Medical Sciences 2020 Vol. 8 (17), p. 68-75

e-ISSN: 2345-0592
Online issue
Indexed in *Index Copernicus*

Medical Sciences

Official website:
www.medicsciences.com

Dilated cardiomyopathy and its complications in a young man caused by synthetic testosterone injection: case report

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Abstract

Background: Dilated Cardiomyopathy (DCM) is a disease of the heart muscle characterized by enlargement and dilation of the ventricles (1). Genetic mutations and non-genetic factors, such as: myocardial inflammation due to infection (usually viral); effects of drugs, toxins or allergens and systemic endocrine or autoimmune diseases, can cause DCM (4). One of the risk factors described in the literature for cardiac remodelling is the use of intravenous steroids. In this report we describe the case of a young patient presenting with DCM caused by synthetic testosterone injections.

Case presentation: A 28 years old man was referred to our hospital suffering fever, cough, frequent cardiac activity and weakness. The patient admitted that four years until now he was using intramuscular injections of synthetic testosterone. Laboratory tests showed slightly elevated levels of inflammatory markers. Transthoracic 2D echocardiography showed significantly impaired left ventricular ejection fraction (LVEF 20%, GLS -5%) and enlarged cardiac chambers. X-ray showed pneumonia. Although the patient was adequately treated, his condition deteriorated, a. mesenterica, a. lienalis, a. poplitea thrombosis was diagnosed and thrombectomy performed. DCM was diagnosed by MRI. After 10 months of adequate heart failure treatment cardiac MRI showed marginally improved LVEF (38%) and RV FAC (-38.6%), dilatation of left cardiac chambers remains the same.

Conclusions: Anabolic steroid use is a rare, reversible cause of dilated cardiomyopathy in young, otherwise healthy athletes. Discontinuation of testosterone use and the initiation of guideline-directed medical treatment may improve and even normalize cardiac function.

Keywords: dilated cardiomyopathy; synthetic testosterone injection.

Sintetinio testosterono injekcijų sąlygota dilatacinė kardiomiopatija ir jos komplikacijos: klinikinio atvejo aprašymas

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Santrauka

Įvadas: Dilatacinė kardiomiopatija – tai širdies raumens liga, sukelianti skilvelių išsiplėtimą bei širdies veiklos sutrikimą (1). Genetinės mutacijos ir negenetiniai veiksniai, tokie kaip: širdies raumens uždegimas dėl infekcijos (dažniausiai virusinis); vaistų, toksinų ar alergenų ir sisteminių endokrininių ar autoimuninių ligų poveikis gali sukelti dilatacinę kardiomiopatiją (4). Vienas iš literatūroje aprašytų širdies ertmių remodeliacijos rizikos veiksnių yra intraveninių steroidų vartojimas. Šiame straipsnyje aprašomas jauno paciento, kuriam dilatacinė kardiomiopatija buvo sukelta sintetinio testosterono injekcijų, atvejis.

Klinikinis atvejis: 28-erių metų vyras, kuris skundėsi subfebriliu karščiavimu, kosuliu, dažnu širdies plakimu, bendru silpnumu, atvyko į mūsų ligoninę 2018 m. sausio mėnesį. Pacientas prisipažino, jog iki šiol ketverius metus jis vartojo sintetinio testosterono injekcijas į raumenis, paskutinė injekcija buvo prieš 4 dienas. Laboratoriniai tyrimai parodė šiek tiek padidėjusias uždegiminių žymenų koncentracijas. Transtorakalinė 2D echokardiografija parodė ženkliai sumažėjusią kairiojo skilvelio išstūmimo frakciją (KSIF 20%, GLS -5%) ir padidėjusias širdies kameras. Rentgenologiniu tyrimu patvirtinta pneumonija. Nepaisant optimalaus gydymo, būklė komplikavosi. Nustatyta *a. mesenterica, a. lienalis, a. poplitea* trombozė, atlikta trombektomija. Dilatacinė kardiomiopatija diagnozuota MRT. Po 10 mėnesių medikamentinio širdies nepakankamumo gydymo, širdies MRT parodė šiek tiek pagerėjusią KSIF (38%) ir DS FAC (-38,6%), kairiųjų širdies kamerų išsiplėtimas išliko tas pats.

