by an autoimmune response through specific antibodies against the acetylcholine receptors. It seems that thymus plays an important role in the initiation of this autoimmune response, in 75% of the myasthenic patients being either hyperplastic (65% of the cases) or tumoral (thymoma – 10% of the cases) [2].

The disease may be localized, involving only some muscle groups (extra ocular muscles, mastication muscles, eyelid elevating muscle, deglutition and mimics muscles) or may have a generalized form (84% of the patients) [1][2].

Cardiac involvement in myasthenia gravis may take several forms, ranging from asymptomatic ECG changes to ventricular tachycardia, myocarditis, conduction disorders, heart failure and sudden death [3–5].

CASE REPORT

We hereby report two cases of patients with myasthenia gravis who developed signs and symptoms of cardiovascular involvement, requiring admission in a cardiology ward for further investigation and treatment.

The first case is that of a 68 year old woman with a generalized form of myasthenia gravis, under chronic treatment with prednisone and neostigmine, admitted for repeated episodes of loss of consciousness (7 episodes of syncope in the latest 9 months).

In this case symptoms began in 1998 (9 years before present admission) with diplopia, muscle weakness, right eye lid ptosis and facial paresthesia. During 1999–2000 the patient has been repeatedly admitted for episodes of loss of postural tone, without loss of consciousness, muscle weakness, slurred speech, diplopia, without a certain diagnosis until 2001, when she was admitted to the...
local hospital on an emergency basis for severe dysphagia, mastication problems and dysarthria. The diagnosis of myasthenia gravis was finally established after a positive neostigmine test. The presence or absence of antibodies against the acetylcholine receptors could not be established at that point. Treatment with neostigmine and theophylline was started, with a partial improvement of symptoms.

After an uneventful period of time the patient was admitted to the local hospital for an episode of loss of postural tone without loss of consciousness, right lid ptosis, diplopia, severe dyspnea and hypotension (BP 60/40mmHg). She was transferred to the Fundeni Clinic Institute, where a CT scan was performed, showing a 5 cm thymic tumor. The patient underwent thymectomy including the resection of both the thymic tumor and the invaded pleura; the final diagnosis was: “Thymic tumor with invasion of mediastinal and visceral pleura (T2N0M0). Generalized form of myasthenia gravis”. Ten sessions of radiotherapy consolidated the treatment. The outcome was favorable, with the complete remission of diplopia, dysarthria, deglutition and mastication altering and the significant improvement of muscle weakness and dyspnea.

Between 2002 and 2006 the patient had a regular follow-up, the evolution being stationary with slight intermittent relapses of the myasthenic weakness during episodes of respiratory infections.

Starting from July 2007 until January 2008 the patient had seven episodes of syncope, both in exertion and while sitting (including supine), the latest episode being two months previous to the admission in our clinic.

At the admission in our clinic we were facing the situation of a patient previously diagnosed with generalized form of myasthenia gravis and a history of repeated episodes of syncope, without relationship to exertion, without prodroma, without angina or palpitations, with no postcritical motor deficits. She presented fatigue, dyspnea at less than ordinary physical exertion and cough with mucopurulent sputum.

The family history was unremarkable; as classical cardiovascular risk factors we can mention severe essential arterial hypertension (highest BP measured value of 180/90mmHg), dyslipidemia and obesity.

Upon admission the physical examination revealed a slightly altered general status, normal body temperature, plethora, ecchymoses on the legs, abdominal type obesity. The muscle examination revealed hypotonia and hypokinesia with preserved reflexes, right lid ptosis. The BP was 120/90mmHg, without postural hypotension, HR 83 bpm, regular heart sounds without murmurs, palpable pulses, without peripheral edema or jugular distension. The patient was in mild respiratory distress with a respiratory frequency of about 35/min, course vesicular sounds and wheezes, cough with mucopurulent sputum.

The laboratory evaluation revealed leucocytosis with neutrophilia, interpreted as secondary to the respiratory infection, dyslipidemia, slightly elevated blood urea nitrogen and uric acid.

ECG showed sinus rhythm, 83bpm, QRS axis –10°, first degree atrioventricular block, complete right bundle branch block with secondary ST-T changes, q wave in aVF and DIII leads (Fig. 1).

