Atrioventricular block: a rare cause of effort intolerance in the young

When the heart does not accelerate and you cannot run ...

Cristiana Poroli Bastone*, Mattia Duchini*, Marcello Di Valentino, Andrea Menafoglio

* These authors equally contributed as first authors
Division of Cardiology, Ospedale San Giovanni, Bellinzona, Switzerland

Summary

Atrioventricular block in the young is a rare condition. It is defined as congenital when diagnosed in utero, at birth or during the first month of life. Childhood atrioventricular block is defined when diagnosis occurs after the first month of life up to the age of 18 years. It can be isolated (in a structurally normal heart), or associated with a congenital or acquired cardiac disease or other primary causes. The definitive treatment consists of pacemaker implantation for high-risk or symptomatic patients. We report a case of probably idiopathic isolated childhood high-degree atrioventricular block presenting with a long-standing history of effort intolerance, successfully treated with a pacemaker. This case emphasises the importance of correct evaluation of a young patient suffering from effort intolerance and the need to record an ECG when faced with an inadequate heart rate, particularly if accompanied by symptoms. We briefly review the classification, the causes, the clinical picture and the treatment of this uncommon condition.

Key words: atrioventricular block; effort intolerance; childhood; pacemaker



Case report

An 18-year-old woman was referred to our cardiology division for a bradycardia at 40 bpm and a long-standing history of effort intolerance with fatigue, shortness of breath and malaise. She never had chest pain, palpitations or syncope. Two years before, exercise-induced asthma was diagnosed, but treatment with bronchodilators did not lead to a significant improvement. Retrospectively, the bradycardia had been known at least since the age of 12 years (heart rate measured as 46 bpm at the age of 12 and 48 bpm at the age of 16). Unfortunately, no ECG was recorded. She had no other medical history. Her only medication was the treatment for asthma. She never used illicit drugs. There was no known family history of heart diseases or premature sudden death.

At clinical examination, she was in excellent general condition, the pulse was regular at 40 bpm, blood pressure was 110/75 mm Hg and oxygen saturation 98%. Heart and lung auscultation were normal, as was the rest of the clinical examination.

The resting ECGs, recorded several times (fig. 1), showed a normocardic sinus rhythm, sometimes with a 2:1 atrioventricular block (AVB) and sometimes with a complete AVB with narrow QRS complexes resulting in a bradycardia of around 40 bpm. In addition, there were nonspecific diffuse repolarisation abnormalities with a moderately prolonged QTc interval. A 24-hour Holter ECG confirmed advanced second-degree AVB (2:1 and 3:1) alternating with complete AVB with an average ventricular rate of 37 bpm (minimum 28, maximum 52 bpm) without significant pauses (maximum RR interval 2.1 seconds) and with only 10 isolated ventricular premature beats. A physical stress test was interrupted after only 80 Watts because of fatigue and dyspnoea. The ECG during exercise (fig. 2) showed a physiological increase in sinus rate up to 165 bpm with, at rest, a 2:1 AVB worsening during exercise to a 3:1 AVB with a maximum ventricular rate of 55 bpm. The echocardiogram and cardiac magnetic resonance imaging confirmed a structurally normal heart; namely, there were no signs of myocardial inflammation, infiltration or scars. Blood tests, including Lyme's serology and anti-Ro/SSA and anti-La/SSB antibodies in both the patient and her mother were negative. The ECGs of the mother and the two younger sisters were normal. The ECG of the father was not available. The patient refused a cardiac genetic analysis.

We retained the diagnosis of high-degree AVB (advanced second degree and third degree), isolated (structurally normal heart), which most likely occurred in childhood since bradycardia was known at least from the age of 12. The AVB was probably idiopathic, although a genetic origin was also possible. We considered the AVB mainly responsible for the patient's symptoms because of chronotropic incompetence, and asthma only as a possible contributing factor.

A dual chamber pacemaker programmed in DDD mode was implanted. The symptoms considerably improved. At a 3-month follow-up, during a new stress test, she reached 160 Watts (previously 80 Watts), with restoration of the chronotropic response during effort (fig. 3). No atrial or ventricular arrhythmias were recorded in the pacemaker memory.

