Third degree atrioventricular block as a rare complication of Graves' thyrotoxicosis

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ARTICLE INFO

Article history:
Submitted: 4. 11. 2018
Accepted: 2. 2. 2019
Available online: 25. 11. 2019

Klíčová slova:
Asystolie
Atrioventrikulární blokáda III. stupně
Gravesova–Basedowova choroba
Sinusová tachykardie
Tyreotoxikóza

SOUHRN

Kompletní atrioventrikulární (AV) blokáda představuje vzácnou, avšak život ohrožující komplikaci tyreotoxikózy. V literatuře bylo dosud popsáno pouze několik případů s nejistou kauzální souvislostí s hypertyroidním stavem. Vzhledem k nedostatku údajů nepanuje absolutní shoda ohledně reverzibility této abnormality AV převodu, a tedy i nutnosti implantace trvalého kardiostimulátoru.

V naší kazuistice popisujeme případ 35leté pacientky, u které se nově diagnostikovaná Gravesova–Basedowova tyreotoxikóza poprvé manifestovala synkopou při kompletní AV blokádě. V úvodu hospitalizace došlo ke spontánní obnově AV převodu v poměru 1 : 1, což vedlo k výrazné sinusové tachykardii s frekvencí 150/min, která byla symptomatická bolestmi na hrudi, prekolapsovým stavem a vedla k rozvoji srdečního selhání v důsledku hyperkinetické cirkulace.

Další komplikací byla epizoda asystolie při recidivě úplné AV blokády bez náhradního rytmu s nutností dvouminutové kardiopulmonální resuscitace a emergentní dočasné transvenózní kardiostimulace. Při léčbě tyreostatiky a kortikosteroidy se po 48 hodinách stabilizoval srdeční rytmus se sklonem k sinusové tachykardii. Další průběh byl již nekomplikovaný, včetně dobré tolerance léčby beta-blokátorem. Komplexní vyšetření (včetně magnetické rezonance srdce) neprokázalo žádnou jinou příčinu vysvětlující kompletní AV blokádu. Zvažovanou implantaci trvalého kardiostimulátoru pacientka odmítla. V následujících třech měsících sledování již nebyla recidiva AV blokády zaznamenána.

Keywords:
Asystole
Graves' disease
Sinus tachycardia
Third degree atrioventricular block
Thyrotoxicosis

ABSTRACT

Complete atrioventricular (AV) block is a rare but life-threatening complication of thyrotoxicosis. In the literature, only a few cases with uncertain causal link to hyperthyroid status have been described so far. Because of the lack of data, there is no clear consensus on the reversibility of AV conduction abnormality and hence on the need for permanent pacemaker implantation.

In the case report, we describe a case of a 35-year-old woman with newly diagnosed Graves' thyrotoxicosis complicated by syncope due to complete AV block. Upon admission to hospital, a spontaneous recovery of the AV conduction with 1 : 1 ratio occurred, resulting in significant sinus tachycardia with a heart rate of 150 bpm, which manifested by chest pain and pre-collapse state and led to the development of heart failure due to hyperkinetic circulation. Further complication was an asystole caused by a recurrence of complete AV block without occurrence of escape rhythm, with the need of a 2-minute cardiopulmonary resuscitation and emergency temporary transvenous pacing. After 48 hours of thyrostatic and corticosteroid treatment, the heart rhythm stabilized, with a tendency to sinus tachycardia. The further course was uncomplicated, including a good beta-blocker tolerance.

A comprehensive examination (including cardiac magnetic resonance) did not show any other cause explaining the complete AV block. The patient refused permanent pacemaker implantation which was considered. During the next 3-month follow-up, a recurrence of AV block did not occur.

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DOI: 10.33678/cor.2019.040

Please cite this article as: Širanec M, Magage S, Válek M, et al. Third degree atrioventricular block as a rare complication of Graves' thyrotoxicosis. Cor Vasa 2019;61:e629–e633.

