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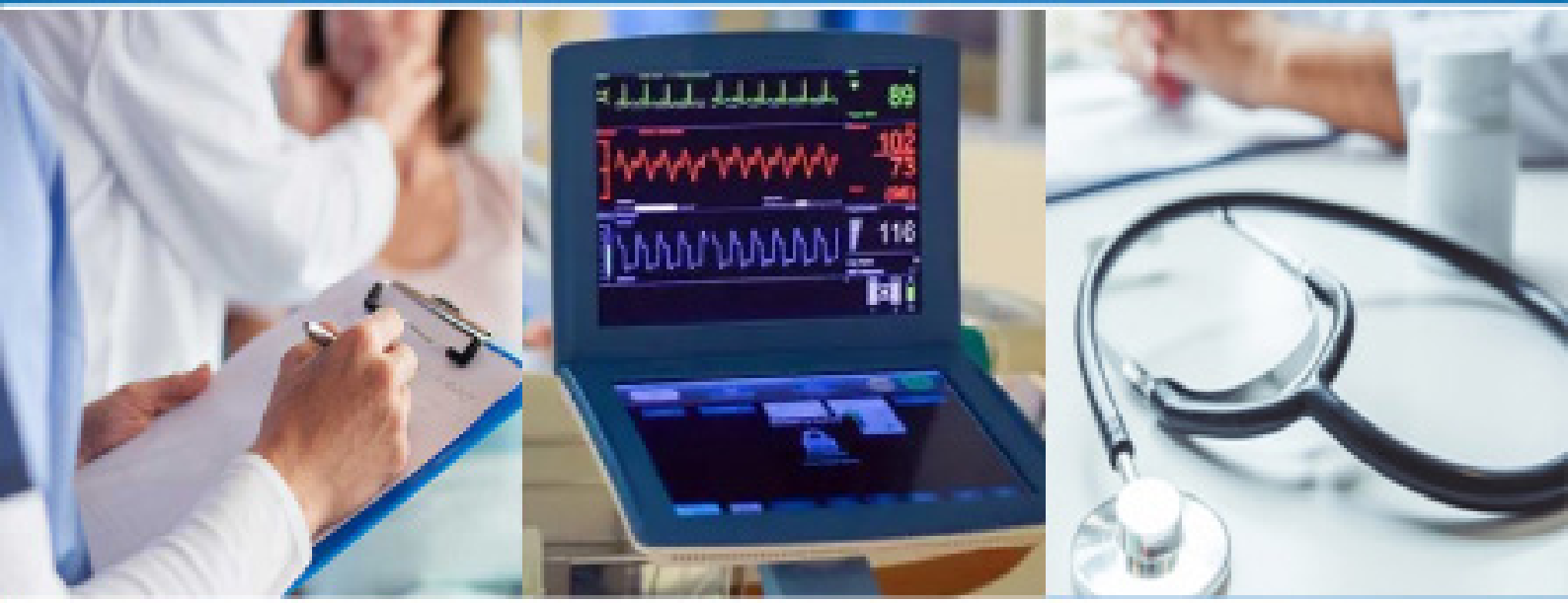

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Original Article

ABO and Rh blood group distribution in ANA positive patients

Ömer Faruk Alakuş[1], İhsan Solmaz[2], Sedrettin Koyun[3]

[1]Department of Internal Medicine, Bismil State Hospital, Diyarbakır, Turkiye
[2]Department of Internal Medicine, Gazi Yaşargil Training and Research Hospital, University of Health Sciences, Diyarbakır, Turkiye
[3]Department of Internal Medicine, Kızıltepe State Hospital, Mardin, Turkiye

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Corresponding Author: Ömer Faruk Alakuş, omerfaruk01@gmail.com

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ABSTRACT

Aims: Antinuclear antibody (ANA) positivity is a common finding in various autoimmune diseases, particularly those of rheumatologic origin. While ANA positivity alone may not be diagnostic, it serves as a valuable marker when supported by clinical findings, aiding in the diagnosis and prediction of autoimmune diseases. The relationship between blood group systems and various diseases has been an area of interest in medical research. In this study, we aimed to investigate the potential association between ABO blood group and ANA positivity, specifically examining whether the ABO blood group status poses a risk for autoimmune diseases in individuals with rheumatologic conditions.