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Fig. 1. – ECG: sinus rhythm, 83bpm, QRS axis –10°, first degree atrioventricular block, complete right bundle branch block with secondary ST-T changes, q wave in aVF and DIII leads.
Postero anterior chest X-ray showed elevated diaphragm, bilateral opacities in the costophrenic angles, enlarged cardiothoracic index, prominent aortic knob, right hilar fibrosis – the same aspect as shown by previous chest X ray films (Fig. 2).

Fig. 2. – Chest X-ray: bilateral opacities in the costophrenic angles, enlarged cardiothoracic index, prominent aortic knob, right hilar fibrosis.

The neurologic evaluation revealed a 6 point QMC score (Quantitative Myasthenia Gravis Score), a score of 39 points representing a significant deficit.

The episodes of syncope in this case raised numerous differential problems. The data were interpreted according to the European Society of Cardiology guidelines for the management of syncope published in 2004 [6]. Based on this, the following types of syncope were excluded:

- **Neurally-mediated syncope** – there was no long history of syncope and the episodes were not related to specific situations like cough, sneeze, swallowing, defecation, urination, visceral pain, did not occur during or after large meals and were not associated with nausea or vomiting.

- **Orthostatic syncope** – the episodes in this patient appeared both in supine and orthostatic position; the examination did not reveal orthostatic hypotension (decrease of SBP>20mmHg or to<90mmHg).

- **Cerebrovascular syncope** – we have considered syncope due to vertebral steal syndrome, but the patient denied loss of consciousness after arm elevation; there were no BP or pulse differences between the two arms.

According to the guidelines, clinical data that raise the suspicion of a cardiac cause of syncope are represented by the occurrence of syncope during exertion and while sitting, structural heart disease, palpitations before the episode of syncope and a family history of sudden death. In this case the data fulfilled the first criteria and the patient needed further evaluation for a possible heart disease.

The first step was to choose between syncope due to valvular disease or rhythm disorders. Echocardiography showed normal heart chambers, normal global and regional systolic function, LV ejection fraction 55%, impaired LV relaxation, tricuspid aortic valve with slight thickening but preserved opening; the examination excluded a significant valvular disease as a possible cause of the syncope.

ECG Holter monitoring showed asymptomatic intermittent second degree type 2 atrioventricular block with 2:1 periods (Fig. 3).

Fig. 3. – Holter ECG monitoring: asymptomatic intermittent second degree type 2 atrioventricular block with 2:1 periods.
The ECG and ECG Holter monitoring (showing complete right bundle branch block, first degree and intermittent second degree type 2 2:1 atrioventricular block) raised the suspicion of a possible arrhythmic cause of syncope, further necessitating the establishment of a specific cause:

- Possible ischaemic etiology – due to the presence of q waves in aVF and D III leads
- Possible involvement of myasthenia gravis in the etiology of conduction disorder
- Possible iatrogenic etiology due to acetylcholinesterase inhibitors for myasthenia gravis.

Ischaemic etiology of the conduction disorder could be excluded based on a coronary angiography, which was not possible at the time of the admission due to logistic problems. However, this etiology is less likely, as the patient denied any history of angina and the echocardiography showed normal LV wall motion at rest.

Based on the clinical and laboratory data, the following diagnosis was established:

Heart failure III NYHA class
Syncope
First degree atrioventricular block
Intermittent second degree type 2 atrioventricular block with periods of 2:1 AV conduction
Severe essential arterial hypertension, high added risk
Dyslipidemia
Generalized form myasthenia gravis – under chronic treatment with glucocorticoids and cholinesterase inhibitors
Operated thymoma (2002)
Chronic bronchitis – acute exacerbation.

Due to the underlying conduction disorder – second degree type 2 atrioventricular block – with symptoms represented by numerous episodes of syncope in the latest 9 months in a patient with known neuromuscular disorder, permanent pacing was performed, without periprocedural incidents.

The treatment at discharge included the myasthenia gravis specific treatment with prednisone 20mg daily, neostigmine 45mg daily with scopalamine, amnophylline 400mg daily, calcium and D3 vitamin, salt without natrium, gastric protection, low-dose diuretic, antiplatelet therapy and statin.

