Case Report

Long-term elevated LDH values preceding heart failure in an elderly patient; a dilemma in the differential diagnosis

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ABSTRACT

Although LDH is one of the markers that can be significantly elevated in patients with tumors, it can also be elevated in patients with inflammation, anemia, tuberculosis, as well as myocardial infarction. Bearing in mind that elevated LDH indicates tissue damage here we monitor the LDH enzyme over time in a 78-year-old patient who previously had rheumatoid arthritis, a heart rhythm disorder with an implanted pacemaker, anemia and weight loss. Elevated LDH values were the reason for a detailed examination, in which the existence of hematological malignancy, lung and digestive system tumors, changes in the kidneys function and hemolysis were excluded. However, during heart rhythm disturbances with disease progression, there was a significant increase in NT pro-BMP (10-11 times from range values, LDH also increased slightly (range 3-5 times) but without a significant increase in troponin or CRP. After cardiology treatment and by adjusting the work of the Pacemaker and with the normalization of the heart rhythm, there is a normalization of NT pro-BMP and LDH values. We conclude that LDH beside NT pro-BMP can also be a useful marker that indicates heart weakness even before the appearance of clinical symptoms, and we recommend it in clinical work.

Keywords

LDH, NT Pro-BMP; troponin; cancer; heart disease; diagnosis; monitoring

INTRODUCTION

Lactate dehydrogenase (LDH) is one of the intracellular enzymes involved in energy metabolism frequently used in the clinical practice. [1]. It is well known that after tissue injury and cell degradation, it is released from intracellular space. In basic research LDH release assay is also used to study cell death following the investigation effects of diverse chemicals, drugs or toxic compounds in the cell cultures in –vitro[2].

In everyday clinical practice LDH is most often used as a biomarker in patients with tumors because increased production and their release into serum are associated with the appearance of metastases and disease progression [3, 4, 5, 6]. The elevated serum LDH are found also in inflammations, tuberculosis, and hemolytic anemia [7-10]. However, as a routine biochemical marker, it is sometimes in general practice not given much importance due to its non-specificity. LDH and its five isoenzymes are used as a marker of myocardial alteration[11]. However with the introduction of much more sensitive assay based on principles of immunology, high-sensitivity troponin I (HS-Troponin I) and other peptide markers including N-terminal pro-B-type natriuretic peptide (NT pro-BNP) was highly recommended together with electrocardiogram

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monitoring [12,13,14] in detection of myocardial alteration.

In this paper, we reported a long-term monitoring of LDH and its clinical significance which proceeds and indicates cardiac disorders.

Case Report

Here we present a 78-year-old patient referred by a Rheumatologist for detailed hematological examinations due to anemia with hemoglobin level of 120 g/L and elevated LDH values which are 880 IU/ml. The patient has been treated for seronegative rheumatoid arthritis since 1995. Previously, the patient received chloroquine and rezoquin therapy, and for the last 2.5 years he has been receiving methotrexate at a dose of 10 mg/week with folic acid. Previously was diagnosed with osteoporosis but without fractures. Dual-chamber rate-modulated (DDDR) pacemaker implanted in June 2023 due to syncope crisis and complete AV block. At that time, coronary angiography was performed and the findings showed LAD 30%, LCx 50%.From 2023, after the pacemaker was installed, LDH ranged between 800 and 880.