Methods: In this retrospective study, we analyzed the blood group data of 536 patients who tested positive for ANA and were receiving treatment for rheumatologic diseases. The blood group status of these individuals was determined using standard serologic techniques. The distribution of ABO and Rh factor blood groups among ANA-positive patients was compared with the blood group distribution in the general population. Statistical analysis was performed to assess any significant differences.

Results: The analysis revealed that the distribution of ABO and Rh factor blood groups among ANA-positive individuals did not show a statistically significant difference compared to the general population. Specifically, there was no significant deviation in the prevalence of ABO blood groups (A, B, AB, O) or Rh factor (positive or negative) among ANA-positive patients compared to expected frequencies based on population data.

Conclusion: Based on our findings, there appears to be no significant association between ABO blood group status and ANA positivity in patients with rheumatologic diseases. The distribution of ABO and Rh blood groups among ANA-positive individuals closely resembled that of the general population. Therefore, our study suggests that current blood group status may not serve as a predictive factor for autoimmune diseases in individuals who test positive for ANA. Further research is warranted to explore other potential factors contributing to autoimmune disease susceptibility.

Keywords: ANA, ABO, blood group

INTRODUCTION

Anti-nuclear antibody (ANA) refers to antibodies developed against nuclear antigens in cells by the immune system that has lost tolerance to its own cells. The ANA test is a test in which anti-nuclear antibodies are measured in the blood by different methods and can be found positive at varying titers in serum in many autoimmune diseases, especially systemic lupus erythematosus (SLE), and guides the clinician.[1] ANA positivity may become positive in autoimmune diseases including SLE, Sjögren's disease, systemic sclerosis, myasthenia gravis, Hashimoto's thyroiditis, and inflammatory bowel disease, as well as in diseases including chronic active hepatitis, infectious mononucleosis, infective endocarditis, tuberculosis, and HIV. A positive test alone is not diagnostically significant. A titer above 1/160 is considered positive by the IFA (immunofluorescent antibody) method.[2] Apart from all these diseases, ANA positivity can also be detected in healthy individuals. Asymptomatic ANA positivity is present in 15-20 percent of the population. The significance of the majority of ANA positivity seen in healthy individuals is unknown, but most of them have benign causes. However, some of these individuals are at risk for autoimmune diseases.[3] Therefore, ANA testing is generally important in rheumatology and immunology practice.

Genetic and environmental factors have been shown to be associated with the incidence of rheumatologic diseases, and many studies have been conducted on this subject. However, the pathogenesis of rheumatic diseases has not been fully elucidated. Many studies have shown that ABO blood groups,

one of the blood grouping systems, are associated with many diseases.[4] In this study, we tried to investigate whether there is a relationship between ANA positivity, which can be a predictor for autoimmune diseases, especially rheumatologic diseases, and the ABO and Rh factor blood grouping systems.

METHODS

The study was carried out with the permission of Ethical Committe of Diyarbakır Gazi Yaşargil Training and Research Hospital (Date: 05.07.2023, Decision No: 2023-25). All procedures were carried out in accordance with the ethical rules and the principles of the Declaration of Helsinki.

This study was planned retrospectively, and the study population consisted of 1419 patients with positive ANA results who were followed and treated for rheumatologic diseases in the Internal Medicine and Rheumatology Outpatient Clinics of University of Health Sciences Diyarbakır Gazi Yaşargil Training and Research Hospital between January 1, 2017 and December 31, 2019. The data of these patients was scanned from the hospital automation system, and 536 patients whose blood group could be determined were included in the study. Patients whose blood group could not be determined were excluded from the study. These ANA test-positive patients were categorized according to their blood groups and compared with the data in the blood group study conducted with 127091 people in our province in 2019 as a control group.[4]

Statistical Analysis

Statistical evaluation was performed using SPSS 22 for Windows (IBM SPSS Inc., Armonk, NY, USA). Chi-square test was used to compare categorical data. In statistical analyses, $p<0.05$ was considered significant.

RESULTS

The blood group distribution of normal individuals in our province was 39.7%, 18.6%, 33.6%, and 8.1% with blood groups A, B, O, and AB, respectively. Rh (+) was 88.4%, and Rh (-) was 11.6%.[4] Data of 1419 patients with rheumatic diseases who were followed up in rheumatology and internal medicine outpatient clinics were examined. The blood group distribution of 536 patients with blood groups in the hospital automation system was determined as A, B, O, AB as 37.12%, 17.72%, 36.3% and 8.76%, respectively. Rh (+) was 88.99%, Rh (-) was 11% (Table).