The second reported case is that of a 69 year old male patient, who presented speech and swallowing problems for about 4 years, diagnosed with myasthenia gravis secondary to a thymoma 6 months before the admission in our clinic. Three months after the diagnosis of myasthenia gravis and the initiation of methylprednisolone and acetylcholinesterase inhibitor therapy the patient presented an episode of acute respiratory failure requiring orotracheal intubation and mechanical ventilation, without a clear precipitating factor. The ECG during the monitoring in the ICU ward (Fig. 4) showed sinus rhythm, QRS axis 60°, diffuse giant negative T waves (leads C2-C5, DI, aVL, DII, DIII, aVF), with a maximum amplitude of 17mm in lead C4, corrected QT interval of 480ms, without ECG criteria for left ventricular hypertrophy. There is also loss of septal q wave in the left leads. In this context the patient was further admitted in a cardiology ward for evaluation.

The patient denied chest pain and had several classical cardiovascular risk factors: smoking, arterial hypertension and dyslipidemia.

This type of ECG, with giant diffuse T wave inversion and prolonged QT interval, recorded in a situation in which the clinical data does not suggest a
specific etiology, imposes several electrocardiographic differentials; this type of repolarisation changes may be seen in subendocardic ischaemia-necrosis, central nervous system (CNS) disorders, pericarditis, myocarditis, obstructive hypertrophic cardiomyopathy, metabolic abnormalities, cocaine use, pheochromocytoma and hyperventilation.

Chest X-ray showed a normal cardiothoracic ratio, without pulmonary or pleural abnormalities.

Electrolytic disorders have been ruled out based on a normal biological panel. Due to the suspicion of myocardial ischaemia the serum troponin was determined (one measurement) – positive qualitative test.

Based on the universal definition of myocardial infarction the positive diagnosis is made on the detection of the rise and/or fall of cardiac biomarkers together with at least one of the following: ischemic symptoms, ECG changes indicative of new ischaemia, new Q waves or imaging evidence of new loss of viable myocardium or new wall motion abnormalities [7].

In this case a second measurement of troponin was not available; although troponin is specific for myocardial necrosis, there are false positive situations – critically ill patients, especially those with respiratory failure or sepsis, myocarditis, hypertrophic cardiomyopathy and so on.

The first echocardiography showed the absence of regional wall motion abnormalities, but revealed moderate concentric left ventricular hypertrophy (interventricular septum 13mm, posterior wall 13mm) (Fig. 5a and 5b) and normal left ventricular systolic function. The left ventricular hypertrophy was considered secondary to the arterial hypertension, a diagnosis of hypertrophic cardiomyopathy being considered unjustified in this case. A small subendocardic necrosis could not be eliminated, as in this case and especially in the presence of LV wall hypertrophy, echocardiography might not detect subtle wall motion abnormalities.

Data on giant T wave inversion shows that myocardial infarction and CNS disorders are major etiologies. In a series of 100 ECGs with T wave inversion analyzed by Walder and Spodick [8] 28 patients presented myocardial infarction and 23 patients CNS disorders.

In the reported case the cerebral CT scan was normal.

Therefore, we were not able to determine a certain cause of the ECG changes, but could not exclude myocardial necrosis in a patient with multiple cardiac risk factors. Coronary angiography on an emergency basis was not performed, in this phase the patient being treated for the acute respiratory failure; although coronary angiography is not contraindicated in myasthenia gravis, iodine contrast usage warrants precaution in these cases, as situations of muscle weakness exacerbation have been reported [9].

The myasthenic crisis had a favorable outcome with remission. During the following week the ECG showed no further evolution. Further myocardial biomarkers determinations were in a normal range.

The physical examination of the patient after the myasthenic crisis showed normal BP measurements under treatment with ACEI and diuretics, without signs of pulmonary or systemic congestion; the following echocardiographic examinations were similar to the first one.

Two months after the myasthenic crisis the ECG shows dynamic changes in the anterior leads, with biphasic T waves in leads C2-C6, DLaVL (Fig. 6), with no ischaemic or heart failure symptoms.
Fig. 6. – ECG recorded 2 months after the myasthenic crisis: sinus rhythm, biphasic T waves C2-C4, negative T waves C5, C6, DI, aVL.

One month later the ECG becomes normal (Fig. 7), without any further changes during the following period.

The evolution of the ST-T makes hypertrophic cardiomyopathy even less likely. In this type of cardiomyopathy the ECG changes, which may appear years before the identification of left ventricular hypertrophy [10], do not alter, especially during short periods of time.

Fig. 7. – ECG recorded 3 months after the myasthenic crisis: sinus rhythm, 65 bpm, QRS axis 15°, no ST-T changes, no pathologic Q waves. Corrected QT interval 350ms.