Published under the copyright license "Attribution – Non-Commercial – NoDerivatives 4.0". No commercial reuse without permission. See: http://emh.ch/en/services/permissions.html

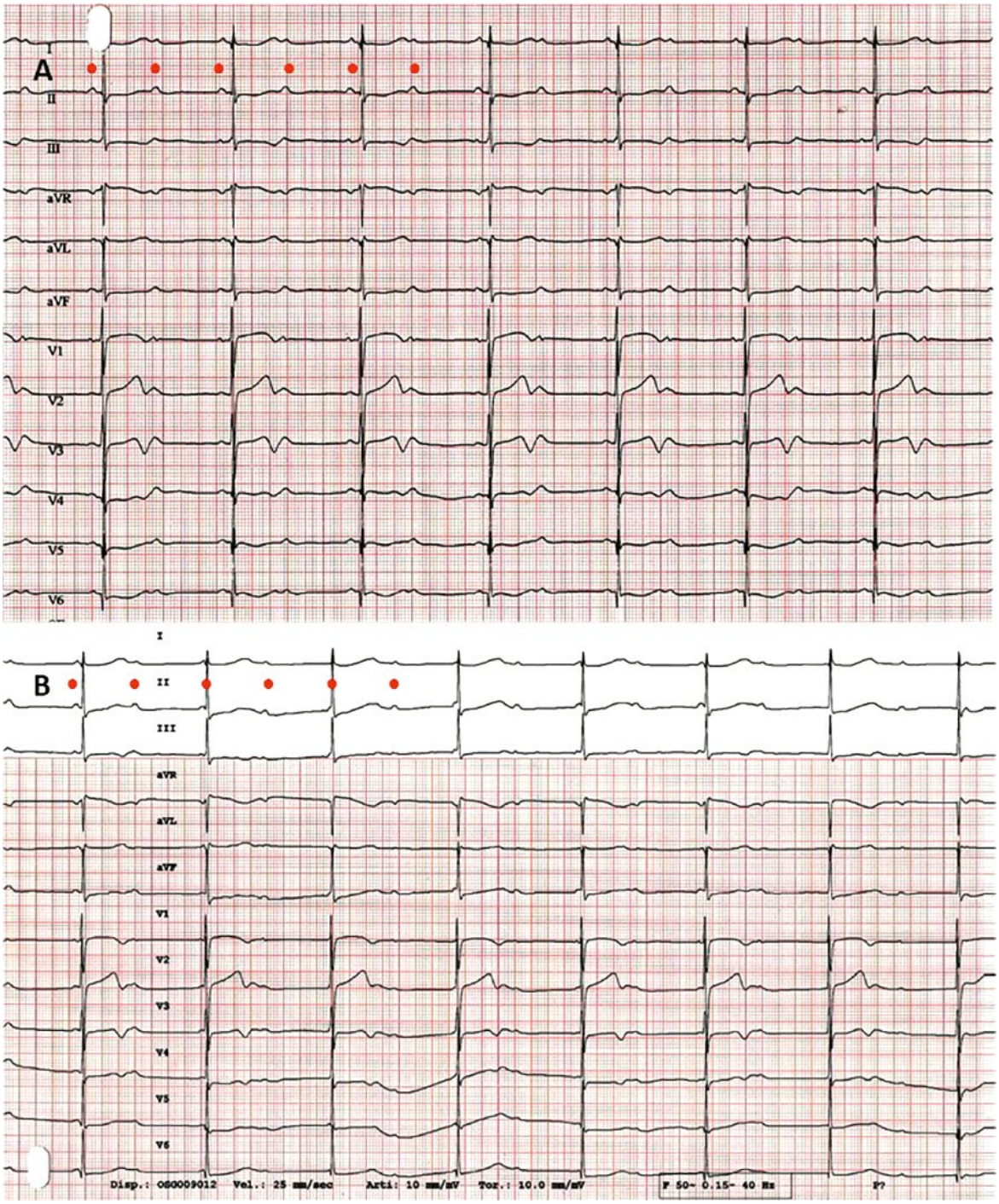


Figure 1: ECG at rest (two tracings). A: sinus rhythm at 84 bpm with 2:1 atrioventricular block (AVB) and narrow QRS complexes at 42 bpm. B: sinus rhythm at 78 bpm with complete AVB and narrow QRS complexes at 40 bpm. The first six sinus P waves are indicated with a red dot. The QRS complexes are normal; there are diffuse nonspecific repolarisation abnormalities. The QTc interval is moderately lengthened to 480 ms (A) and 508 ms (B).

Discussion

We have described the case of a young girl suffering from chronic effort intolerance related to AVB. We would like to emphasise some important aspects of the assessment of young people with limited effort capacity. In addition, we will briefly review the main characteristics of this rare condition.