Table. Blood group distribution and analysis of ANA+patients and healthy individuals

	ANA (+) patients (%)	Blood group distribution in the population of Diyarbakır, n (%)	X^2	p
Blood group A	199 (37.12)	50449 (39.7)	1.471	0.225
Blood group B	95 (17.72)	23678 (18.6)	0.290	0.590
Blood group O	195 (36.3)	42728 (33.6)	1.822	0.177
Blood group AB	47 (8.76)	10236 (8.1)	0.368	0.554
Rh+	477 (88.99)	112390 (88.4)	0.164	0.686
Rh-	59 (11)	14701 (11.6)	0.164	0.686

ANA: Anti-nuclear antibody

DISCUSSION

Many studies have been conducted on the role of blood groups in different diseases. It has been shown that the risk of thromboembolic events and cardiovascular diseases is higher in individuals with blood groups other than blood group 0.[5] In addition, it has been found that the likelihood of severe plasmodium falciparum infection is high in individuals with blood group 0.[6] In a study on blood group distribution in COVID-19 patients during the recent COVID-19 pandemic, it was found that ABO blood group distribution was the same as the normal population in individuals with COVID-19, Rh factor negativity was protective against COVID-19, and Rh factor positivity was predisposed to the disease.[7]

Many studies have been conducted on the relationship between rheumatic diseases and blood groups. In a study conducted by Çildağ et al.[8] in the immunology-rheumatology clinic, it was found that Rh factor positivity was higher in all rheumatic diseases. In this study, although there were no data on the normal population, the most common blood group in all rheumatic diseases was A, followed by 0, B, and AB, respectively, as in other studies conducted in our country. In this study, it was shown that the blood group distribution in rheumatic diseases was generally the same as in the normal population when compared with other studies. However, it was found that blood group A was higher in rheumatoid arthritis and spondyloarthropathies, and blood group 0 was higher in systemic lupus erythematosus and FMF. In our study, the blood group of patients found to be ANA positive was A>0>B>AB, respectively. Considering those rheumatologic diseases such as SLE and Sjögren's disease have the highest rate of ANA positivity, the most common blood group in this group was blood group A in our study, which was the same with the normal population.

In our study, when the ABO blood groups of ANA-positive patients and normal individuals taken as the control group were compared in terms of ABO blood groups, it was found that they were proportionally similar. In the statistical analysis, no statistically significant difference was observed between ANA-positive patients and healthy individuals.

ANA-positive individuals were also classified according to Rh-factor results and compared with the normal population in terms of Rh-factor results. No statistically significant difference was observed between the groups in terms of Rh factor results.

It is obvious that the ANA test, which is associated with many diseases, especially autoimmune diseases, is an important marker for clinicians in the diagnosis and treatment follow-up of many diseases if it is performed at the right time and in cases of significant clinical suspicion. The main diseases in which ANA positivity is important are autoimmune diseases, whose etiologies are still not fully elucidated. In our study of 536 patients with ANA positivity, we investigated whether there was a relationship between ANA positivity, which can be a predictor for autoimmune diseases, and blood group. We concluded that there was no significant difference from the normal population. Further studies on the relationship between genetic and environmental factors and autoimmune diseases, especially rheumatologic diseases affecting many systems, are needed.

Limitations

Our study has some limitations. First of all, we did not classify the patients included in our study according to rheumatological disease subgroups. Additionally, our study, which included 536 patients, was conducted using data from

a single center. If our study was multicenter, we could make additional contributions to our study by including a larger patient population in different geographies.

CONCLUSION

Conditions that predispose to autoimmune diseases are the subject of current studies. Studies in this field aim to predict individuals with autoimmune diseases and to determine the treatment strategy accordingly. In our study, we aimed to determine whether blood group is a predictor for autoimmune diseases by comparing the blood group of ANA test positive individuals followed up for rheumatologic diseases with the normal population. The retrospective design of our study and the fact that it was a single center study, we think that the current findings should be confirmed by studies conducted in larger populations. In addition, we believe that further research on the relationship between autoimmune diseases and genetic and environmental factors is needed.

ETHICAL DECLARATIONS

Ethics Committee Approval

The study was carried out with the permission of Ethical Committe of Diyarbakır Gazi Yaşargil Training and Research Hospital (Date: 05.07.2023, Decision No: 2023-25).