On admission in April 2025 she was conscious, oriented, eupnoic, afebrile, without signs of hemolytic syndrome. On admission, the cardiac action is arrhythmic; tones are quiet, without murmurs are heard. Pressure was 150/80mmHg. In the electrocardiogram, the frequency is around 60/min, without ST and T changes present. Finding on the lungs has been shown diffusely weakened respiratory noise, more on the left basal side and in the left apex. Oxygen saturation was 99%. Examination of the abdomen shows that the soft tissue is painfully insensitive to palpation, and the liver and spleen are within physiological limits. Due to her age and the LDH value of the findings, she was sent for consideration to have a bone marrow biopsy and suspicion of possible malignancy because in the last year she has lost about 6 kg in weight and has no appetite. The performed results have been shown that the fecal occult blood (FOB) assay is negative. Further, an ultrasound examination of the abdomen was performed and results showed that there were no pathological masses. Gastroscopy and colonoscopy indicated that pathological changes or tumor mass were not seen. In laboratory data from January 2025, hemoglobin was 120 g/L, MCV 91.0, RDW 15.7, platelets 208, LDH 880, iron was 6, 8. By looking at the computer system since the lab data was generated, for the last ten years, LDH has been over 560 all the time (Figure1). The Coombs test was negative, the number of reticulocytes was normal, while the performed tumor markers, CEA, CA 19-9, CA 125, CA 15-3 were all within physiological values. Creatinine clearance and 24h proteinuria were in reference range. The Bence-Jones protein in urine is negative. The serum and urine protein electrophoresis are in reference values. Therapy with folic acid and vitamin B12 amp was prescribed. On regular control hemoglobin was 135g/L, Red blood cells 4.53 and the patient was without palpable peripheral lymphadenopathy. All other biochemical findings including C-reactive protein and sedimentation rate were in the physiological range. In order to rule out malignancy, a CT scan of the thorax was performed. Standard axial sections with coronal and sagittal reconstructions were performed natively, and after i.v. application of contrast, no pathological changes were observed on the sections through the base of the neck. Axillaries on both sides were without pathological enlargement of the lymph nodes. In the lung parenchyma, there are no signs of consolidation or other pathological changes. The trachea and both main bronchi are patent. The mediastinum was without significantly enlarged lymph nodes. The pleural spaces are free. On high sections through the abdomen, the finding is without pathological signs. The diffusely reduced mineralization of the shown bone structures of the appendicular skeleton. Apart from the degenerative ones, no other pathological changes can be observed on the bone structures shown. The spirometry finding was in range values, but the arterial acid-base status indicated hypoxemia with oxygen saturation of 70mmHg while pCO_2 was 45mmHg.

On 17 April 2025, the main symptom that dominates at admission in hospital is fatigue during exertion. The data has been shown that high-sensitivity troponin I (hs-Troponin I) was 212, 4 pg/mL and NTpro-BNP was 4975.0 pg/mL (Figure 1 and Figure 2). The patient was immediately transportedand admitted to the coronary unit with acute heart failure. At admission in coronary units she is normotensive, but a pacemaker rhythm that goes from 150to 60/min was seen on the monitor with chest pains. The patient had an irregular atrial rhythm; sinusarrhythmia which activated ventricular pacing and consequent heart failure (figure3 and figure 4). A control checkof the pacemaker activity was performed with optimization of the parameters. A coronaryangiography was performed which is identical to the description from 2023 year. Echocardiography

Aorta at root: 27 Left atrium: 35 LV EDD: 45 LV ESD: 33Septum: 0.9 Posterior wall: 0.9. TMP (E/A) / V max (m/sec): 0.7/0.6 TMP (E/A) /Regurgitate: + Ao flow / V max (m/sec): 1.5, EF preserved. During hospitalization, the patient was treated with anti- arrhythmic drugs, low dosesof diuretics, anti-hypertensive drugs and beta blockers. General condition was better and after five days hospitalization in Coronary units values for HS Trop I was 219.0 pg/mL, NT pro-BNP was2253.0 pg/mL while LDH 537, first time after two years of routine monitoring. The degree of changes in LDH and NT Pro-BMP in comparison to the range is shown in Figure 2 for better comparison. Follow-up data over time indicate that LDH is increased all the time from 2-3 times compared to control. However, NT pro-BMP is increased from 10-11 times but only during disease progression with a rapid decrease after therapy, while LDH remains slightly elevated. The patient was discharged with advice for regular controls. At the next regular check-ups, the patient feels better and tolerates the effort better.