Thereafter, in this case in which other causes of giant T waves have been ruled out, a coronary angiography was performed and showed normal epicardic coronary arteries (Figs. 8, 9).

Myocardial infarction with angiographically normal coronary arteries is a well-known entity, with a prevalence of 1–12%. It is more frequent in young patients and the etiology is still unclear; the proposed mechanism includes coronary vasospasm, thrombosis, platelet dysfunction or vasospastic syndromes [11]. However, this diagnosis seems unlikely in a 69 year old male with cardiovascular risk factors, evolving ECG changes and positive troponin in a situation which may elicit a false positive result.

In the current situation other disorders with similar presentation must be considered. The ECG changes occurred during a myasthenic crisis in a patient with myasthenia gravis secondary to a thymoma.

Based on the data about the most frequent cardiovascular signs and symptoms in myasthenia gravis [3][5][12](Table I) and the data in the reported case, myocarditis should be considered as a differential; it may be quite frequently encountered in patients with myasthenia gravis, especially in the thymoma associated group (with an up to 61% prevalence of
Fig. 8. – Coronary angiography – RAO – no significant stenosis of the left coronary artery.

Fig. 9. – Coronary angiography – LAO – normal right coronary artery.

Table 1
Cardiovascular disorders in patients with myasthenia gravis (after Guglin[3])

<table>
<thead>
<tr>
<th>Disorder</th>
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<tbody>
<tr>
<td>Myocarditis</td>
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<tr>
<td>Giant cell myocarditis</td>
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<tr>
<td>Cor pulmonale</td>
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<tr>
<td>Post thymectomy:</td>
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<tr>
<td>Pericarditis</td>
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<tr>
<td>Arrhythmia</td>
</tr>
<tr>
<td>Medication related:</td>
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<tr>
<td>Cyclosporine – arterial hypertension</td>
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<tr>
<td>Cholinesterase inhibitors:</td>
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<tr>
<td>Bradycardia, asystole</td>
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<tr>
<td>Paroxysmal tachycardia</td>
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<tr>
<td>ECG abnormalities:</td>
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<tr>
<td>Nonspecific ST-T changes</td>
</tr>
<tr>
<td>Prolonged QT interval</td>
</tr>
<tr>
<td>Arrhythmia</td>
</tr>
<tr>
<td>Atrial fibrillation/flutter</td>
</tr>
<tr>
<td>Sinus bradycardia</td>
</tr>
<tr>
<td>Bundle branch block</td>
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<tr>
<td>Atrioventricular block</td>
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<tr>
<td>Thymoma related</td>
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<td>Post-irradiation injury</td>
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histological evidence of myocarditis versus 0.6% prevalence in unselected autopsy series) [3].

In this case, although a specific moment of acute heart failure is missing, the final two diagnostics considered are myocarditis or NSTEMI with angiographically normal coronary arteries.

The patient was discharged on medical treatment for myasthenia gravis (neostigmine, corticosteroids) and ACE inhibitors, diuretic and statin. Until this article was written the thymectomy has not been performed yet, so we lack histopathological data.

DISCUSSION

The aforementioned cases have been chosen in order to underline the peculiarities and polymorphism of heart involvement in myasthenia gravis and the differential problems that they raised.

The first case portraits a typical myasthenia gravis, with a classical onset with involvement of the cephalic muscles with further generalized involvement. The positive diagnosis was established based on the clinical signs and symptoms and neostigmine test; due to technical problems the presence of antibodies against acetylcholine receptors was not established; this would have been useful because clinical trials have found a connection between the antibody type and clinical subtype.

As already mentioned, the pathological mechanism of this disease is the decrease of the acetylcholine receptors at the neuromuscular junction due to an autoimmune answer mediated through specific antibodies against the acetylcholine receptors. The acetylcholine receptor has five units ($2\alpha$, $1\beta$, $1\delta$, $1\gamma$ or $\varepsilon$) around a central pore; the $\alpha$ unit contains both the acetylcholine binding site and the primary immunogenic site). Anti-AchR antibodies are positive in 85% of the generalized form myasthenia gravis and in 50% of the ocular form; a negative result does not exclude the diagnosis, because as far as 40% of the cases with negative antibodies have anti-MuSK (specific muscle kinase) receptors, which play an important role in the post-synaptic differentiation of acetylcholine receptors [1]. The positive antiMuSK antibodies are more frequently found in female patients and the respiratory and bulbar muscles are frequently involved. Other types of antibodies in myasthenia gravis are anti-smooth muscle antibodies (84% of the patients younger than 40 years without thymoma or patients older than 40 years with thymoma) and striational...
antibodies (antimuscle protein titin and anti ryanodinic receptor) which connect themselves in a cross linked pattern on different epitopes on the skeletal and heart muscles [1]. Almost all patients with myasthenia gravis and thymoma and half of the patients with late onset myasthenia (>50years old) have these antibodies [1].