Informed Consent

Because the study was designed retrospectively, no written informed consent form was obtained from patients.

Referee Evaluation Process

Externally peer-reviewed.

Conflict of Interest Statement

The authors have no conflicts of interest to declare.

Financial Disclosure

The authors declared that this study has received no financial support.

Author Contributions

All of the authors declare that they have all participated in the design, execution, and analysis of the paper, and that they have approved the final version.

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Review

Current treatment approaches in the management of the heart failure patient

Bilgin Bahadır Başgöz[1], Cansu Öztürk[2], Caner Varhan[3], İhsan Solmaz[3]

[1]Department of Internal Medicine, Gülhane Faculty of Medicine, University of Health Sciences, Ankara, Turkiye
[2]Department of Cardiology, Gazi Yaşargil Training and Research Hospital, University of Health Sciences, Diyarbakır, Turkiye
[3]Department of Internal Medicine, Gazi Yaşargil Training and Research Hospital, University of Health Sciences, Diyarbakır, Turkiye

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Corresponding Author: Caner Varhan, drcvarhan@gmail.com

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ABSTRACT

Heart failure is a clinical syndrome in which the function of the heart muscle and neurohormonal regulation are impaired, resulting in an inability to meet the metabolic needs of tissues. Many different mechanisms are involved in the pathophysiology of heart failure. Therefore, this disease is defined as a chronic disease in which treatment management is difficult for both the patient and the physician. Therefore, although the main goal is to take the necessary precautions before the disease develops, this may not always be possible. The management of the disease and the treatment options are being provided by finding drugs that are effective against existing mechanisms or against new mechanisms that have been discovered. The main goal of treatment is to stop the chain of events that cause and worsen heart failure based on the physiopathology. For this reason, there are various treatment modalities accepted in current guidelines to manage the current process. The aim of these treatments is to reduce symptoms, improve quality of life, and reduce mortality and morbidity rates. Recently, many important developments in the field of heart failure have started to come one after another. In this article, the mechanisms of action of the current treatment options and their effects on mortality have been mentioned, but rather than the current pharmacologic treatments, promising new treatment options, especially phase 3 and phase 4 trials, have been evaluated.

Keywords: Heart failure, current treatment, medications, phase trials

INTRODUCTION

Heart failure (HF), to which millions of new cases are added every year, is still one of the most important health problems, despite improved diagnostic and therapeutic methods. In 2019, estimated 56.2 million people were living with HF across 204 countries globally, although the estimate likely underrepresents the true prevalence of HF because of data and diagnostic gaps in low-resource regions.[1] Despite high treatment costs, 1 out of every 2 patients diagnosed with HF dies within the following 5 years, and 1 out of every 3 patients hospitalized for HF dies within the following year. Therefore, it is very important to take the necessary preventive measures before the development of HF and to ensure that it is treated effectively for a long time after its development.

The primary goals of HF treatment are to reduce symptoms, improve quality of life and functionality, and reduce hospitalization and mortality. To achieve these goals, all factors that have an impact on the disease process and outcomes, such as lifestyle modification, identification and treatment of comorbidities, determination of the stage of the disease, and appropriate pharmacological and/or device therapies, should be addressed by a knowledgeable and experienced clinical team, and all of them should be effectively combated.

Considering the breadth of the subject and the existence of international consensus reports, this article will focus mainly on promising new treatment options rather than current pharmacological treatments.

CURRENT PHARMACOLOGIC TREATMENT AGENTS IN HEART FAILURE

Management of risk factors such as smoking and alcohol use, obesity, hypertension and diabetes mellitus, which have proven adverse effects on outcomes, is the first line of treatment in patients with HF.

Sodium-Glucose Cotransporter-2 Inhibitors (SGLT2I)

SGLT2i is suggested for people with symptoms of reduced ejection fraction HF (HFrEF) to lower the risk of hospitalization and death from cardiovascular disease, even if they also have type 2 diabetes. Following recent updates,

SGLT2i has also become the primary treatment option in patients with HF with preserved ejection fraction (HFpEF).[2]

Angiotensin Receptor-Neprilysin Inhibitors (ARNI)

Neprilysin, a neutral endopeptidase, mediates the degradation of many endogenous vasoactive peptides, especially natriuretic peptides, and decreases their levels. Sacubitril, an inhibitor of neprilysin, decreases the degradation of vasoactive peptides by inhibiting neprilysin and increasing their blood levels. This prevents water and sodium retention, vasoconstriction, and neurohumoral overactivation, leading to inappropriate remodeling.