Our patient had suffered from effort intolerance since childhood, initially attributed to asthma. However, treatment did not lead to a satisfactory response. In situations like this, other pathological conditions should

Published under the copyright license "Attribution – Non-Commercial – NoDerivatives 4.0". No commercial reuse without permission. See: http://emh.ch/en/services/permissions.html

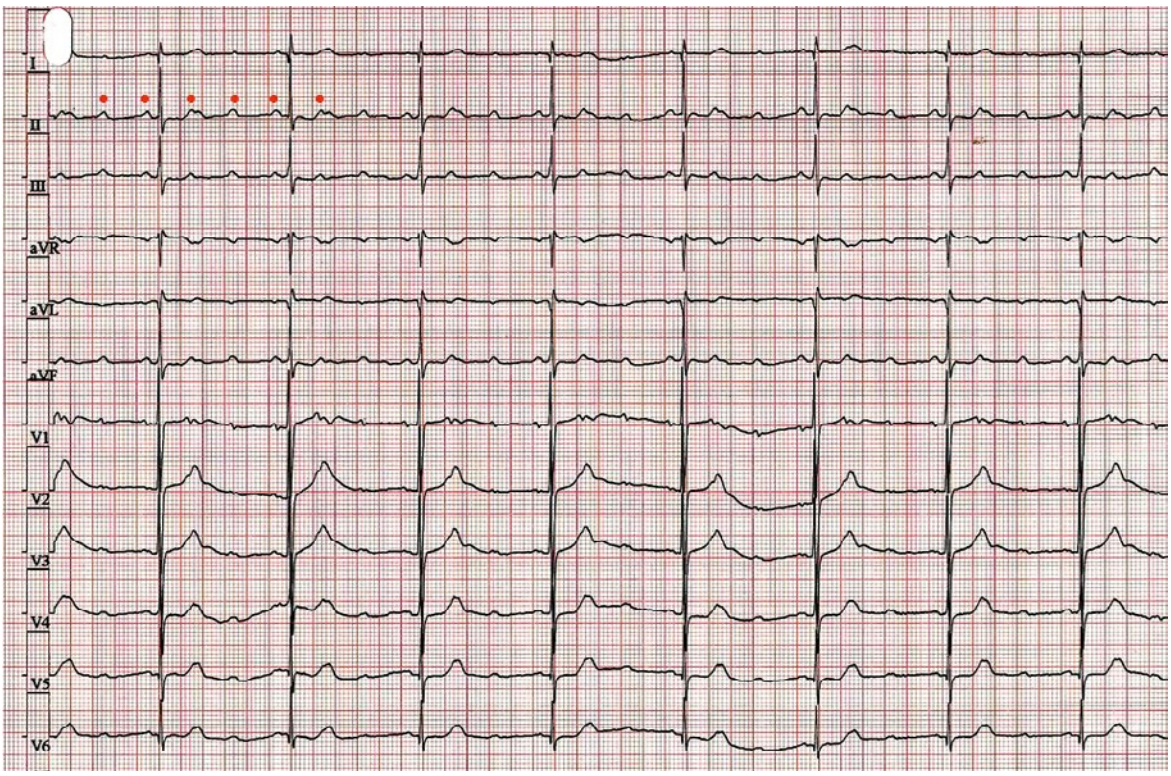


Figure 2: ECG during exercise: physiological sinus tachycardia at 150 bpm (the first six sinus P waves are indicated with a red dot) with 3:1 atrioventricular block and ventricular rate of 50 bpm. Compared with the resting ECG, note the normalisation of repolarisation and of the QTc interval (422 ms).

be investigated to explain the reduced exercise capacity in an otherwise healthy young patient.

