What Is High Enough? Elevated NT-pro-BNP in Decompensated Paroxysmal Supraventricular Tachycardia

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Abstract

Since the late 1980s, elevated atrial natriuretic peptide (ANP) was considered the cause of brisk diuresis in adult patients with paroxysmal supraventricular tachycardia (PSVT). Pro-brain natriuretic peptide (pro-BNP) and related molecules, e.g., N-terminal pro b-type natriuretic peptide (NT-pro-BNP) are known biomarkers of heart failure in adult patients from many causes with probable relevance in children. Perhaps, pro-BNP or related molecules such as NT-pro-BNP are useful in the management of PSVT in infants, thus hastening treatment in children who may otherwise significantly decompensate. Case series of one infant and two neonates presenting with cardiogenic shock and evidence of heart failure are presented. Cardiac monitoring or electrocardiogram (ECG) confirmed the presence of PSVT. Adenosine was administered resulting in successful chemical cardioversion with each case. Significantly elevated NT-pro-BNP levels correlated with heart failure prior to cardioversion. In each case, patients were discharged home with lower NT-pro-BNP levels and maintenance with a β -blocker. Due to documented relationships between elevated pro-BNP level and heart failure in adults, the authors measured the related biomarker NT-pro-BNP in each case, as the relationship could be similar in pediatric PSVT. Based on our experience with children in acute heart failure from other causes, NT-pro-BNP can increase to potentially extreme levels in infants. It appears to correlate with clinical signs of insufficient cardiac output, such as tachycardia, respiratory distress, and moribund appearance. Indeed, in the case series, extremely high NT-pro-BNP values were obtained when the patients appeared moribund from decompensated PSVT. The question arising from these observations is:

Keywords

- BNP
- brain natriuretic peptide
- NT-pro-BNP
- paroxysmal supraventricular tachycardia
- infant(s)
- neonate(s)
- cardiogenic shock

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At what level of elevated NT-pro-BNP, would patients be identified for cardioversion prior to appearance of other signs and symptoms? For each patient within the case series, NT-pro-BNP levels of approximately 20,000 pg/mL were indicative of decompensated heart failure, which was subsequently confirmed by examination of the patient. Further investigation is needed to determine the clinical significance of NT-pro-BNP and related peptides in pediatric patients with PSVT and intermittent PSVT. However, the possibility exists that an increase in NT-pro-BNP and related peptides could be a biomarker for cardiac decompensation after prolonged or intermittent PSVT, thereby shortening the time of diagnosis and intervention, and hence, potentially preventing morbidity, mortality, and extended hospitalization. Additional evidence-based research would help provide biomarker information during PSVT allowing practitioners to more objectively analyze risks.

Introduction

Paroxysmal supraventricular tachycardia (PSVT) may lead to cardiogenic shock in infants and children requiring emergency cardioversion. Optimal timing of cardioversion rests on the perception of “decompensation.” Subjective clinical assessment of distress and need for intervention before development of end-organ dysfunction varies among even experienced practitioners. Cardioversion poses varying risks, but early intervention is critical. Since the late 1980s, it has been known that atrial natriuretic peptide (ANP) becomes elevated in adult patients with PSVT and is considered the cause of brisk diuresis.^{1,2} Pro-brain or b-type natriuretic peptide (pro-BNP) and related molecules such as N-terminal pro b-type natriuretic peptide (NT-pro-BNP) are known biomarkers of heart failure from many causes in adults³ and are proposed to have relevance in children.^{4–6} Elevated pro-BNP levels have been demonstrated during PSVT in adults⁷ but are not routinely measured in infants and children with suspected or noted PSVT. Demonstration of elevated NT-pro-BNP during or between PSVT events might lead to earlier treatment in children prior to development of decompensation.

Cases

Case 1

Our initial patient was a 6-month-old female noted to be tachycardic and tachypneic by her pediatrician during a well visit. History revealed persistent emesis with inability to retain formula or infant electrolyte solution for 12 hours, since 8:00 PM the previous evening. History included a 1-month neonatal intensive care unit (NICU) stay with multiple episodes of PSVT managed with digoxin and subsequently with atenolol 2 months prior to presentation.

The infant was referred to a local emergency department (ED) of an outlying hospital at 12:30 PM in severe respiratory distress. RSV and influenza tests were negative. She was given two albuterol treatments and two 20 mL/kg boluses of normal saline. There was no improvement in her condition and an electrocardiogram (ECG) revealed PSVT. Unsuccessful chemical conversion was attempted twice with adenosine (0.1 mg/kg) administered via a dorsal metacarpal vein IV. The

patient was then transferred by ground to our pediatric intensive care unit (PICU). No emergency medical service (EMS) records were available to document whether the patient remained in PSVT during the 3-hour transport.