A recent study identified correlations between the clinical subsets and antibodies type. Anti-Kv1.4 antibodies have been associated with bulbar involvement, myasthenic crisis, thymoma and myocarditis and/or myositis; anti-Ach antibodies correlate with an early onset of the disease and seronegativity is associated with ocular form myasthenia.

All these data underline the fact that the autoimmune answer in myasthenia gravis may involve the myocardium.

Thymus plays an important role in the initiation of the autoimmune answer in myasthenia gravis. Antibodies in this disease are IgG, T-lymphocyte dependent. It seems that the myoid thymic cells, which express acetylcholine receptors, may serve as an autoantigen source and can trigger the autoimmune reaction [2]. Thymectomy improves the symptoms in 85%, and in 35% of the patients they enter the remission phase without further need of medical treatment continuation [2].

In the first case we presented thymectomy improved symptomatology, with the complete disappearance of diplopia, dysarthria, deglutition and mastication problems and the significant improvement of muscle weakness and dyspnea.

The association between myasthenia gravis and cardiovascular diseases is known for over 100 years, but there is no specific etiologic link between the two conditions. Most of the data derive from series of patients or case reports. Guglin and associates [3] studied 108 patients with myasthenia gravis and found signs of cardiac involvement in 16% of the cases (atrial fibrillation, atrioventricular heart blocks, asystole, sudden death) that could not be explained by other causes and interpreted as due to myocarditis that occurs during the autoimmune involvement. Clinical signs of unexplained cardiovascular involvement occur especially in myasthenia gravis with thymoma (50%), more often than in myasthenia gravis without thymoma (only 12%). Arrhythmia is the most common clinical manifestation and these patients are at an increased risk of sudden death.

ECG abnormalities may be found in 16 to 88% of patients with myasthenia gravis; the most common forms are nonspecific ST-T changes, abnormal T wave, prolonged QT interval, sinus tachycardia, sinus arrhythmia, bundle branch blocks [3]. According to our data there is only one reported case of transient ECG changes during a myasthenic crisis suggesting anterior acute myocardial infarction [14]. The necropsy in that case showed no coronary abnormalities, but discovered partial areas of interstitial fibrosis.

The mechanism of myocardial involvement in myasthenia gravis is still unknown. Some isolated reports described autoimmune myocarditis. Similar anatomical changes in the myocardium (focal myocarditis) and skeletal muscles [15] have led to the idea of myocardium involvement in the pathological process of the disease.

The earliest evidence of heart involvement goes back to 1901, when Weigert described abnormal cells in the myo- and epicardium of a patient with thymoma. In 1942 Rottino described polymorphic myocardial histological lesions in the myocardium of myasthenia gravis patients, from scarce lymphocytic infiltration, to diffuse myocarditis [16]. The microscopical lesions include myofibrillar necrosis, inflammatory changes with edema, hemorrhages, lymphocytic infiltrations, large irregular histiocytes. These pathological changes are non specific, as they can also be found in thyreotoxicosis, Addison’s disease and rheumatoid arthritis. Furthermore, the non specific inflammatory changes associated with hypoxia, hypercapnia and metabolic acidosis associated with myastenic crisis cannot be neglected [3][17].

Some authors also described myocarditis with focal cellular infiltration, possibly due to antibodies against β1 and β2 receptors, with prolonged QT interval and non specific ST-T changes [18].

The presence of more frequent, more serious myocardial involvement in thymoma patients has led some investigators to interpret the myocarditis in these cases as a paraneoplastic phenomenon [3].

Some of the non specific ECG changes may be induced by myocarditis, as autopsy series described myocardial abnormalities in young patients with myasthenia gravis and ECG changes [7][14].

Besides myocarditis, not always with clinical symptoms (especially as one of the cardinal symptoms of myasthenia is fatigue), some cases of giant cells myocarditis with rapid progression have also been described, more frequent in a perioperative setting.
Most of the studies concerning ECG changes and myocardial infiltration in myasthenia gravis were conducted before the era of coronary angiography, so that there is difficult to interpretate them especially in thymoma patients, who are usually older male patients, with a high probability of ischemic heart disease. A contemporary review of these data with modern technique would be of real interest.