Išvados: Testosterono injekcijų vartojimas yra reta, grįžtamosios dilatacinės kardiomiopatijos priežastis, pasitaikanti tarp jaunų, sveikų bei atletiškų pacientų. Nutraukus testosterono vartojimą ir pradėjus adekvatų medikamentinį gydymą, širdies funkcija gali pagerėti ar net regresuoti širdies nepakankamumo simptomai.

Raktažodžiai: dilatacinė kardiomiopatija; sintetinio testosterono injekcijos.

2. Introduction

Dilated cardiomyopathy (DCM) is a disease of the heart muscle characterized by enlargement and dilation of the ventricles (1). This causes heart failure (HF) when the left ventricular ejection fraction (LVEF) becomes less than 40% (1). HF is characterized by structural and metabolic cardiac remodelling (2).

DCM is not explained by abnormal loading conditions like hypertension and valvular heart disease or coronary artery disease (4). Genetic mutations involving genes that encode cytoskeletal, sarcomere, and nuclear envelope proteins, among others, account for up to 35% of cases (5). Non-genetic forms of DCM can result from different etiologies, including myocardial inflammation due to infection (usually viral); effects of drugs, toxins or allergens and systemic endocrine or autoimmune diseases (4). One of the risk factors described in the literature for cardiac remodelling is the use of intravenous steroids. There are studies of testosterone side effects on blood vessels tissue from mice. They found that the hormone triggers cells from the blood vessels to produce calcification (3). In humans, who use intravenous testosterone, it was noticed expression of androgenic receptors (ARs), through which the biological effects of testosterone occur, in calcified cardiovascular tissue, including the femoral artery and aortic valve (3).

The most common presenting symptoms relates to congestive heart failure, but can also include circulatory collapse, arrhythmias, and thromboembolic events (5). Secondary, neurohormonal changes cause permanent myocytes damage and rearrangement of cardiac configuration. Cardiac chamber measurements, especially LV size and LVEF, obtained by transthoracic 2D echocardiography (TTE) are one of the most important diagnostic modalities confirming the diagnosis of DCM (6). MRI is also very important for the diagnosis of DCM. Cardiac biopsy confirms histologically evidence of pathological myocyte hypertrophy and apoptosis, myofibroblast proliferation and interstitial fibrosis (7). Diagnosis and prognosis of DCM have improved in recent decades largely due to elucidation of the etiology of the disease, improved and earlier diagnosis, optimized drug and non-drug treatment (8).

Despite improved diagnostic and treatment options, DCM remains a major cause of heart failure and heart transplantation (9).

3. Case

A 28 years old man was referred to our hospital suffering fever, cough, frequent cardiac activity and weakness. Symptoms appeared five days till hospitalization. The patient admitted that four years until now he was going to the gym and using intramuscular injections of synthetic testosterone. No other drugs were used.

Laboratory tests showed slightly elevated levels of inflammatory markers (CRP 18,94 mg/l, WBC 7,5 x 10^9/l) and extremely elevated NT-proBNP (3731 ng/l), ECG showed sinus tachycardia, Q wave in V1-V3, negative T wave in V5-V6 and poor R wave progression in chest leads.

2D TTE showed significantly impaired left ventricular ejection fraction (LVEF 20%, GLS -5%) (Fig. 1 -2) , dilated left ventricle (LVEDDi 31,8 mm/m^2, LVEDV 245 ml, LVESV 210 ml), LV was globally akinetic, trabeculated, spherical shaped, in the apex four thrombus was noticed (the largest 36x14mm) (3 pav.) , dilated mitral anulus, moderate (II-III*) MV insufficiency, RV function was impaired (FAC -22.7%). Chest x-ray showed pneumonia in the right lung.

In the course of adequate heart failure, pneumonia treatment, anticoagulation therapy patient's status got worsening, negative clinical signs showed up such as new onset pain in the chest with elevated cardiac enzymes (TnI 11 μg/l), abdominal pain, numbness in both foots and right foot skin discoloration, so for a detailed work up chest-abdomen-pelvis CT was performed and thrombosis of a. mesenterica, a. lienalis, a. poplitea was diagnosed.

Surgical trombectomia of a. poplitea, a. mesenterica superior and inferior was performed. Coronary angiography was with no lesions. Cardiac MRI confirmed dilated cardiomyopathy with preserved LV and RV function, suspicion of edema in LV anterior and lateral walls, ischaemia induced fibrotic areas in LV mid-inferior, posterior and apical inferior segments.