Assessment upon arrival to PICU at 7:10 PM revealed a distressed, pale, and lethargic infant with a documented capillary refill time of 3 seconds and a liver edge palpable 2 cm below the right costal margin. Heart rate was 280 beats per minute (bpm) and a 12-lead ECG confirmed PSVT (►Table 1). A right external jugular IV was immediately placed and adenosine (0.1 mg/kg) was rapidly administered for cardioversion without success. The dose was immediately doubled and administered via the same IV. After the second dose, a 12-lead rhythm strip transiently revealed no atrial activity during atrioventricular node block. Successful conversion to sinus tachycardia (rate, 162 bpm) was then noted with the presence of p waves (►Table 1).

Follow-up ECG during normal sinus rhythm demonstrated the presence of delta waves with right axis deviation and nonspecific ST-T wave abnormalities consistent with Wolf-Parkinson-White syndrome and possible myocardial strain/inflammation/injury along with intraventricular conduction delay (►Fig. 1). After stabilization, two-dimensional (2-D) echocardiography identified a fenestrated atrial septal defect (ASD) with bidirectional flow, severe pulmonic stenosis, normal left ventricular dimensions, low-normal function, and a right pleural effusion. No significant pericardial effusion was noted. Plasma NT-pro-BNP level initially was elevated to 19,534 pg/mL on admission and decreased to 1,310 pg/mL at discharge (►Table 1). Of note, the patient had a second episode of PSVT on day 2 of hospitalization and was discharged 3 days later.

Case 2

Two neonates with PSVT were subsequently admitted to the PICU the following year. The first was a 4-day-old term male who presented to newborn nursery for a weight check and was found to have severe tachycardia, tachypnea (80 s), and poor femoral pulses. Pulse oximeter revealed a heart rate of 280 to 290 bpm, confirmed on cardiac monitor. The patient was immediately admitted to the PICU for resuscitation and

Table 1 Pre/post adenosine ECG and admission/discharge NT-pro-BNP results

	Pre-adenosine ECG	Post-adenosine ECG	NT-pro-BNP admission	NT-pro-BNP discharge
Patient #1	HR: 289 bpm, QRS: 256 ms, QT/QTc: 191/419 ms	HR: 162 bpm, PR int: 66 ms, QRS: 102 ms, QT/QTc: 271/361 ms	19,534 pg/mL	1,310 pg/mL
Patient #2	HR: 280–290 bpm, No preadenosine ECG obtained	HR: 125, PR int: 160 ms, QRS: 64 ms, QT/QTc: 285/359 ms	21,680 pg/mL	3,078 pg/mL
Patient #3	HR: 280 bpm, QRS: 175 ms, QT/QTc: 168/281 ms	No post adenosine ECG obtained	24,572 pg/mL	2,575 pg/mL

Abbreviations: BNP, b-type natriuretic peptide; bpm, beats per minute; ECG, electrocardiogram; HR, heart rate; PR int, PR interval; NT-pro-BNP, N-terminal pro-b-type natriuretic peptide; QRS, Q, R, and S waves.

Note: Normal values for NT-pro-BNP are age related: 3–11 d: 28–7, 250 pg/mL

>1 mo to ≤ 1 yr: 5–1, 121 pg/mL^a

^a(22)

cardioversion. Documented arrival PICU examination revealed a dusky, mottled, drowsy neonate with weak femoral pulses. Emergent right external jugular venous access was obtained. Administration of adenosine (0.1 mg/kg) for cardioversion was unsuccessful, but cardioversion was successful with doubling of the dose. The heart rate decreased to 160 bpm with rapidly improving perfusion. Propranolol (0.5 mg/kg orally) was started immediately every 6 hours after stabilization. The 2-D transthoracic echocardiography (TTE) revealed trace tricuspid insufficiency, small patent ductus arteriosus, and slightly decreased left ventricular function. Subsequent TTE showed adequate biventricular function without chamber enlargement or hypertrophy, and ECG showed normal sinus rhythm. Initial NT-pro-BNP level, drawn at admission, was elevated to 21,680 pg/mL. It continued to trend downward throughout hospitalization, reaching 3,078 pg/mL at the time of discharge 36 hours later (►Table 1). Of note, the mother indicated that she thought the “heart was racing” during the night prior to admission.

Case 3

The third patient was a previously healthy, nearly 4-week-old term male. In the afternoon on the day of admission, mother reported a decreased oral intake to his pediatrician, who recommended infant electrolyte solution, which was also refused by the patient. He developed intermittent emesis and the mother observed a “prominent” heartbeat. He was taken to the ED, where initial heart rate was recorded as 140 bpm. Two 20 mL/kg boluses of normal saline were administered and he was observed. Assessment by a different provider 2 hours later revealed tachypnea, grunting, and tachycardia with pallor and poor capillary refill times in the extremities. PSVT was noted on ECG (►Table 1).

Initial administration of adenosine (0.1 mg/kg) via a dorsal metacarpal vein failed to induce cardioversion, but a second administration of 0.2 mg/kg was successful. After conversion, the patient was in normal sinus rhythm with a heart rate of 150 bpm. He was transferred to the PICU for further PSVT therapy and monitoring.

