By colleagues for colleagues
Cardiology: Mitral valve insufficiency

Nt-proBNP as a deciding factor for further cardiological testing of stage B2 patients

Clinical signs and preliminary report
A 13-year-old, uncastrated male Miniature Schnauzer was presented at the clinic. The owner reported that the dog had shown symptoms of diminished capacity for exercise for several months, for example, tiring easily, reduced desire for exercise and increased need for sleep. Other symptoms, such as cough, panting, loss of appetite, increase in abdominal circumference, paralysis, etc. were not observed.

Clinical examination
<table>
<thead>
<tr>
<th>Nutritional status:</th>
<th>healthy muscle status, well-defined ‘waist’</th>
</tr>
</thead>
<tbody>
<tr>
<td>Conjunctivae/mucous membranes:</td>
<td>pale pink, smooth and shiny</td>
</tr>
<tr>
<td>Capillary refill:</td>
<td>&lt;2 seconds</td>
</tr>
<tr>
<td>Tip of nose:</td>
<td>dry</td>
</tr>
<tr>
<td>Oral cavity/teeth:</td>
<td>NSF</td>
</tr>
<tr>
<td>Skin turgor:</td>
<td>preserved</td>
</tr>
<tr>
<td>Cough reflex larynx:</td>
<td>active</td>
</tr>
<tr>
<td>Heart rate:</td>
<td>86 bpm, regular, distinct heartbeats, strong systolic heart murmur grade I-II/Vi over the mitral valve</td>
</tr>
<tr>
<td>Heart murmur:</td>
<td>I-II/Vi</td>
</tr>
<tr>
<td>Pulse:</td>
<td>regular, strong, no pulse deficit</td>
</tr>
<tr>
<td>Respiratory rate:</td>
<td>18 breaths/min., slightly increased upon inspiration</td>
</tr>
<tr>
<td>Palpation of abdomen:</td>
<td>borders of organs palpable without pain, no indication of fluid or increase in size</td>
</tr>
<tr>
<td>Body temperature:</td>
<td>38.3°C</td>
</tr>
<tr>
<td>Body weight:</td>
<td>10 kg</td>
</tr>
</tbody>
</table>

Laboratory tests

<table>
<thead>
<tr>
<th>Haematology</th>
<th>NSF</th>
</tr>
</thead>
<tbody>
<tr>
<td>Biochemistry</td>
<td></td>
</tr>
<tr>
<td>ALT</td>
<td>112 U/l (reference range 10-100 U/l)</td>
</tr>
<tr>
<td>ALP</td>
<td>436 U/l (reference range 23-112 U/l)</td>
</tr>
<tr>
<td>Na/K/Cl</td>
<td>NSF</td>
</tr>
<tr>
<td>Other biochem. parameters</td>
<td>NSF</td>
</tr>
<tr>
<td>Cardiopet® proBNP</td>
<td>1987 pmol/l</td>
</tr>
</tbody>
</table>

Evaluation for the range >1800 pmol/l:
The likelihood that clinical signs (e.g. respiratory and/or exercise intolerance) are due to heart failure is high. Further cardiac workup or cardiac consultation recommended.

Further cardiological testing

Radiographic examination
The latero-lateral projection of the chest radiograph showed a vertebral heart score (VHS) of 11.5 vertebral bodies and left atrial enlargement with loss of cranial tapering in the transition from the right atrium to the right ventricle. The trachea was elevated, the two mainstem bronchi were divergent and the mitral triangle was diminished. There was moderate peribronchial alveolar oedema and the pulmonary veins were slightly distended.

Right latero-lateral chest projection

Dorsoventral chest projection
The dorsoventral chest projection showed left atrial and left ventricular enlargement, as well as diverging mainstem bronchi superimposed on the left atrium.
Echocardiography

**From the right:**

- Dimension measurements in B-mode
  - L/AW = 6.7 mm
  - (norm 5.8 – 6.9 mm)
  - LV = 32.6 mm
  - (norm 21.5 – 33.2 mm)
  - VS = 8.2 mm
  - (norm 7.3 – 8.5 mm)
  - LA = 29.6 mm
  - (norm 118 – 27.2 mm)
  - Mild enlargement of the left atrium