Despite adequate antibacterial treatment and reduction of inflammatory markers clinical signs of infection remained - nasopharyngeal specimen confirmed Influenza A virus. In suspicion of viral induced myocarditis endomyocardial biopsy was performed and histological study ruled out myocarditis diagnosis.

After 10 months of guideline-directed medical HF treatment, cardiac MRI showed marginally improved LVEF (38%) and RV FAC (-38.6%), dilatation of left cardiac chambers remains the same. Subendocardial late gadolinium enhancement remains in left inferior and apical segments.

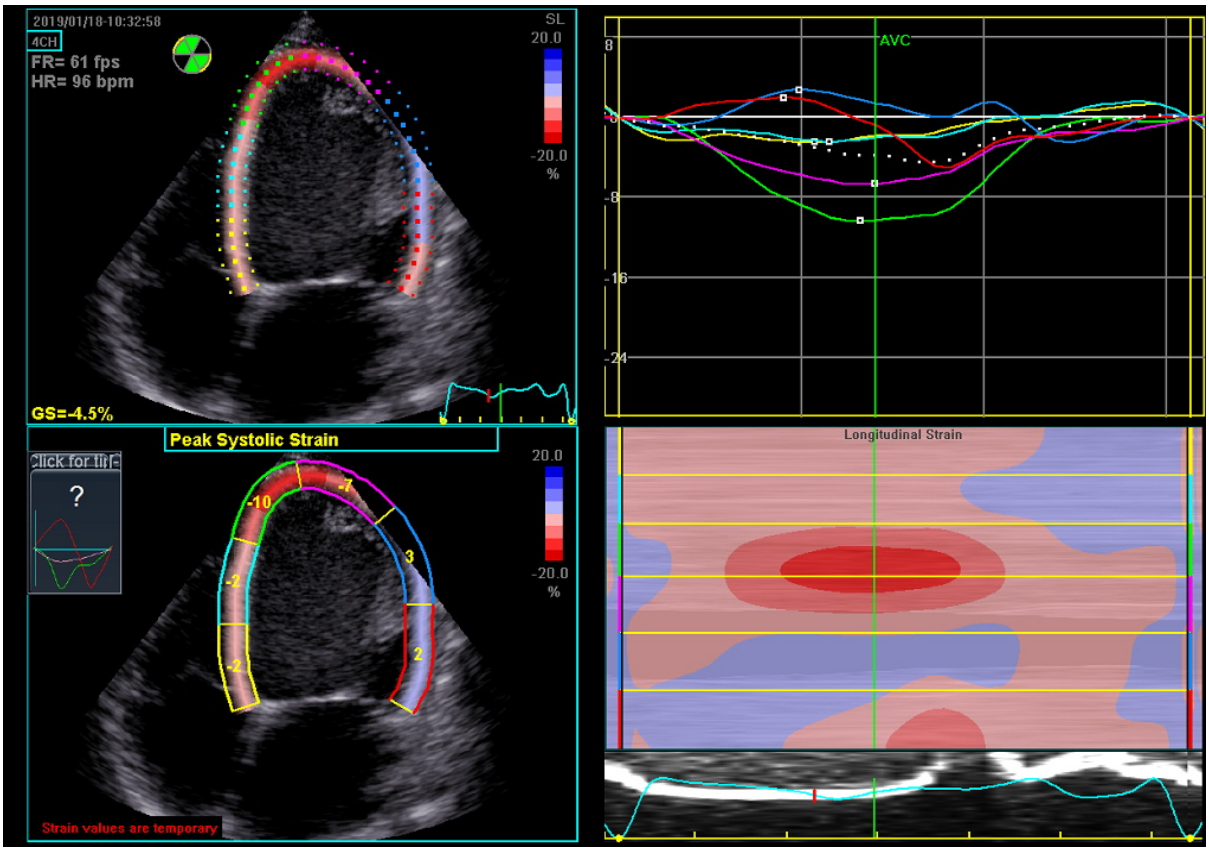

Figure 1. *Two-dimensional speckle tracking-derived longitudinal strain curves from 6 myocardial segments on standard 4-chamber view. A patient with DCM with reduced global longitudinal strain.*