Case report

A 35-year-old woman, active smoker, with a history of hepatitis B in childhood, otherwise without serious comorbidities, was admitted to the coronary care unit after an episode of syncope.

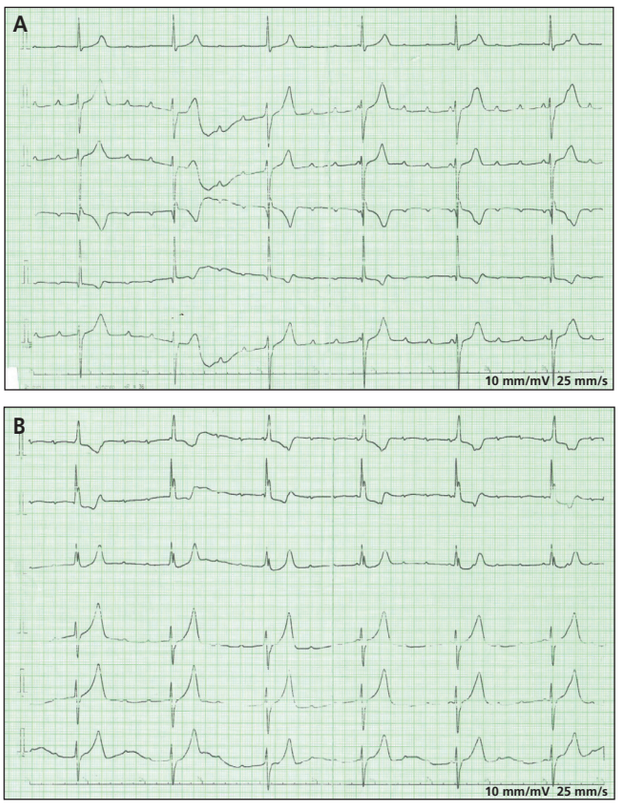

Fig. 1 – ECG on admission: (A) limb leads, (B) precordial leads. Sinus tachycardia with an atrial rate of 150 bpm and third degree AV block with infra-Hisian escape rhythm and ventricular rate of 36 bpm (RBBB and LAFB morphology), probably from the area of left posterior fascicle.

An electrocardiogram (ECG) upon admission showed sinus tachycardia with an atrial rate of 150 bpm and infra-Hisian third degree AV block with a ventricular rate of 36 bpm and morphology of right bundle branch block (RBBB) and left anterior fascicular block (LAFB; Fig. 1). The patient was normotensive, eupnoeic, and slightly anxious. Physical examination revealed mild exophthalmos and systolic murmur (grade III/VI) over the precordium. Shortly after admission, a spontaneous recovery of the AV conduction with 1 : 1 ratio occurred, resulting in significant sinus tachycardia with a heart rate of 150 bpm and morphology of left bundle branch block (LBBB; Fig. 2), which manifested by chest pain and pre-collapse state. A few minutes later, recurrence of complete AV block without escape rhythm (Fig. 3) occurred, leading to asystole with loss of consciousness, with the need of a 2-minute cardiopulmonary resuscitation during which sinus rhythm with third degree AV block and ventricular escape rhythm was recovered. Emergency temporary transvenous pacing was performed and the patient remained intermittently dependent on ventricular pacing for the next 48 hours, but was completely hemodynamically stable.

