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Increased baroreceptor sensitivity in a patient with hereditary spastic paraplegia – type SPG11

A case report

Abstract: An 18 years old male patient was diagnosed with genetically confirmed hereditary spastic paraplegia of type SPG11 - a rare disease of neurodegeneration. During normal clinical routine investigation, he presented with a moderate sinus bradycardia. The function of the cardiovascular system was investigated by recording electrocardiogram, impedance cardiogram and continuous blood pressure non-invasively. Cardiac function appeared normal in all modalities. Baroreflex sensitivity was strongly increased by a factor of 2.8. Results indicate that further to hyperactivity of deep tendon reflexes, also the responsiveness regarding control of heart rhythm by baroreceptors is significantly increased. This finding provides evidence for the impact of a neurological disorder onto the cardiovascular system and its autonomic control.

Keywords: Hereditary spastic paraplegia, baroreflex sensitivity, SPG11.

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1 Introduction

Hereditary spastic paraplegia (HSP) is a rare inborn progressing disease of neurodegeneration causing progressing ataxia of the lower limbs [1], [2]. Its prevalence is approximately 5–8:100,000 inhabitants.

In an 18-year-old male patient, HSP of the complex type SPG11 [3] was confirmed by routine genetic testing. In SPG11

patients, neurodegeneration affects the central and peripheral nervous system. Upon routine ECG recording, the patient presented with a sinus bradycardia. We hypothesized that bradycardia might be caused by the impact of the primary neurological disease onto the nervous control of circulatory activity.

Heart rate variability (HRV) and sensitivity of the arterial baroreflex (BRS) are frequently used methods for investigating autonomic nervous system control of cardiac function. HRV and BRS can be assessed at low risk profile within a few minutes [4]. Therefore, we chose these methods for testing our hypothesis.

2 Methods

2.1 Clinical history

Clinically, a male patient presented with over the years increasing spasticity particularly of the lower limbs. At an age of 18 years, the patient was dependent on walking aids and wheel chair. HSP was genetically confirmed with two non-sense mutations at location SPG11. In a twelve-lead ECG recorded at rest, a moderate sinus bradycardia (first degree sinoatrial block) was manifested. The morphology of P, QRS and T wave was normal providing no evidence for an underlying structural heart disease. Furthermore, no history of a cardio-vascular disease was documented.

2.2 Measurement

The subject gave written informed consent to the study. Recordings were performed in a quiet room and ambient temperature was between 20°C and 24°C. The subject was studied 2 hours after consuming a light meal while in the supine position and breathing spontaneously at a comfortable tidal volume. Lead I and II of the ECG, continuous finger blood pressure and impedance cardiogram (ICG) were

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continuously recorded for 20 minutes at physical rest (Task Force Monitor, CN-Systems, Graz, Austria). All signals were digitized by a 16-bit analog-to-digital converter. Sampling rate was 1000 Hz for ECG, 500Hz for ICG and 100 Hz for blood pressure. The last 75 seconds of the interval were used for evaluation.

After the recording, the walking ability of the subject was documented performing a short distance walking test and a stair stepping test [2]. Linear regressions taken from [2] were used for estimating the spastic paraplegia rating score (SPRS) value. Live style with respect to physical exercise was documented.

2.3 Data Analysis

The built-in software analysis tools of the Task Monitor System [4] were used for studying HRV parameters and BRS [5]. The result obtained for BRS where compared to data of a normal, healthy population as described in [6]. According to this reference data, the age depended normal mean $BRS_m(age)$ value is defined by:

$$\ln(BRS_m) = 3.3 - 0.027 \times age. \quad (1)$$

where the age is entered in years. Data was normalized by the normal value expected at an age of 18 years for analysis.

3 Results

After starting measurement of circulatory parameters an initial time interval was used for calibration of the sensors and for allowing the subject to obtain a comfortable resting state. The last 75 seconds out of 20 minutes were evaluated. Mean heart rate was 58 beats per minute. P-QRS-T morphology of the ECG was normal. Mean systolic and diastolic blood pressure was 118 and 72 mmHg. HRV revealed that both sympathetic and parasympathic activity contribute to the control of the circulatory system. A mean stroke volume (SV) of 109 ml was estimated from the ICG. Hemodynamic values like cardiac output, SV and total peripheral resistance obtained from ICG showed normal pumping performance of the heart.

A BRS value of 46.8 ms/mmHg was obtained. The normal mean value at an age of 18 years is 16.7 ms/mmHg. Thus, the value is increased by a factor of 2.8. Comparing this value to the data presented in [6] 1132 out of 1134 normal subjects do have a smaller BRS. Thus, the probability to obtain such a high BRS in a normal cohort is estimated by 0.002. When limiting the analysis to the youngest age group in [4] (18 to 29 years,

235 individuals) the probability for observing such a high BRS is estimated by 0.004.

The time needed for walking a 10-meter distance including a 180° turn after 5 meters was 34 seconds. The time needed for stepping five stairs down and back up again was 62 seconds. Both values correspond to an SPRS value of approximately 30. Live style assessment revealed that the subject performs no sportive activity not even by using a wheel chair or a home trainer device. Once a week, a one-hour physiotherapeutic training was performed under the guidance of a professional coach.

4 Conclusion

Assessment of walking ability revealed a progressed state of the HSP – type SPG11 disease close to the complete loss of independent walking ability [2]. A moderate sinus bradycardia was confirmed by measurements performed with the Task Force monitor system. Both ECG and ICG provided no hint for an underlying structural heart disease.

Most prominently a 2.8-fold increase of BRS was observed. While a high BRS in normal subjects is typically related with a physically trained body condition [6], life style assessment of our patient did not reveal any hint of regularly practicing physical exercise. Hence, it suggests that BRS increase is a consequence from the disease itself. Spasticity is caused hyperactivity of deep tendon reflexes. In other words, reflexes are overexpressed causing spastics. This overexpression of reflexes was also observable for the baroreceptor reflex in the investigated subject. Our finding provides initial evidence, that HSP – type SPG11 can also affect the nervous control of the cardiovascular system.

Author Statement

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