Bradycardia has been documented in our patient at least since the age of 12. Bradycardia can be physiological in healthy young people, in athletes or during sleep as a sign of vagotonia. On the other hand, when it is inadequate for the clinical condition, or if it is accompanied by symptoms, as in our case, or by abnormal clinical signs, it can be the result of rhythm or conduction disorders and requires an ECG recording. In our patient, the diagnosis of high-degree AVB was finally made only at the age of 18, but very likely it had been present at least from the age of 12.

AVB in the paediatric age group is rare. It is defined as congenital when diagnosed in utero, at birth or during the first month of life. Childhood AVB is defined when diagnosis is made after the first month of life up to the age of 18 [1]. The AVB can be isolated (occurring in a structurally normal heart without other predisposing conditions), or associated with a congenital or acquired cardiac disease or other primary causes [2] (fig. 4).

Congenital AVB has an incidence of 1:15,000–20,000 newborns. About one third are associated with anatomical abnormalities or rare acquired causes, the remaining two thirds are isolated. Isolated congenital AVB is a passively acquired autoimmune disease of the fetus. In fact, in about 95% of the mothers of newborns with isolated congenital AVB, anti-Ro/SSA and anti-La/SSB antibodies are detected. These antibodies cross the placenta to reach the fetal circulation, where they can generate an inflammatory response in the cardiac conduction system at the level of the atrioventricular junction, potentially leading to local fibrosis. This can result in an AVB, which is usually complete and irreversible. Note that these antibodies can be detected in 1–2% of all pregnant women (of whom the great majority are asymptomatic), but only 2–5% of the fetuses whose mothers are antibody positive develop an AVB [2–4].

Childhood AVB is more commonly associated with other heart conditions. The causes are multiple. Among the congenital heart diseases, corrected transposition of the great vessels and endocardial cushion defects are typically associated with AVB. Infectious or inflammatory myocarditis, infiltrative, ischaemic or valvular heart diseases, cardiomyopathies, tumours, sequelae of cardiac surgery or percutaneous interventions, radiotherapy, drugs, multisystem neuromuscular or metabolic diseases, can all be accompanied by AVB [2] (fig. 4). When facing a young patient with AVB, it

Published under the copyright license "Attribution – Non-Commercial – NoDerivatives 4.0". No commercial reuse without permission. See: http://emh.ch/en/services/permissions.html