DISCUSSION

In this case report it is shown that high LDH values require complex analyses to reveal the true cause in elderly patients. The patient had rheumatoid arthritis for many years, then a Pacemaker was implanted due to a heart rhythm disorder, but her main symptoms were fatigue and weight loss with anemia. Due to the clinical symptoms, the existence of malignancy was correctly suspected first, and all tests were carried out, as well as the determination of tumor markers. Suspicions of malignancy, which is the most common cause of elevated LDH values in the elderly (6,7, 8, 9) were eliminated by correct but complicated differential diagnosis and long-term and complex examinations. Procedures were applied here that excluded all other possible reasons for elevated LDH values, as well as hematological tests for the presence of malignant melanoma and hemolytic anemia (10). However, based on the further worsening of weakness and rhythm disturbances, cardiac disease was evident as the primary reason for elevated LDH.

Fast and timely admission of the patient to the cardiology department during fatigue and quick control of the Pacemaker as well as adjustment of the Pacemaker prevented further worsening of the disease and the patient was stabilized in the eventual further progression of the disease and cardiac dysfunction. The finding of coronarography made in the phase of worsening of the disease, which was similar to the one two years ago and without significant narrowing of the coronary arteries, excludes myocardial infarction regarding possible metabolic disease or arteriosclerosis but indicates weakening of the heart muscle (15,16). High serum level of LDH can be a predictor in infectious myocarditis and literature data indicated its association with mortality (17). However, in this case, high LDH is associated with heart failure which leads to tissue ischemia, and here, even without the presence of infection, LDH was elevated.

Of course, the sudden increase in other biomarkers including NT Pro-BMP together with heart rhythm disturbances was the key reason for the urgent referral to the cardiology department and the application of cardiac therapy. Release of NT Pro-BMP from cardiomyocytes in this case can be a consequence of increased end-diastolic wall stress due to ventricular volume or pressure (18). Several studies as well as a report from American Heart Association confirmed that the elevated NT Pro-BMP can be also a good predictor of the development of heart disease including subclinical manifestation (18, 19). In this patient we saw that LDH was always elevated over a longer period of time. NT pro-BMP is much more increased but only during cardiac rhythm disturbance and that it returned quickly to normal while LDH remained elevated afterwards. This most likely indicated significant structural damage to the cardiomyocytes in elderly patients, considering that LDH is localized in the cytoplasm and is released when the cell membrane is damaged or when the cell structures are destroyed by any form of cell death (2,12).

What is particularly interesting is when, over time, as well as during the worsening of the disease and irregular rhythm, the percentage of increase in the LDH enzyme is observed in relation to the percentage of increase in NT Pro-BMP, which is considered an important marker of heart failure. In this case we see that the percentage of LDH increase is twice as high as compared to the reference values. However, increases in NT-Pro-BMP values are more than ten times higher, but only in the case of irregular rhythm and during hospitalization due to cardiac dysfunction. It is most likely the changes in cardiomyocytes because the enzyme LDH has been shown in many scientific papers to be a reliable and

good marker of cell apoptosis, necrosis and ferroptosis; both in experimental conditions, in an animal model and also in humans (2, 11, 13, 19, 20). So in this case, we see that LDH is indeed a good marker of cardiomyocyte metabolism damage. Improving the function of cardiomyocytes after pacemaker correction and with regular rhythm, increasing the force of contraction and better oxygenation after drug administration leads to a decrease in LDH and NT pro-BMP.

With this work, we want to point out that, based on the long-term increase in the value of the LDH enzyme, it is still necessary to regularly monitor the patient on an electrocardiogram frequently and monitor the Pacemaker when elevated values appear, because they still indicate tissue damage. This case indicated the importance of the LDH analyses in clinical practice and for patients with cardiac problems.

Author contributions

V.J: Writing – review & editing, supervision, Corresponding. J.Lj: Data preparation and first draft; V.I., Data Curation and Formal cardiology analyses; I. I., Data preparation; N.C. Formal hematology analyses.

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Declaration of conflicting interests

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Ethics approval

The authors declare that the work is written with due consideration of ethical standards and in line with the principles of the Declaration of Helsinki. Our institution does not require ethical approval for reporting individual cases.