Laboratory examination revealed severe autoimmune hyperthyroidism (Graves' thyrotoxicosis) with an extremely low level of thyroid stimulating hormone (TSH), elevated free thyroxine (fT4), free triiodothyronine (fT3), and TSH receptor antibodies (TRAK). The diagnosis was also supported by a history of tremor, excessive sweating, weight loss, and palpitations in the few months preceding admission to hospital. Other laboratory results showed mildly elevated inflammatory markers (however, without evidence of any source of infection), mild hypokalaemia, metabolic acidosis, elevated NT-proBNP, lactate, and liver tests (Table 1). Antithyroid (thiamazole) and glucocorticoid treatment was initiated. Heart rhythm was stabilized, with a tendency to sinus tachycardia with a heart rate of 130 bpm, prolonged AV conduction, and morphology of incomplete RBBB. Tachycardia and hyperkinetic circulation led to development of heart failure (present clinical signs and laboratory findings). Consequently, beta-blocker therapy was initiated and carefully up-titrated

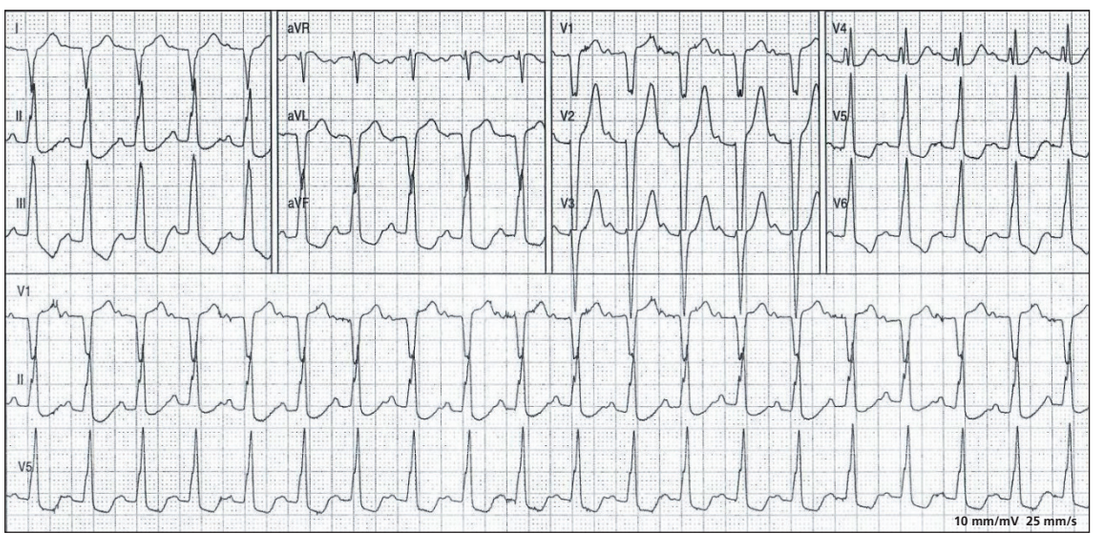

Fig. 2 – ECG shortly after admission – sinus tachycardia with a rate around 150 bpm and LBBB morphology.