- Measurement of the EPSS in M-mode
  - Mildly increased EPSS due to mitral valve insufficiency

- Teichholz formula for LV in B-mode
  - Normal motion of the wall of the left ventricle

- Measurement of the shortened cycle in B-mode
  - Hyperechogenic papillary muscles with partly hyperechogenic exterior wall of the left ventricle

**From the left:**

- Visualization of the LA, the mitral valve and the LV in B-mode in systole
  - Mildly dilated left atrium, mitral valve thickened at the tips of the leaflets

- Visualization of the blood flow at the mitral valve in systole using PW Doppler
  - Marked insufficiency flow profile in systole with 3 m/sec

- Visualization of the flow conditions at the mitral valve in systole using colour Doppler in systole
  - Turbulence (green) and regurgitation flow (blue) into the left atrium in systole with closed mitral valve
Diagnosis
The patient was diagnosed with moderate stage B2 mitral valve insufficiency (ACVIM Consensus Statements). This is a structural heart disease without or with earliest clinical symptoms, however, with haemodynamically significant regurgitation and radiological and echocardiographic signs, such as enlargement of the left side of the heart and enlargement of the atrium.

Differential diagnoses
Subaortic stenosis (SAS)
Subaortic stenosis is a congenital deformity of the aortic valve. Clinical symptoms include diminished capacity for exercise, weakness upon effort and syncope. Respiratory symptoms of left-sided heart failure (dyspnoea, cough) are possible. A weak, small pulse is characteristic. Findings on auscultation include a systolic heart murmur on the left in the area of the apex of the heart. In dogs with mild SAS, the radiological changes of pulmonary oedema may be mild or absent. The echocardiogram shows left ventricular hypertrophy with subaortic stenosis. Furthermore, dilatation of the ascending aorta, thickening of the aortic valve and left atrial enlargement with hypertrophy may occur. Doppler echocardiography can visualize systolic turbulence and detect high systolic outflow velocities within the aorta. Mitral regurgitation is a frequent occurrence.

Exclusion:
In the dog’s history as a puppy, there were no pathological findings on auscultation. Prior to the first visit, the dog had only very minor clinical symptoms. The dog’s pulse was normal and the systolic heart murmur could be auscultated left of the apex. There were no morphological changes in the left ventricular outflow tract and the flow profile and flow velocity at the aorta were normal.

Mitral valve dysplasia
Mitral valve dysplasia is a congenital deformity of the mitral valve. It occurs most frequently in large dog breeds. Echocardiography shows visible morphological changes, including thickened or shortened leaflets, prolapsed leaflets, papillary muscles that are shifted upwards or deformed and excessive dilatation of the valve annulus. The functional disorder is caused by the regurgitation being clinically relevant. As soon as ventricular filling is impaired, left atrial pressure increases and pulmonary oedema can occur. This leads to clinical symptoms including diminished capacity for exercise, respiratory symptoms of left-sided heart failure (dyspnoea, cough), loss of appetite and atrial arrhythmia. A systolic heart murmur can be auscultated at the left apex. Enlargement of the left atrium and a dorsal shift of the mainstem bronchus are characteristic radiographic findings.

Exclusion:
The dog is a Miniature Schnauzer, i.e. a small dog breed. In the patient’s history prior to the first visit, only slight impaired performance was reported. In the echocardiogram, no morphological deformities could be detected.

Treatment
The patient was prescribed an ACE inhibitor and a diuretic for treatment.

Treatment guidelines for chronic atrioventricular valve disease
Patients without symptoms/with mild symptoms (stage B)
- Inform the patient’s owner about the course of disease and early signs of heart failure
- Perform routine measures (blood pressure measurement, chest radiograph and echocardiography) and annual check-ups, ensure normal body weight, maintain fitness, regular exercise
- Monitor and treat other medical problems
- Low-sodium diet
- In dogs with dilatation of the LA and/or of the LV, prescribe ACE inhibitors and diuretics.