In the PARADIGM-HF trial, sacubitril/valsartan, an ARNI, was shown to be superior to enalapril in reducing hospitalizations for worsening HF, CV mortality, and all-cause mortality in patients with LVEF≤40% (HFrEF).[2] In recent heart failure guidelines, ARNI has taken its place as the RAASi of first choice with a high level of evidence.

Angiotensin Converting Enzyme Inhibitor (ACE-I)

Effective dose ACE-I use has been shown to reduce mortality and morbidity in patients with HFrEF. Therefore, its use is recommended with a high level of evidence in all patients with CHF who cannot use ARNI, who have no contraindications for ACE-I use, and who can tolerate ACE-I. In survivors of acute MI with asymptomatic LV dysfunction (LVEF<35%-40%), RCTs have shown that ACEi reduced mortality, HF hospitalizations, and progression to severe HF compared with placebo.[3,4]

Beta Blocker (BB)

BB and ACE-I are known to have complementary effects and are recommended to be used together in patients with HF unless there is an obstacle. In combination, these two classes provide a comprehensive neuroendocrine blockade targeting both the heart, where beta blockade reduces cardiac output, and the vessels, where ACE inhibition induces vasodilation among other actions.[5] Carvedilol, extended-release metoprolol, nebivolol, and bisoprolol are the main molecules that have been shown to increase the duration of the symptom-free period and survival and are recommended for use in HF indications.

Angiotensin Receptor Blocker (ARB)

Although they are widely used, they are only recommended as an alternative for patients who cannot tolerate ACE-I. ARBs have significantly lower withdrawal rates than ACEi and most of the ARBs are nearly as effective as ACEi in the treatment of HF.[6]

Mineralocorticoid Receptor Antagonists (MRA)

Evidence has shown that aldosterone and MR activation may play a significant role in cardiovascular events.[7] MRAs (Spironolactone or Eplerenone) are recommended to reduce mortality and HF-related hospitalization in patients with persistent HF-related symptoms and left ventricular ejection fraction (EF)≤35% as measured by echocardiography despite receiving optimal doses of ACE-I and BB therapy.[8]

Eplerenone causes less gynecomastia development because it causes a more specific aldosterone blockade. Patients given MRA should be closely monitored, especially in terms of renal function and hyperpotassemia.

Diuretics

Expansion of extracellular fluid volume is central to the pathophysiology of heart failure. Increased extracellular fluid leads to elevated intracardiac filling pressures, resulting in a constellation of signs and symptoms of heart failure referred to as congestion.[9]

Although their positive effects on mortality and morbidity have not been demonstrated in randomized controlled trials, they have been used for a period of time in almost all patients, mainly loop diuretics and thiazides, to reduce the signs and symptoms of fluid overload.

Diuretics are recommended for HF patients with signs and/or symptoms of congestion to alleviate HF symptoms, improve exercise capacity, and reduce HF hospitalizations.[2]

The ADVOR study showed a significant increase in the incidence of successful decongestion within 3 days with the addition of IV acetazolamide to IV loop diuretics compared to placebo in acute decompensated heart failure, regardless of baseline EF and renal function.[10]

Others

Ivabradine reduces heart rate by inhibiting action on "funny" sodium channels (If) responsible for spontaneous diastolic depolarization of the sinoatrial node. It is indicated for use in patients with HFrEF who have persistent symptoms despite receiving maximally tolerated doses of beta-blockers, ACE-I (or ARB) and an MRA, heart rhythm in sinus rhythm, heart rate above 70 beats/min, and EF<35%.[2]

Treatment with Hidralazine+Isosorbid dinitrate is guideline-recommended for HFrEF patients who cannot receive either angiotensin-converting enzyme inhibitors or angiotensin receptor blockers due to intolerance or contraindication.[11] Hydralazine and isosorbide dinitrate should be considered in self-described black patients with LVEF<35% despite treatment with ACE-I (or ARNI), beta-blockers, and MRA or LVEF<45% with dilated left ventricle in NYHA class 3-4 to reduce the risk of HF hospitalization and death.[2]

Although digoxin has no favorable effect on mortality, it can be used for resting rate control in HF patients with atrial fibrillation accompanied by a high ventricular response.