Two additional PSVT events occurred in the PICU that were treated successfully with 0.2 mg/kg adenosine. An esmolol infusion was initiated, but three more PSVT events occurred

that evening and the next morning. The 2-D TTE revealed mild left and right atrial enlargement with mild tricuspid insufficiency and normal function. Esmolol was discontinued on day 3 with no further PSVT. Initial NT-pro-BNP level, drawn in the PICU 3 hours after normal sinus rhythm was initially achieved, measured 24,572 pg/mL (►Table 1). The NT-pro-BNP level had decreased to 2,575 pg/mL by the time of discharge 5 days later (►Table 1).

Literature Review

A focused search for reviews published in English and human subjects using the terms “pro-BNP,” “natriuretic peptides,” “pro-BNP AND heart failure,” “pro-BNP AND supraventricular tachycardia,” “pro-BNP AND heart failure,” “NT-pro-BNP AND supraventricular tachycardia,” “brain natriuretic peptide,” and “brain natriuretic peptide AND pediatric heart failure” via the online database PubMed resulted in 40 publications. Additionally, the authors queried the Cochrane Library for controlled clinical trials using “pro-BNP” and “NT-pro-BNP.” Among resultant reviews, a trend can be seen that from 2002 to 2007, pro-BNP was being seriously considered as an important biomarker in acute coronary syndrome and heart failure, as rapid bedside assays became available.^{7–10} After 2007, importance of pro-BNP appeared accepted as illustrated by its inclusion in many therapeutic trials; its role in diverse populations, such as dialysis patients,^{11,12} postoperative pediatric patients,¹³ atrial fibrillation patients,¹⁴ pediatric septic patients,¹⁵ and pediatric oncology patients,¹⁶ became of interest. There has even been an attempt to use troponin I and NT-pro-BNP to risk stratify emergency room adult patients with palpitations.¹⁷ The authors found no studies demonstrating the utility of pro-BNP or related peptides in the risk stratification of pediatric patients in PSVT.

Discussion

Cardiac ventricular myocytes release a precursor protein, pro-BNP (108 amino acids), in response to pressure overload, volume expansion, and increase in myocardial wall stress. The precursor is then converted to biologically active and inactive forms, BNP (77–108 amino acids) and NT-pro-BNP

Fig. 1 (A) Initial ECG showing paroxysmal supraventricular tachycardia (PSVT) with presence of mild left ventricular strain in patient 1. (B) Follow-up ECG showing presence of delta waves on anterior chest leads. ECG, electrocardiogram.

(1–76 amino acids), respectively.¹⁸ When released, BNP binds to and activates the natriuretic factor receptors A and B, although to a lesser extent to B. Physiological actions of BNP are similar to those of ANP and include decrease in systemic vascular resistance and central venous pressure as well as an increase in natriuresis. The net effect of these peptides is a decrease in blood pressure due to the decrease in systemic vascular resistance, and thus, afterload. Additionally, the actions of both BNP and ANP result in a decrease in cardiac output due to an overall decrease in central venous pressure

and preload as a result of the reduction in blood volume that follows natriuresis and diuresis.¹⁹

All three patients with PSVT in our series had clinically apparent, cardiac decompensation. Due to previously reported relationships between elevated pro-BNP levels and heart failure in adults, serum levels of the related molecule, NT-pro-BNP, were measured in the first infant and then in the second and third after finding the elevation in the first. NT-pro-BNP levels have been reported to be slightly elevated at birth but decreased to accepted normal levels for infants in the first

2 days.²⁰ The levels on presentation of these three patients during PSVT were extremely elevated. Based on our experience with children in acute heart failure from other causes, this increase appears to correlate with clinical signs of inadequate cardiac output/cardiogenic shock such as tachycardia, respiratory distress, and moribund appearance. Indeed, in the current cases, the extremely high NT-pro-BNP values were present when the patient appeared moribund from decompensated PSVT and decreased significantly prior to discharge.

Conclusion

The case series highlighted here appears to be the first report of elevated NT-pro-BNP levels in neonates and an infant with PSVT. Importantly, all three patients were *in extremis* at the time the samples were drawn. The fact the biomarker decreased markedly after conversion confirmed that the high levels of it resulted from PSVT and were not the result of some other etiology.²¹ The length of time between the onset of PSVT and the timing of first serum sample drawn for measurement of the pro-BNP is not known for any of these patients, although the elevation of NT-pro-BNP most likely is dependent upon duration of arrhythmia, degree of heart failure, and patient age.²² Therefore, no definite conclusion can be drawn about the cardiovascular status at the time of PSVT onset or NT-pro-BNP increase. Would the measurement of the inactive and longer lasting NT-pro-BNP level show a continued myocardial wall stress in the already converted infant or neonate? As this is a more stable cardiac marker protein due to its increased half-life in comparison to BNP, it has been used as a surrogate marker.²³ Moreover, like in other causes of heart failure, there could be a lower limit of NT-pro-BNP after treatment of PSVT that would correlate with subjective signs of recovery, whereby discharge planning can begin earlier. Additionally, trending the presence of NT-pro-BNP after conversion could be a useful tool for monitoring ventricular strain associated with PSVT, particularly in areas or regions of limited resources or in an outpatient setting for signs of impending heart failure or risk for developing further PSVT.

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Conflict of Interest
None.

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