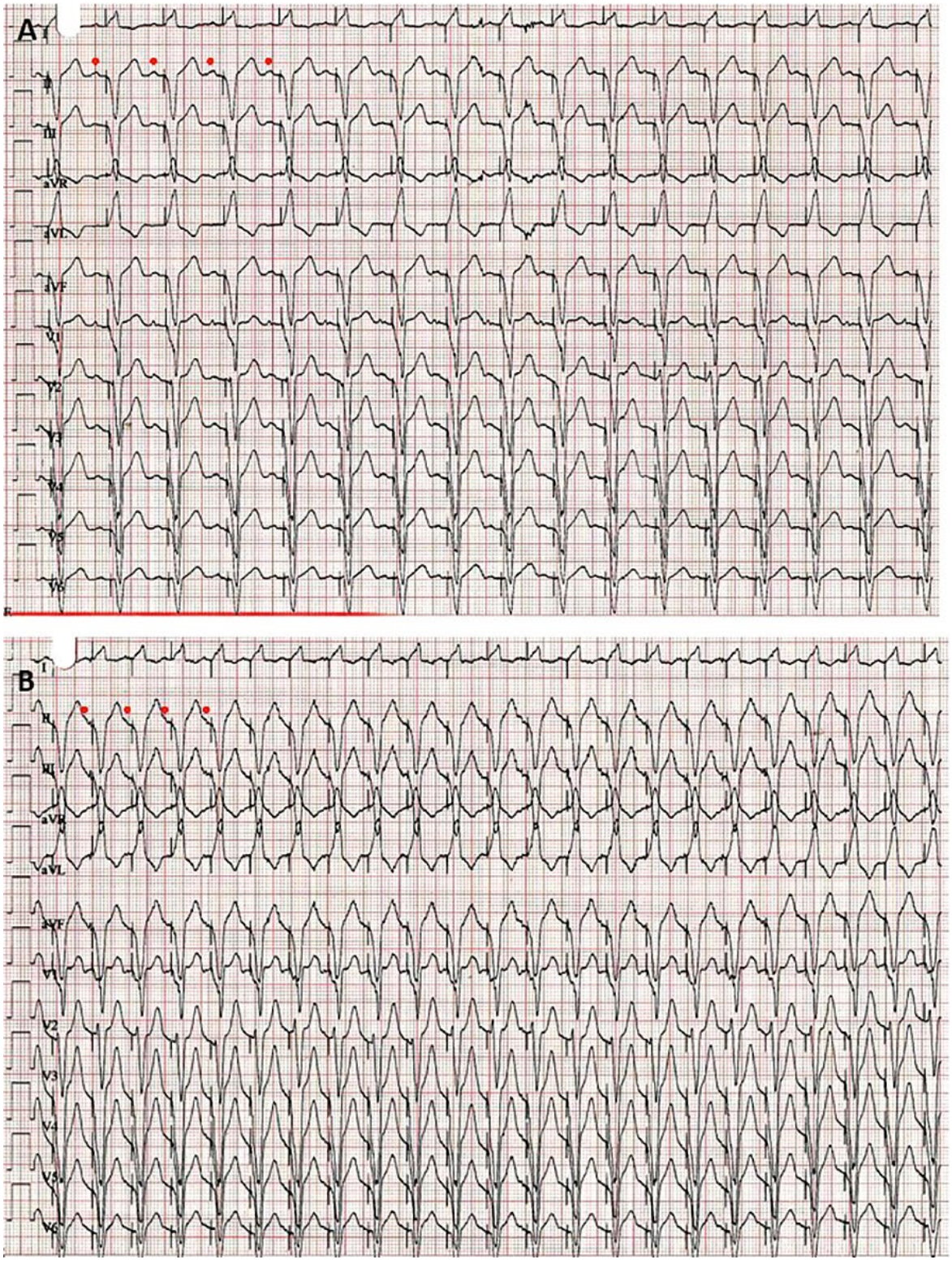


Figure 3: ECG after implantation of a dual chamber pacemaker programmed in DDD mode. A: resting ECG with sinus rhythm at 96 bpm with electro-stimulated ventricular rhythm synchronous to the P wave. B: ECG during exercise showing sinus tachycardia at 139 bpm with synchronous ventricular rhythm. The first four sinus P waves of each trace are indicated with a red dot.

Published under the copyright license "Attribution – Non-Commercial – NoDerivatives 4.0". No commercial reuse without permission. See: http://emh.ch/en/services/permissions.html