Discussion
The formation and release of atrial natriuretic peptide (ANP) and B-type natriuretic peptide (BNP) in the heart is primarily triggered by stretching of the myocardium. In dogs with heart failure, levels of ANP and BNP in the blood are elevated. In patients with heart disease, this results in overstimulation of the renin-angiotensin-aldosterone system. The natriuretic peptides

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ECG

<table>
<thead>
<tr>
<th>Lead II measurements</th>
<th>(reference ranges in brackets)</th>
</tr>
</thead>
<tbody>
<tr>
<td>P wave</td>
<td>0.04 sec (0.04 sec)</td>
</tr>
<tr>
<td>P wave</td>
<td>0.6 mV (0.4 mV)</td>
</tr>
<tr>
<td>PR interval</td>
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</tr>
<tr>
<td>QRS complex</td>
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</tr>
<tr>
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</tr>
<tr>
<td>ST segment deviation</td>
<td>&gt; 0.2 mV depression</td>
</tr>
<tr>
<td></td>
<td>(&lt; 0.2 mV depression)</td>
</tr>
<tr>
<td>T wave</td>
<td>&lt; 25% of R wave height, +ve,</td>
</tr>
<tr>
<td></td>
<td>(&lt; 25% of R wave height, +ve,</td>
</tr>
<tr>
<td></td>
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Physiological Doppler flow profile at the aorta

MITRAL VALVE DYSPLASIA

Four-chamber view, left scanning; visualization of the physiological mitral valve leaflets

ECG

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P wave 0.04 sec (0.04 sec)
P wave 0.6 mV (0.4 mV)
PR interval 0.06 sec (0.06 sec)
QRS complex 0.04 sec (0.05 sec)
R wave 1.6 mV (2.5 mV)
ST segment deviation > 0.2 mV depression (< 0.2 mV depression)
T wave < 25% of R wave height, +ve, (< 25% of R wave height, +ve, -ve or biphasic)

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ST segment deviation > 0.2 mV depression (< 0.2 mV depression)
T wave < 25% of R wave height, +ve, (< 25% of R wave height, +ve, -ve or biphasic)
counteract this activity by stimulating natriuresis, increasing blood flow in the kidneys, promoting diuresis and vasodilatation and strengthening diastolic heart function. The circulating concentrations of the atrial natriuretic peptide (ANP) and the B-type natriuretic peptide (BNP) are elevated primarily as a reaction to the increased burden on the myocardial wall.\(^9\)

NT-proBNP occurs when serum endopeptidases split proBNP in order to form BNP.\(^6\) Whilst NT-proBNP is biologically inactive, it possesses a higher stability than the biologically active BNP. Since NT-proBNP and BNP are formed at a ratio of 1:1, the measurement of NT-proBNP measured in the context of heart disease precisely reflects the amount of active BNP formed.\(^9\)

Due its better stability and longer half-life, NT-proBNP is used for immunoassay.

It is difficult to determine the underlying reason for respiratory symptoms in older small breed dogs, in which concomitant mitral valve diseases and primary chronic respiratory disorders are not uncommon. In these cases, an elevated NT-proBNP concentration may be helpful if the patient does not have a history of symptoms or there are no clinical symptoms or radiographic findings at present.\(^4\)

The measurement of the natriuretic peptides in the blood can support the diagnosis of heart disease when combined with physical examination, radiographic examination and echocardiography.


The combination of different biomarkers, such as cTnl (troponin I) and NT-proBNP, may be able to provide better diagnostic results in dogs with early symptoms than the determination of cTnl alone.\(^9\)

Two published studies evaluated the efficacy of treatment with angiotensin-converting enzyme inhibitors (ACE inhibitors) in dogs in the early stage of disease.\(^7,10\)

ACE inhibitors combined with diuretics improve clinical symptoms and prolong survival times.\(^2\)

**Treatment control/screening**

Dogs that are apparently healthy with an only slightly elevated individual NT-proBNP level should undergo repeat testing.\(^5\)

In the Miniature Schnauzer examined here, an ACE inhibitor and diuretic were administered based on the radiographic and echocardiographic findings. Cardiac troponin I levels are elevated in the blood in dogs with congestive heart failure. For the diagnosis of acute heart failure, it can be detected 4 hours to one week after myocardial damage.\(^8,12\)

NT-proBNP can be detected in the blood for more than one week. For this reason, a combination of troponin I and NT-proBNP testing may be recommended.

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**Literatur**

13. Vollmer, A. Atrioventrikular-(AV-)Klappenerkrankungen. Kleintierpraxis 2010; 55; Heft 9; 505-522