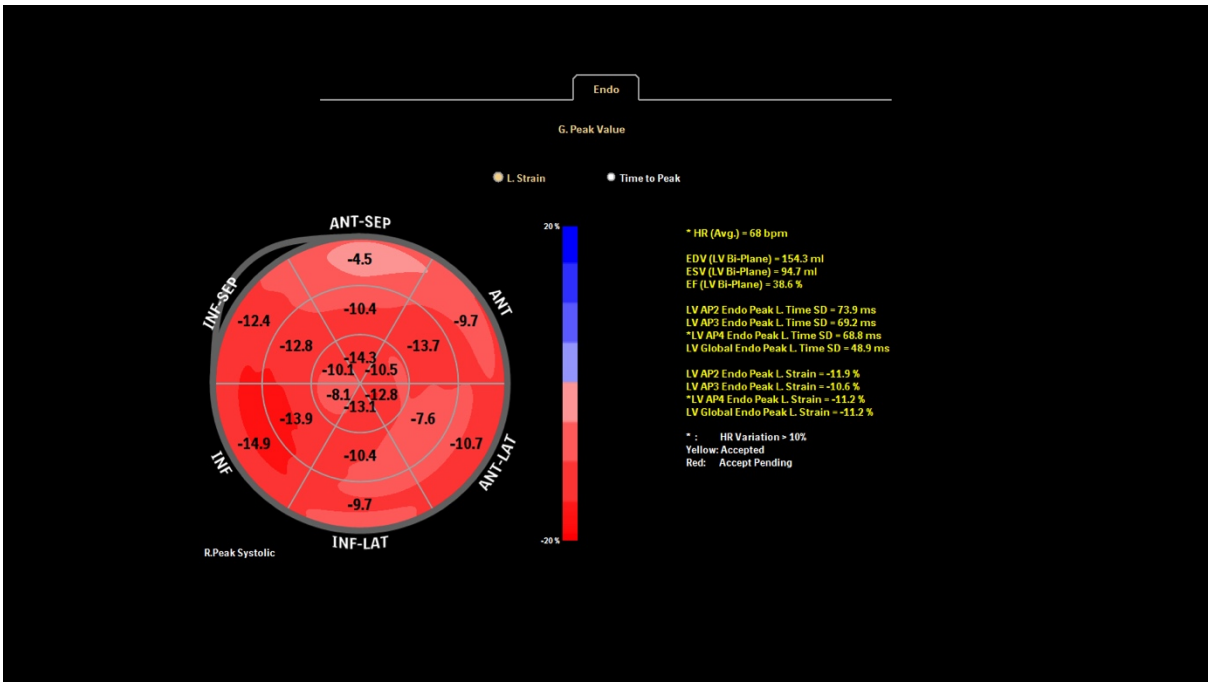

Figure 2. *Two-dimensional speckle tracking echocardiography showing reduced global longitudinal strain.*