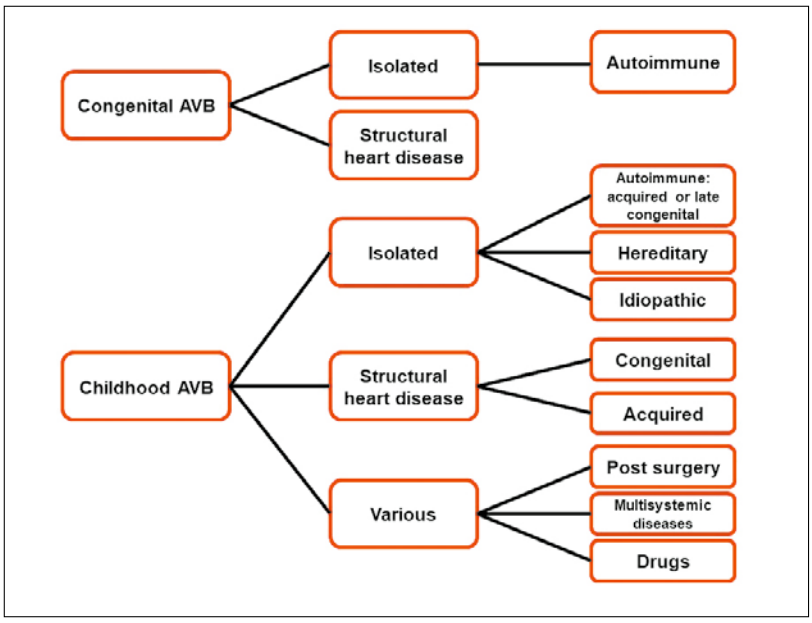


Figure 4: The main causes of paediatric atrioventricular block (AVB) (modified from reference [2]).

is therefore essential to perform an overall clinical evaluation to exclude primary causes. In our patient, there was no clue to a primary pathology linked to the AVB and the heart was structurally normal, leading us to conclude that this was an isolated AVB. Among the isolated childhood AVBs, three causes can be identified: autoimmune, genetic and idiopathic. There are two types of autoimmune AVB: a late progressive congenital form where anti-Ro/SSA and anti-La/SSB antibodies are found only in the mother, and an acquired form where these antibodies develop during childhood (and are found only in the patient). Together, they can represent up to 20% of cases of isolated childhood AVB [5, 6]. In our case, an autoimmune cause was excluded by the absence of antibodies in the patient and her mother. Recently, it has been found that a significant proportion of isolated AVBs in young people have a hereditary basis in the form of a genetic mutation [7, 8]. Some mutations (for example in the *SCN5A* gene) can lead to overlap syndromes with sinus disease, conduction disturbances, QTc prolongation and a Brugada ECG pattern. In our patient, the prolongation of the QTc interval could suggest such an origin. However, there was no clinical evidence for a hereditary origin. Unfortunately, a genetic analysis was not performed. The diagnosis of idiopathic isolated AVB was therefore retained, although a genetic origin was also deemed possible.

Unlike isolated congenital AVBs, isolated childhood AVBs can be partial (first or second degree), but they often evolve to complete AVB. In the vast majority of cases, the escape QRS complexes are narrow, indicating an injury of the atrioventricular junction [9–12], as in our case. The site of block can be determined by non-invasive manoeuvres: exercise or atropine improve atrioventricular nodal blocks but worsen infranodal blocks (which have a worse prognosis). Vagal manoeuvres, such as carotid sinus massage, have the opposite effect [13]. In our case, QRS complexes were narrow and the AVB worsened during exercise, suggesting that the block was in the bundle of His.

The clinical manifestations of isolated AVBs are variable, but usually more severe in the congenital form than in the childhood one. Sometimes AVBs remain asymptomatic and are discovered incidentally. Sometimes they cause nonspecific symptoms such as fatigue, discomfort, dizziness and sleep disorders. They may also manifest as exercise intolerance, as in our case, or, more rarely (particularly in the congenital form), as major symptoms such as syncope, cardiac failure and even cardiac arrest. Without treatment, the mortality of congenital isolated AVBs reaches 14–34% in the fetus and newborn, 8–16% in infants and 4–8% in children and adults [2, 3, 11, 12].