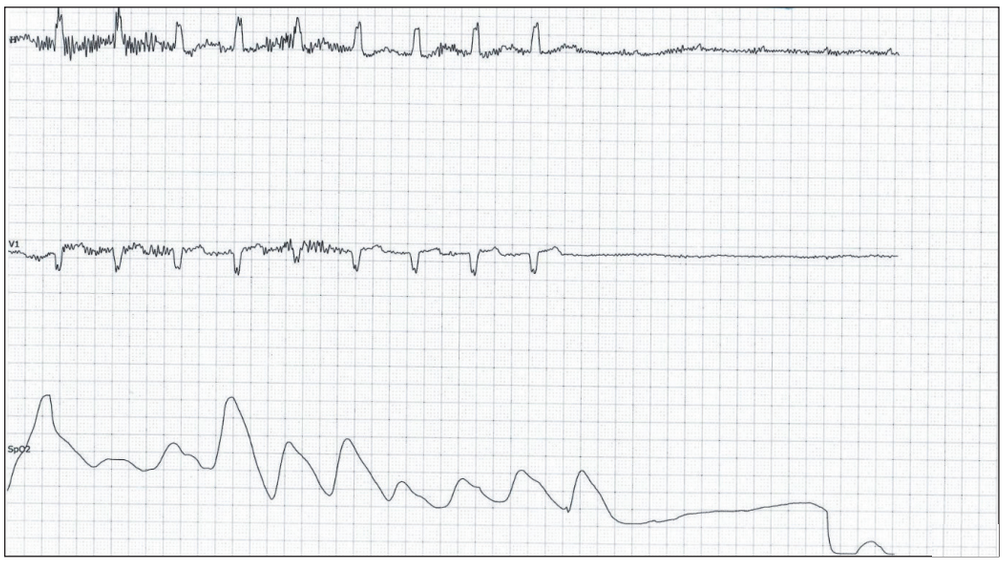

Fig. 3 – Two ECG leads and pulse oxymetry curve – sinus tachycardia followed by an asystole due to complete AV block without escape rhythm.

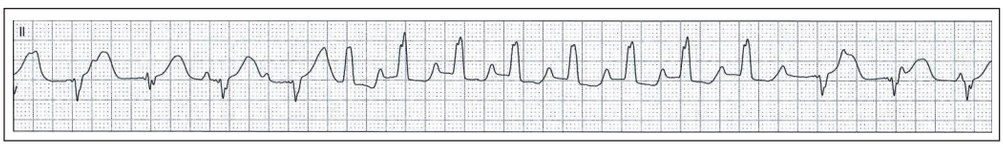

Fig. 4 – One ECG lead from cardiac monitor – initially third degree AV block with junctional rhythm of 75 bpm, further spontaneous recovery of 1 : 1 AV conduction ratio with a rate around 130 bpm and LBBB morphology, and eventually complete AV dissociation with escape rhythm.

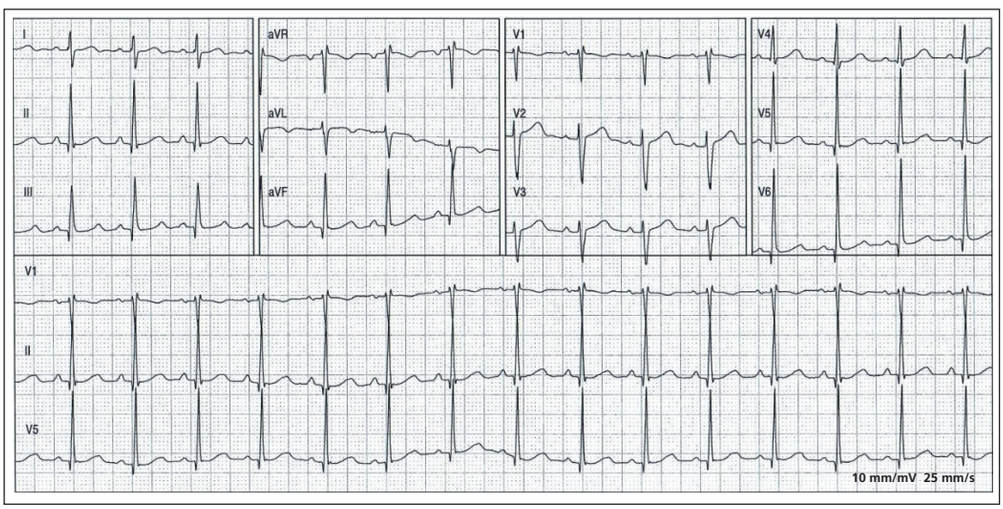

Fig. 5 – ECG before hospital discharge – sinus rhythm with a rate of 95 bpm and incomplete RBBB morphology.

to the dose of 5 mg of bisoprolol daily with good effect and tolerance. Echocardiography detected moderate mitral and tricuspid regurgitation and preserved left ventricular ejection fraction. Since AV block is an atypical manifestation of thyrotoxicosis, cardiac magnetic resonance imaging was also performed to rule out another coincidental heart disease. No signs of myocarditis or any other serious pathology were found. Systolic function of both ventricles was normal and both atria were mildly enlarged. There was no bradyarrhythmia recurrence on the established treatment. On her own request, the patient was discharged on the 12th day of hospitalization to the outpatient care. Permanent pacemaker implantation was rejected by the patient. At three-month follow-up, the patient had no recurrent syncope, and a stable sinus rhythm persisted.