Informed consent

Written informed consent was obtained from the patient for their anonymized information to be published in this article.

Trial registration number/date N/A

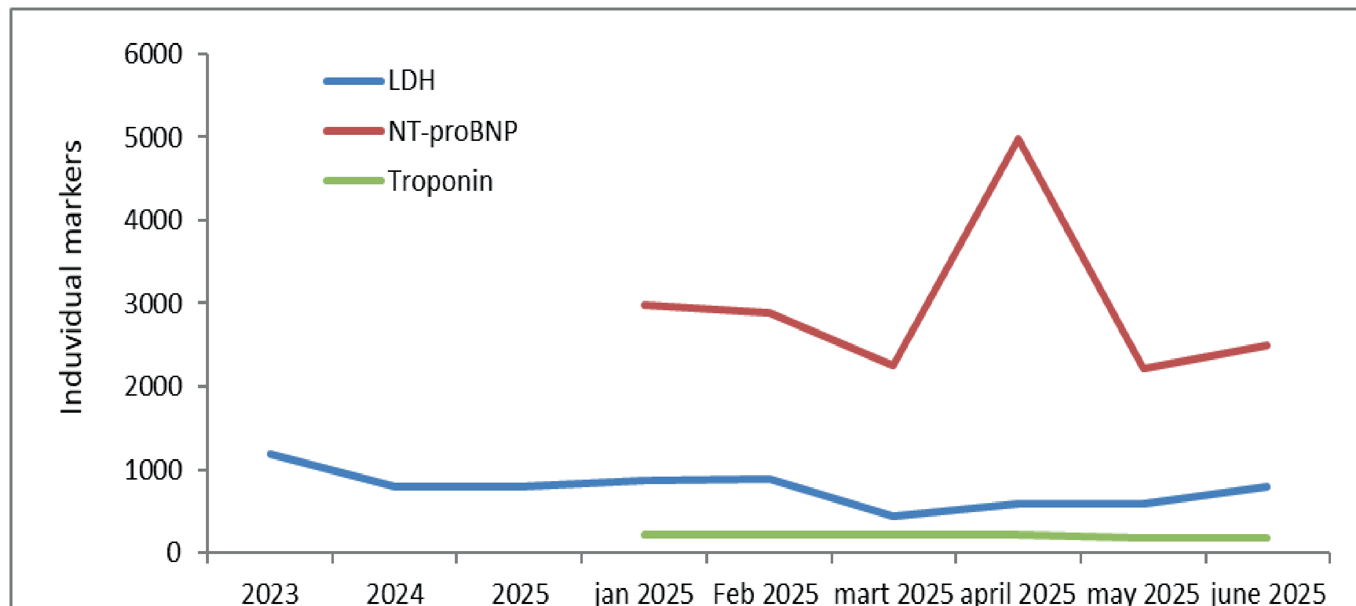

Fig1. Values of LDH, NTpro-BNP and Troponin markers over time

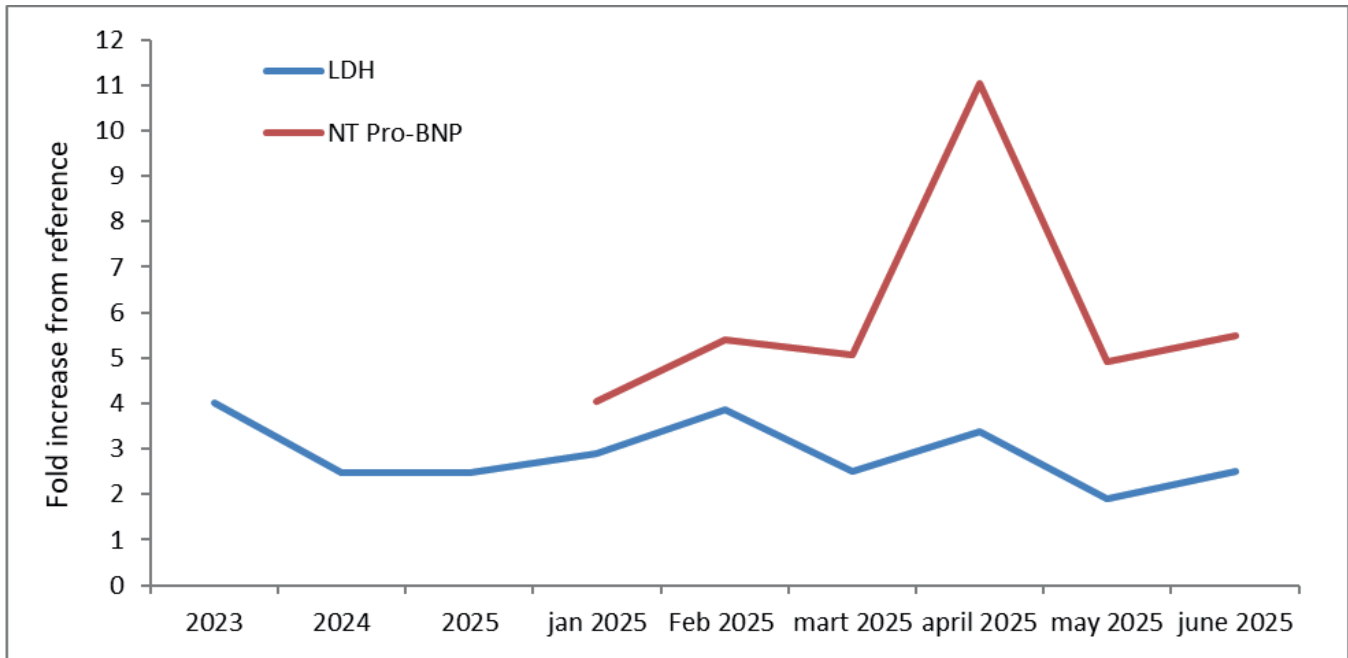

Fig 2. Changes in LDH and NTpro-BNP values over time, but calculated as fold increase compared to control