The definitive treatment of congenital or childhood high-degree AVB consists of implanting a pacemaker. Pacing is recommended in patients with symptoms related to the AVB (syncope, heart failure, exercise intolerance). Patients with syncope or heart failure should be implanted without delay. In asymptomatic patients or those with nonspecific symptoms, the prognostic significance of the AVB should be evaluated. A number of parameters are considered risk factors for adverse outcome, although the results of several studies are controversial. Ventricular dysfunction, resting bradycardia <55 bpm up to 1 year of age or <50 bpm beyond one year, asystole >3 seconds, wide escape QRS complexes, complex ventricular arrhythmias and QTc prolongation are considered markers for increased risk of mortality and may represent an indication for prophylactic pacemaker implantation [2, 3, 14, 15]. Our patient suffered from reduced effort tolerance, and she had resting bradycardia <50 bpm and prolongation of the QTc interval. Therefore, in our case the pacemaker was indicated for both symptomatic and prognostic reasons. If in the past a pacemaker was implanted mainly for symptomatic reasons (about 50% of the patients were implanted in some old studies [12]), in more recent series the indication is often prophylactic and the great majority of the patients finally benefited from the pacemaker (between 79 and 95% in recent series [9–11]). The broader use of pacemakers appears to be the main reason for the improved prognosis of patients with an isolated AVB. For example, in a recent multi-

Published under the copyright license "Attribution – Non-Commercial – NoDerivatives 4.0". No commercial reuse without permission. See: http://emh.ch/en/services/permissions.html

centre study of 141 patients with isolated AVB of whom 79% received a pacemaker, there were no deaths during an average follow-up of 11.6 years [9]. Therefore, the arising problem concerning asymptomatic patients is mainly to know when to implant the pacemaker rather than deciding whether implanting it or not. The decision must consider the risk related to the AVB, the risk of the procedure itself and particularly the high risk of serious long-term complications in the face of a lifetime of pacing. An epicardial lead is commonly used in children weighing less than <20 kg (<6 years) because of the high risk of venous obstruction if a transvenous lead were used in a small size venous network. Epicardial pacing requires a major operation and lead dysfunctions are more frequent than in transvenous systems, reaching 27% at 5 years [3, 16–18]. The endovascular approach is usually chosen in children weighing more than 20 kg. The major long-term complications are related to the lead. Lead dysfunction occurs more frequently in children than in adults because of the increased mechanical stress (small space between clavicle and ribs, somatic growth, more physical activity). The 5-year rate of lead dysfunction in children ranges between 5 and 24% [3, 16–18], in adults between 1 and 9% [19]. Over several decades it is likely to be close to 100%. This will lead to a series of reinterventions, including lead extraction, an especially high-risk procedure in children. Venous occlusion is another frequent complication, involving 20–30% of patients, and can be an important obstacle in the event of reintervention. Infectious complications are relatively rare but very serious, usually requiring the extraction of the whole system. Tricuspid regurgitation due to entrapment of the lead can occasionally be severe [3, 16–19]. In a large study, the overall complication rate at 5 years in pacemaker therapy was 19.7%, with a reintervention rate of 8.2% [20]. Therefore, over a lifetime of pacing, complication rates can be extremely high. Another concern in these patients, who are expected to be paced 100% through life, is the deleterious effect that right ventricular apical pacing may have on left ventricular function. His bundle pacing has recently generated interest as a feasible and more physiological stimulation with encouraging clinical results [21, 22]. Therefore, His bundle pacing could be a potential beneficial technique in these young patients and could encourage an implantation at an earlier stage.

Correspondence:
Cristiana Poroli Bastone, MD
Division of Cardiology
Ospedale San Giovanni
CH-6500 Bellinzona
cristiana.porolibastone[at]eoc.ch

Disclosure statement
No financial support and no other potential conflict of interest relevant to this article was reported.