Table 1 – Abnormal admission laboratory test results

Laboratory marker	Value	Reference range
Sodium	133 mmol/L	137–146 mmol/L
Potassium	3.6 mmol/L	3.8–5.0 mmol/L
Chloride	94 mmol/L	97–108 mmol/L
Gamma-glutamyl transferase	2.46 µkat/L	0.14–0.68 µkat/L
Alkaline phosphatase	2.88 µkat/L	0.66–2.20 µkat/L
C-reactive protein	43.3 mg/L	0.0–5.0 mg/L
pH	7.248	7.350–7.440
Lactate	4.8 mmol/L	0.50–2.00 mmol/L
High-sensitive troponin I	29.7 ng/L	0.0–11.6 ng/L
NT-proBNP	2763 ng/L	0–125 ng/L
TSH	0.004 mIU/L	0.500–4.900 mIU/L
fT3	22.1 pmol/L	3.4–6.3 pmol/L
fT4	71.4 pmol/L	10.0–18.7 pmol/L
TRAK	13.24 IU/L	0.00–1.75 IU/L
Anti-TPO	136 kIU/L	0–60 kIU/L
Anti-TG	401.3 kIU/L	0,0–60,0 kIU/L

Anti-TG – anti-thyroglobulin; anti-TPO – antithyroid peroxidase antibodies; fT3 – free triiodothyronine; fT4 – free thyroxine; NT-proBNP – N-terminal pro B-type natriuretic peptide; TRAK – TSH receptor antibodies; TSH – thyroid stimulating hormone.

Discussion

Hyperthyroidism is a common endocrinological disease with the prevalence of 1.2–1.6% (0.5–0.6% overt and 0.7–1.0% subclinical). Its most common cause is, as in our case, Graves' disease, which is typical for women aged 30–60 years.[1–3] It is an organ specific autoimmune disease in which circulating antibodies stimulate TSH receptors, and lead to thyroid hyperplasia and pathological overproduction of thyroid hormones.[4] These hormones have pleiotropic effects on the cardiovascular system. Indirect effects include increased sensitivity to adrenergic stimulation and increased expression of adrenergic receptors in a number of tissues.[5,6] Direct effects on myocardial cells constitute of increased adenosine transport into myocardial cells and its phosphorylation, as well as the activation of membrane Na^+/K^+-ATPase and sarcoplasmic reticulum Ca^{2+}-ATPase, which together with increased synthesis of myosin heavy chain alpha isoform contribute to increased myocardial contractility.[7,8] Clinical manifestations include sinus tachycardia, systolic hypertension with widened pulse pressure, and chest pain which may occur in patients with known coronary atherosclerosis as well as in young patients with normal coronary arteries. This can be caused by increased metabolic demands of the myocardium but also by coronary spasms.[9,10] Longstanding, untreated thyrotoxicosis can result in a development of congestive heart failure due to hyperkinetic circulation and an accentuation of regurgitant valve disease.[11,12] These conditions were quite typically manifested in the described patient.