In the second case we reported, myocarditis is a plausible cause of ECG evolving changes in the context of angiographically normal coronary arteries.

Some technical limits in the paraclinical investigations have led to the impossibility of establishing a certain diagnosis: lack of quantitative measurements of troponin level in dynamics, lack of ECG for comparison, BNP measurement in the acute episode, of myocardial scintigraphy with monoclonal Indium labeled antimyosin antibodies or Galium scintigraphy or cardiac MRI exam.

A recent study [19] suggested that functional changes are frequent in myasthenia gravis. Autonomous nervous system, both sympathetic and parasympathetic, is affected in myasthenia gravis, but the impact of these changes on heart function is still unclear. It has also been proven that the patients with myasthenia gravis and autoimmune autonomous neuropathy [20] have antibodies against the nicotinic receptor for acetylcholine located in the skeletal muscle (a classical finding in myasthenia gravis) and specific antibodies against the acetylcoline receptors located in the ganglia on the nerves. This finding may explain the rare, but possible clinical association between myasthenia gravis and autonomous system dysfunction.

Another important part is the possible iatrogenic heart involvement during treatment with cholinesterase inhibitors which may cause bradycardia, hypotension, syncope, atrioventricular heart blocks due to the increased quantity of acethylcoline in the synapse. Some reports mention cases of vasospastic angina [21], acute myocardial infarction due to coronary artery spasm during the colinergic crisis [22] and proarrrhythmic effects of cholinesterase inhibiting drugs [23].

In the first reported case we do not have enough data to strictly link the conduction abnormalities to the pathogeny of the disease (myocarditis or autonomous nervous system dysfunction) because of lack of immunologic panel of the patient. The patient followed a long treatment (2001–2008) with colin-esterase inhibitors, a iatrogenic etiology must be considered in this case, with no possibility of stopping or decreasing the dosage due to the relapsing of myasthenic symptoms.

In the cases of symptomatic heart blocks with syncope in patients with myasthenia gravis under treatment with colinesterase inhibitors the usual management implies permanent pacing, as in the described case.

A recent published case report describes the situation of a patient with myasthenia gravis under piridostigmine treatment who developed high grade atrioventricular block with frequent episodes of syncope. In this case the authors chose the simultaneous treatment with hiosciamine, a muscarinic antagonist used to block the deleterious cholinergic side effects. Under the association of therapy the atrioventricular block completely disappeared, there was no further syncope, thereafter avoiding the permanent pacing. This situation is an isolated report, moreover the treatment with hiosciamine is not available in Romania.

There is also a case report of atrioventricular block and pericardial effusion in a myasthenia gravis patient, with favourable course under immuno-suppressive therapy and plasmapheresis [4].

In the first case we considered that the patient had an increased risk of sudden death, no matter the cause of the conduction abnormalities and chose a permanent pacing attitude, even if the current guidelines do not include myasthenia gravis among the neuromuscular disorders with conduction abnormalities that impose pacing. According to the ACC/AHA 2002 guidelines for implantation of cardiac pacemakers and antiarrhythmia devices the pacing indication in our patient is class IIb, level of evidence B. The guidelines mention that in neuromuscular disorders like myotonic muscular dystrophy, Kearns Sayre syndrome, Erb dystrophy and peronier muscular atrophy, the presence of an atrioventricular block of any grade (including grade I atrioventricular block) with or without symptoms permanent pacing is indicated given the impredictable progression of conduction abnormalities in these patients. According to the ESC Pacing and CRT Guidelines, neuromuscular disorders with second or third degree atrioventricular block represent a class I level of evidence B recommendation for cardiac pacing, while the association with first-degree atrioventricular block is a class IIb level of evidence B recommendation.
The particular characteristics of the first case may be summarized as follows:

The symptomatic conduction disturbances with frequent episodes of syncope in a patient with myasthenia gravis who necessitated permanent pacing.

The difficulties we encountered in the establishment of conduction disturbances etiology (due to the disease or to the treatment with acetylcholinesterase inhibitors).

The second case shows a different kind of cardiac involvement in myasthenia gravis – the ECG changes (giant diffuse T waves in a patient with cardiovascular risk factors) which needed further investigation and long term surveillance.

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