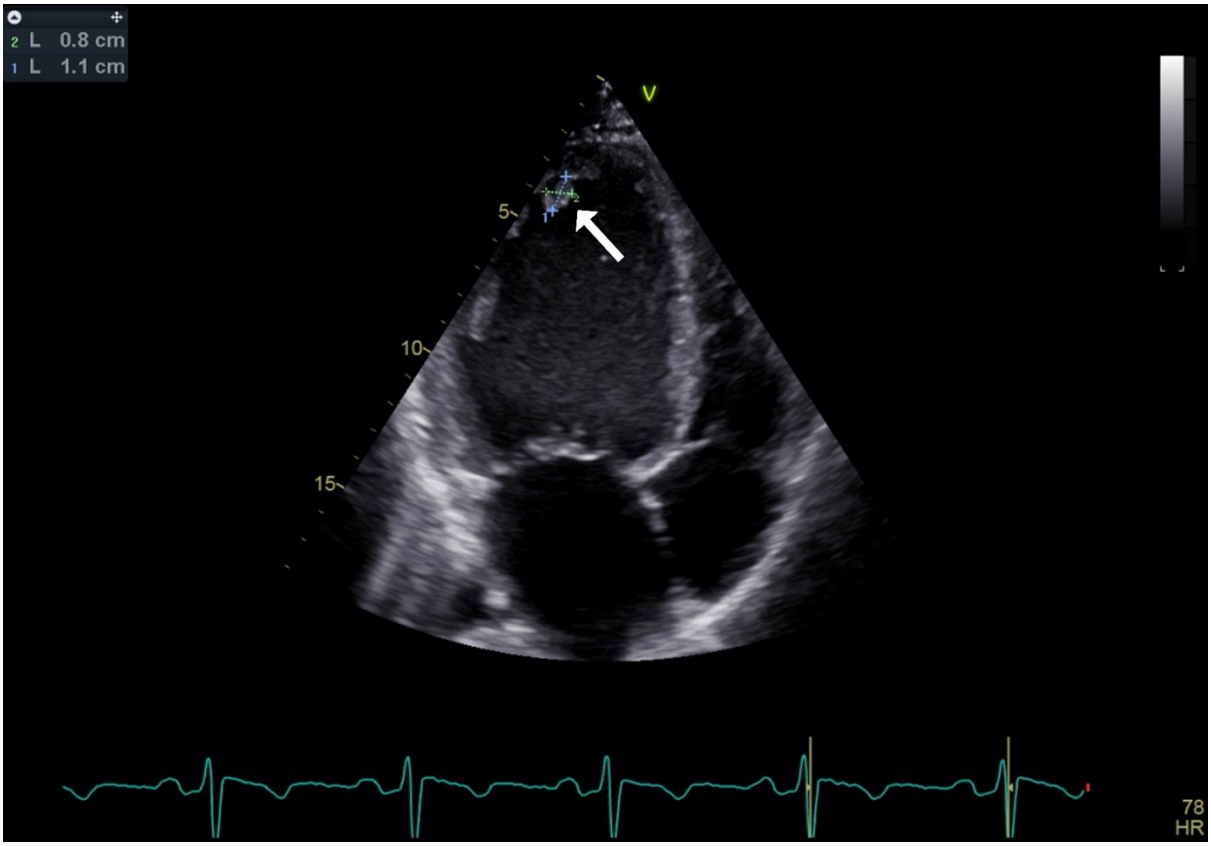

Figure 3. *Transthoracic echocardiography. Thrombus in left ventricular apex.*

4. Discussion

DCM is more common in men than in women (14). A large proportion of patients with DCM do not experience any symptoms and have a long latency period. Our patient did not have classic symptoms and signs of DCM such as fatigue, edema in legs, ankles or feet and heart murmurs. The main symptoms of our patient were fever, cough, frequent cardiac activity and weakness. DCM was found accidentally by TTE. And the main question was - what was the cause of DCM in young, previously healthy individual? For this reason, every patient with suspected DCM should be evaluated by TTE or MRI.

The most common etiology of DCM is idiopathic and without an identifiable cause (14). The secondary causes include infectious myocarditis, ischemic disease, hypertension, medication-induced, alcohol abuse, human immunodeficiency virus, peripartum cardiomyopathy, or infiltrative disease (14). It was difficult for our patient to differentiate the main cause – DCM induced influenza virus was first suspected. Infections are believed to account for ~30% of the etiology of DCM and are typically associated with myocarditis, as it has been demonstrated in animal models and human patients (4). One of the most common groups of viruses associated with DCM are the enteroviruses, adenoviruses and herpesviruses (12). The positive identification of viral genome with biopsy is associated with a more-rapid progression to DCM and worse clinical outcomes (13). Our patient was diagnosed with influenza A virus. A biopsy was performed to differentiate etiology of this disease. However, histological examination ruled out the diagnosis of myocarditis, so we began to search for another cause of DCM.

Taking into account patients' previous history, the most reasonable cause of cardiac damage was synthetic testosterone. Anabolic-androgenic steroid (AAS) is the synthetic derivative of the male hormone testosterone that is often used by athletes to increase muscle mass (10). This can produce side effects such as gynaecomastia, testicular atrophy, liver adenomas and severe cardiac effects. Steroids are thought to cause changes in heart muscle structure through their effect on androgen receptors expressed on cardiac myocytes (11). In men without any risk factors, long-term testosterone use may lead to cardiac death, myocardial infarction, hypertension, cardiomyopathy including ventricular hypertrophy and dilatation and HF. Other cardiotoxic events are changes in lipid metabolism, hypercoagulable states and polycythaemia. AAS can directly harm the myocardium by causing tissue fibrosis and apoptosis.

5. Conclusions

1) Anabolic steroids use is a rare, reversible cause of cardiomyopathy in young, otherwise healthy athletes. Therefore, it is very important to know patient's anamnestic data well. In this case, patient admitted the use of injections of synthetic testosterone.
2) Discontinuation of testosterone use and the initiation of guideline-directed medical treatment are advocated and, as demonstrated in our case, may improve cardiac function.
3) It is important to prevent complications that DCM can cause, such as: circulatory collapse, arrhythmias, and thromboembolic events.

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