Besides common sinus tachycardia, atrial tachycardia and atrial fibrillation, as a consequence of rapid depolarization and repolarization, shortening of action potential duration and refractory period of atrial myocardium and AV node, are present in 6 to 12% of patients (even in the subclinical form of hyperthyroidism).[13–15] In contrast, AV block in thyrotoxicosis is very rare and paradoxical. In the literature, only few case reports have been described so far, and there is only one study which associated AV block with direct autoimmune involvement of the cardiac conduction system.[16] In other studies, AV block was explained by a different factor such as electrolyte imbalance (hypercalcaemia, hypokalaemia), infection, or digoxin administration.[17–22]

There is a wide spectrum of potential aetiologies of complete AV block,[23] but in our case clear triggering factor other than thyrotoxicosis was not detected. Mildly abnormal laboratory results were not able to explain AV block. Infectious focus despite mild elevation of inflammatory parameters was not confirmed. The AV block was already present before the administration of any medication. Not even imaging methods, including cardiac magnetic resonance, showed signs of structural myocardial involvement. The diagnosis of thyrotoxicosis as an underlying cause of AV block was also supported by the fact that antithyroid treatment led to the resolution of the AV conduction abnormality.

Knowing the aetiology of AV block plays a role in distinguishing the reversible and irreversible cause and the subsequent determination of the treatment strategy, i.e. the pacemaker implantation. Complete AV block can lead to prolonged asystole, ventricular tachycardia, or ventricular fibrillation triggered by bradycardia, and may be the cause of sudden cardiac death. Other negative consequences are associated with bradycardia itself, which can lead to development of heart failure with low cardiac output and consequently to multiorgan dysfunction. According to the European Society of Cardiology and European Heart Rhythm Association guidelines, permanent pacemaker implantation is indicated in patients with third degree AV block, not only for symptom improvement but also for prognostic reasons – to reduce the recurrence of syncope and prevent sudden death. This, however, applies to patients with irreversible causes of AV block. In patients with reversible causes of AV block, permanent pacemaker implantation is not recommended.[24]

Thyroid disease is considered to be a potentially reversible cause of AV block, although opinions are not always consistent. One study followed 50 patients with thyropathy (21 with hyperthyroidism) and second or third degree AV block. Persistent or recurrent AV block was found in 40 patients (18 with hyperthyroidism), who consequently underwent permanent pacemaker implantation.[21] However, one of the limitations of this study was a very short follow-up period (21 days). Since sinus rhythm recovery can occur after prolonged euthyroid state, it is not possible to draw conclusions about the causal link between AV block and hyperthyroidism.

In our case of a young female patient, the decision whether to implant permanent pacemaker or not was not unequivocal. Nevertheless, the patient strictly refused the pacemaker implantation.

Treatment of Graves' disease is based on antithyroid drugs (ATD), and on glucocorticoids in addition to ATD

in case of severe thyrotoxicosis or thyroid storm. The effect of thyroid hormones on the cardiovascular system is supressed by beta-blockers. Beta-adrenergic blockade is recommended in all symptomatic patients, particularly in those with a resting heart rate over 90 bpm or coexistent cardiovascular disease to supress tachycardia, tremor, and anxiety. The following beta-blockers are used: nonselective beta-blocker propranolol, which can inhibit conversion of T4 to T3 at high doses (40 mg 4 times daily), selective beta-blockers atenolol, bisoprolol, metoprolol, and in the case of thyrotoxic crisis parenterally administered esmolol.[1,2] Calcium channel blockers verapamil and diltiazem can be used as an alternative in case of beta-blocker contraindication. However, the use of beta-blockers in patients with advanced AV blockade (even if only intermittent) has to be carefully considered due to their negative dromotropic effect. Nevertheless, there was no worsening of AV conduction disorder in our case. During the 12-day hospitalization, treatment consisting of antithyroid drug, glucocorticoids, and beta-blocker led to a complete stabilization of the heart (sinus) rhythm and heart failure sign regression.

Conclusion

Complete atrioventricular blockade is a prognostically significant heart rhythm disorder. In order to determine the treatment it is necessary to clarify the underlying cause. The presented case shows third degree AV block with syncope as a rare complication of Graves' thyrotoxicosis. Opinions on the optimal management, including permanent pacemaker implantation and especially its timing, differ because of insufficient data on the extent of reversibility of AV blockade with adequate antithyroid treatment.

Conflict of interests
None declared.

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