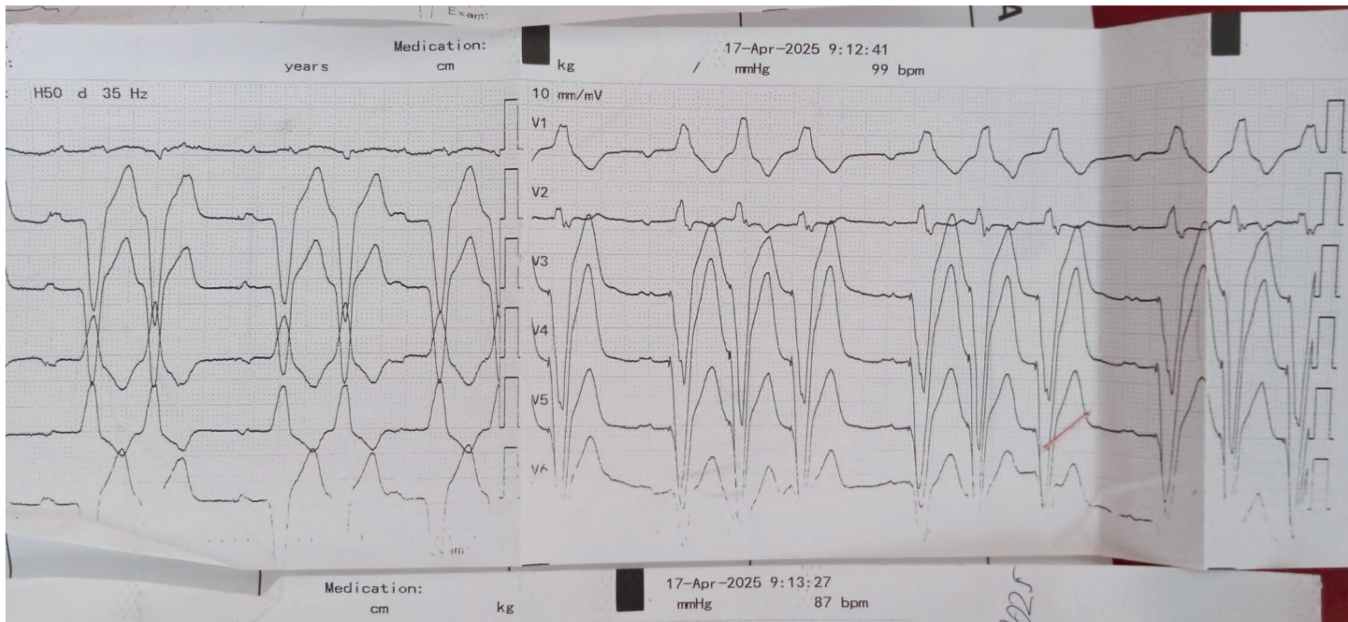

Fig 3. The ECG record on 17 April 2025 shows paced QRS complexes, but they are of higher frequency, i.e. faster pacing chambers with irregular chamber rhythm Frequent atrial premature beats with consequent activation