

Japanese type cardiomyopathy associated with preexcitation / Japanese type cardiomyopathy without deep negative T waves and with findings of preexcitation on ECG

Preeksitasyon ve Japon tipi kardiyomiyopati birlikteliği / EKG'de derin negatif T dalgaları izlenmeyen, preeksitasyon bulguları izlenen Japon tipi kardiyomiyopati

Dear Editor,

I read with great interest the case report presented by Emiroğlu et al. (1) for which I would like to congratulate all the authors. They described a case with Japanese type cardiomyopathy associated with pre-excitation, but without associated classical finding of deep negative precordial T waves. The authors pointed out that this case might represent a rare case of this type of cardiomyopathy and they could not give a plausible explanation for the absence of deep T wave negativity. However, I would suggest that one explanation for the absence of deep negative T waves might be pre-excitation itself. According to the surface electrocardiogram given in Figures 1 and 2 the accessory pathway seems to be located to the anteroseptal region and as it is well known that preexcitation might be responsible for abnormal repolarization vector. Hence, the normal axis of ventricular activation, namely depolarization and repolarization directions might both be changed according to the location and direction of the accessory pathway. We all are aware that residual T wave axis changes occur after ablation of accessory pathways and cardiac T wave memory are implicated for this behavior. Therefore, in this particular case deep negative T waves usually observed in patients with apical hypertrophic cardiomyopathy representing abnormal repolarization might be masked by the repolarization changes of pre-excitation. It might be interesting to see how T waves would appear after ablation of the accessory pathway. Therefore, I think that the case presented by Emiroğlu et al. (1) should not be considered as a unique entity. It might be merely related to accessory pathway mediated change of repolarization vector.

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Author's Reply

Dear Editor,

We are very contented to take feedbacks from other authors about our article. Though the 'Japanese Type Cardiomyopathy' is easily diagnosed with echocardiography, not all secrets about the disease are evident yet, because of its rare incidence. As, we mentioned in our letter, deep negative T waves may resolve or normalize with the advance of disease to another form (i.e dilated cardiomyopathy) or with developing a new concomitant cardiac disease (i.e coronary artery disease) (1). It is well known that preexcitation syndromes may cause repolarization anomalies. Because we did not perform electrophysiological study (EPS) or ablative therapy to our patient, we refrained from attributing T wave anomalies to the existed preexcitation entirely. If EPS had been done, it would have been very interesting to survey T wave changes. However, to say more would be speculation. The point that we would like to draw attention in our letter is that sometimes, some diseases, in spite of well-known criteria, may manifest with different findings.

Many thanks for your comment.

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The beneficial effects of allopurinol in cardiology practice: decrease in uric acid and vascular oxidative stress/ The effects of lowering uric acid levels using allopurinol on markers of metabolic syndrome in end-stage renal disease patients: a pilot study

Allopurinolün kardiyoloji pratiğindeki faydalı etkileri: Ürik asitte ve vasküler oksidatif strese azalma/ Ürik asit seviyelerinin allopurinol ile azaltılmasının son dönem böbrek hastalarındaki metabolik sendrom belirleyicilerine etkisi: Pilot çalışma

Dear Editor,

We have read the article of Shemaldine et al. (1) with great interest. They evaluated the effects of allopurinol on lipid parameters in 12 hemodialysis patients with gout and showed low-density lipoprotein (LDL) lowering and triglyceride increasing effects of the treatment.

Although there are numerous studies evaluating effects of allopurinol on endothelial function, this trial is the first to show LDL lowering effect of allopurinol. The novel findings of this study are very interesting; however, the very small study population and the lack of the control group are the two major limitations of this trial. We have previously shown in metabolic syndrome patients that allopurinol reduces oxidative stress, improves endothelial function and ameliorates myeloperoxidase levels (2). Furthermore, although we did not exhibit our lipid results in detail in the published article, we could not find any significant change in lipid parameters with the treatment. This difference may be the result of the different study population.