References

1 Brucato, A, Jonzon, A, Friedman, D. Proposal for a new definition of congenital complete atrioventricular block. Lupus. 2003;12:427–35.
2 Baruteau A-E, Pass RH, Thambo J-B, et al. Congenital and childhood atrioventricular blocks: pathophysiology and contemporary management. Eur J Pediatr. 2016;175:1235–48.
3 Bordachar P, Whinnett Z, Ploux S, Labrousse L, Haissaguerre M, Thambo J-B. Pathophysiology, clinical course and management of congenital complete atrioventricular block. Heart Rhythm. 2013;10:760–6.
4 Brito-Zerón P, Izmirly PM, Ramos-Casals M, Buyon JP, Khamashta MA. Autoimmune congenital heart block: complex and unusual situations. Lupus. 2016;25:116–28.
5 Lazzerini PE, Capecchi PL, Laghi-Pasini F. Isolated atrioventricular block of unknown origin in adults and anti-Ro/SSA antibodies: clinical evidence, putative mechanisms, and therapeutic implications. Heart Rhythm. 2015;12:449–54.
6 Bergman G, Skog A, Tingström G, et al. Late development of complete atrioventricular block may be immune mediated and congenital in origin. Acta Paediatr. 2014;103:275–81.
7 Baruteau A-E, Behaghel A, Fouchard S, et al. Parental electrocardiographic screening identifies a high degree of inheritance for congenital and childhood non-immune isolated atrioventricular block. Circulation. 2012;126:1469–77.
8 Baruteau A-E, Probst V, Abriel H. Inherited progressive cardiac conduction disorders. Curr Opin Cardiol. 2015;30:33–9.
9 Baruteau A-E, Fouchard S, Behaghel A et al. Characteristics and long-term outcome of non-immune isolated atrioventricular block diagnosed in utero or early childhood: a multicenter study. Eur Heart J 2012;33:622–9.
10 Villain E, Coastedoat-Chalumeau N, Marijoin E, Boudjemline Y, Piette J-C, Bonnet D. Presentation and prognosis of complete atrioventricular block in childhood, according to maternal antibody status. J Am Coll Cardiol. 2006;48:1682–7.
11 Jaeggi ET, Hamilton RM, Silverman ED, Zamora SA, Hornberg LK. Outcome of children with fetal, neonatal or childhood diagnosis of isolated congenital atrioventricular block. A single institution's experience of 30 years. J Am Coll Cardiol. 2002;39:130–7.
12 Michaëlsson M, Jonzon A, Riesenfeld T. Isolated congenital complete atrioventricular block in adult life. A prospective study. Circulation. 1995;92:442.
13 Wellens HJJ, Conover MB. The ECG in emergency decision making. Philadelphia, 1992, Sauders, pp. 115–128.
14 Brignole M, Auricchio A, Baron-Esquivias G, et al. ESC guideline on cardiac pacing and acrdiac resynchronisation therapy: the task force on cardiac pacing and resynchronisation therapy of the European Society of Cardiology (ESC). Developed in collaboration with the European Heart Rhythm Association (EHRA). Eur Heart J. 2013;34:2281–329.
15 Epstein AE, Di Marco JP, Ellenbogen KA, et al. 2012 ACCF/AHA/HRS focused update incorporated into the ACCF/AHA/HRS 2008 guidelines for device-based therapy of cardiac rhythm abnormalities. A report of the American College of Cardiology Foundation/American Heart Association Task Force on Practice Guidelines and the Heart Rhythm Society. J Am Coll Cardiol. 2013;61:e6-75.
16 Takeuchi D, Tomizawa Y. Pacing device therapy in infants and children: a review. J Artif Organs. 2013;16:23–33.
17 Janousek J, Kubus P. What's new in cardiac pacing in children? Curr Opin Cardiol. 2014;29:78–82.
18 Chandler SF, Fynn-Thompson F, Mah DY. Role of cardiac pacing in congenital complete heart block. Expert Rev Cardiovasc Ther. 2017;15:853–61.
19 El-Chami, MF, Rao B, Shah AD, et al. Long-Term Performance of A Pacing Lead Family: A Single Center Experience. Heart Rhythm 2018. doi.org/10.1016/j.hrthm.2018.10.024.
20 Udo EO, Zuithoff NPA, van Hemel NM et al. Incidence and predictors of short-and long-term complications in pacemaker therapy: The FOLLOWPACE study. Heart Rhythm. 2012;9:728–35.
21 Vijayaraman P, Chung MK, Dandamudi G et al. His bundle pacing. J Am Coll Cardiol. 2018;72:927–47.
22 Burri H, Stettler C. Direct His bundle pacing in routine clinical practice. Cardiovasc Med. 2018;21:249–54.

Published under the copyright license "Attribution – Non-Commercial – NoDerivatives 4.0". No commercial reuse without permission. See: http://emh.ch/en/services/permissions.html