of ventricular pacing as cause of irregular heart rhythm

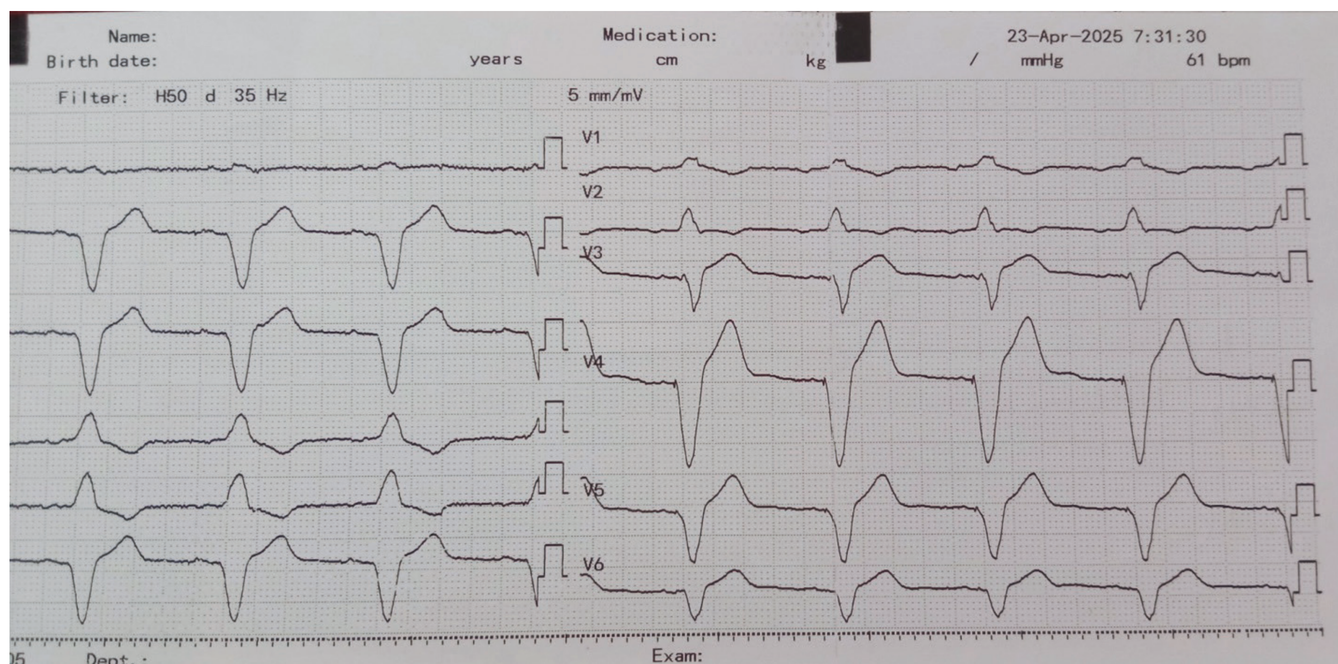

Fig 4. The ECG record on 23 April 2025 indicated that most pre-ventricular P waves are also paced

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