In end-stage renal disease patients, hyperuricemia generally results from the decrease in renal excretion. Uric acid (UA) crystals clearly have the potential to induce inflammation given their role in pathogenesis of gout. Serum UA levels have also been linked to levels of proinflammatory cytokines and may have a role in perpetuating the inflammatory response that characterizes atherosclerosis. UA may also increase oxygenation of LDL, and UA crystals have also been shown to stimulate release of the platelet constituents serotonin, ATP and ADP. Perhaps most importantly, UA has a putative role in the development of hypertension via effects on nitric oxide production in the macula densa. It is also possible that higher levels of UA reflect higher levels of xanthine oxidase activity and oxidative stress. Oxidative stress plays an important role in the progression of vascular endothelial dysfunction. The two major systems generating vascular oxidative stress are the NADPH oxidase and xanthine oxidoreductase (XOR) pathways. It has been shown that inhibition of XOR with allopurinol or oxypurinol reduces oxidative stress in vasculature and reverses endothelial dysfunction evaluated by forearm blood flow responses to administration of acetylcholine or hyperemia in diabetic and hypercholesterolemic patients. There are no adequately powered clinical endpoint trials of UA lowering strategies. However, three drugs known to reduce cardiovascular mortality have been shown to reduce serum UA, which, hypothetically, may explain some of their beneficial effects. Fenofibrate and losartan reduce serum UA level in healthy volunteers and hypertensive patients via increased renal UA excretion (3, 4). As a further example, atorvastatin has been shown to reduce serum UA even after adjustment for risk factors including change in renal function (5). In addition to these large trials, the effect of probenecid (a uricosuric agent with no effect on xanthine oxidase) has been studied in a group with heart failure. Probenecid reduced UA. This reduction was similar to that observed with allopurinol but no improvement in endothelial function was seen (whereas it was with allopurinol) suggesting that the mechanism of benefit of allopurinol is UA-independent (6). Effects of XOR inhibition on outcome in heart failure patients have also been assessed in OPT-CHF trial (7). This medium-sized prospective study identified no overall difference following oxypurinol treatment but suggested potential benefit amongst hyperuricemic patients.

Consequently, XOR is the unique modifiable enzyme system generating reactive oxygen species. Although there is no evidence dictating usage of allopurinol and/or oxypurinol in cardiology practice, there are numerous small mechanistic trials implying beneficial effects of them.

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Author's Reply

Controlling uric acid as a means to control cardiovascular disease, metabolic syndrome and lipids

Lipidler, metabolik sendrom ve kardiyovasküler hastalıkların kontrol aracı olarak ürik asidin kontrolü

We are pleased with the interest of Yiğiner et al. in our observational and pilot study looking at the effects of allopurinol on markers of the metabolic syndrome, specifically lipids. Most end-stage renal disease (ESRD) patients have a comorbid condition of hyperuricemia (1) with some patients presenting with clinical gout as well. Also, we believe uric acid may be another marker of the metabolic syndrome (2) that could possibly be treated in patients who exhibit other comorbid conditions of the metabolic syndrome (central obesity, glucose intolerance, hyperinsulinemia, dyslipidemia, and hypertension). We are in agreement with Yiğiner et al. that these other comorbid conditions are contributing and possibly responsible for cardiovascular events (3). Novel treatments may be necessary for improvement in cardiovascular disease (CVD) profiles in such patients.

One of the reasons for the unusual effect of lipid lowering with concomitant increases in triglycerides in our study may be explained by another comorbid condition in ESRD patients and mentioned in our

manuscript. ESRD patients may have a tendency of enhanced very-low density lipoprotein (VLDL) catabolism with a downstream effect of smaller and denser low-density lipoprotein (LDL) particles with more oxidation of triglycerides and less production of lipoprotein lipase (4). This defect has been difficult to overcome in some of our previous studies in ESRD patients who did not present with significant hyperuricemia.

Secondly, we support the comments of Yiğiner et al. about the linkages between uric acid and proinflammatory cytokines. We have specifically added a number of markers of inflammation [C-reactive protein (CRP), interleukin-6 (IL-6), interleukin-1 (IL-1), interleukin-13 (IL-13) and tumor-necrosis factor alpha (TNF- α)] in our projects that are tracking uric acid through treatment with allopurinol. The inflammatory cytokines are associated with increased morbidity and mortality (5). It is our belief that inflammation may also play as significant a factor in the development of metabolic syndrome as the other well-supported comorbidities.

Finally, we agree with Yiğiner et al. that our pilot study has a major limitation regarding sample size and lacked a control group. Yet, since these patients were diagnosed with severe hyperuricemia with clinical gout and were treated with allopurinol, it made sense to see what effects allopurinol might have on lipids following previously published work (5-9). Our results suggested the need for further research. Consequently, we have launched a more longitudinal study with random selection of both a treatment group and control group that we believe will be a better powered study and add to the literature.

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