RECENTLY REPORTED ADVANCES FROM HEART FAILURE TRIALS

Soluble Guanylate Cyclase Stimulator

The VICTORIA study evaluated the efficacy and safety of the oral soluble guanylate cyclase stimulator vericiguat in patients with reduced EF and recently decompensated CHF. The incidence of the primary endpoint of death from CV causes or hospitalization for HF was lower in those receiving vericiguat than in those receiving placebo.[12] No reduction in all-cause or CV mortality was seen. Therefore, vericiguat may be considered as an adjunct to standard treatment for HF.

Cardiac Myosin Activator

The GALACTIC-HF study looked at how well and safely the cardiac myosin activator omecamtiv mecarbil worked in both inpatients and outpatients with HF. The primary endpoint of the first HF event or CV death was reduced by 8%. There was no significant reduction in CV mortality. Currently, this drug

is not licensed for use in HF. However, it may be considered in the future as an adjunct to standard treatment for HFrEF to reduce the risk of CV mortality and hospitalization for HF.[13] Disease modifying drugs in important randomized trials in patients with heart failure were summarized in Table.

Table. Disease modifying drugs in important randomized trials in patients with heart failure

ARNI	SGLT2I	ACE-I	ARB	β-blockers	MRA
Sacubitril-Valsartan	Dapagliflozin Empagliflozin Canagliflozin	Captopril Enalapril Lisinopril Ramipril Trandolapril	Candesartan Losartan Valsartan	Bisoprolol Carvedilol Metoprolol Nebivolol	Spironolactone Eplerenone
Other Agents					
Ivabradine, Vericiguat, Digoxin, Hydralazine/Isosorbide dinitrate					

ARNI: Angiotensin receptor-neprilysin inhibitors, SGLT2I: Sodium-glucose cotransporter-2 inhibitors, ACE-I: Angiotensin converting enzyme inhibitor, ARB: Angiotensin receptor blocker, MRA: Mineralocorticoid receptor antagonists

RECENT IMPORTANT STUDIES ON THE TREATMENT OF HF

Circulating NEP and NEP Inhibition in Heart Failure with Preserved Ejection Fraction Study (Phase 4)

To determine biomarker responses to Entresto™ in patients with heart failure with preserved ejection fraction (HFpEF) and high or low serum neprilysin (NEP) levels.[14]

Entresto™ (LCZ696) in Advanced Heart Failure (LIFE Study) (Phase 4)

The primary objective of the study was to determine whether treatment with LCZ696 for 24 weeks would improve Pro-B-type Natriuretic Peptide (NT-proBNP) levels reflecting hemodynamic and clinical status compared to treatment with valsartan in patients with symptomatic, advanced heart failure due to left ventricular systolic dysfunction.[14]

STEP-HFpEF Study (Phase 3)

This study aims to evaluate the efficacy of semaglutide treatment compared to placebo in achieving weight loss in addition to improvement in symptoms, physical limitation and exercise function in patients with CHF and obesity.[15]

Combined Loop-Thiazide Diuretic Therapy (Phase 3)

In the Spain-based study titled "Safety and Efficacy of the Combination of Loop with Thiazide-type Diuretics in Patients with Decompensated Heart Failure (CLOROTIC)", which included patients with decompensated HF, it was planned to compare loop diuretic therapy alone with combined loop-thiazide diuretic combination therapy in one arm and loop diuretic therapy with placebo in the other arm and to evaluate the effects on the primary endpoints of body weight and dyspnea.[16]

Randomized Placebo-Controlled Trial of FCM as Treatment for Iron Deficient Heart Failure (Phase 3)

The primary objective of this study was to determine the efficacy and safety of iron therapy using intravenous (IV) ferric carboxymaltose (FCM) compared to placebo in the treatment of heart failure participants with iron deficiency and reduced ejection fraction.[14]

Efficacy and Safety of LCZ696 Compared with Valsartan on Morbidity and Mortality in Heart Failure Patients with Preserved Ejection Fraction (Phase 3)

The aim of this study was to evaluate the effect of LCZ696 compared to valsartan in reducing cardiovascular death and HF hospitalizations in HF patients with preserved ejection fraction.[14]

Evaluating the Safety and Efficacy of Allogeneic Mesenchymal Precursor Cells in the Treatment of Heart Failure (Phase 3)

The primary objective of this study was to determine whether transendocardial delivery of allogeneic human bone marrow-derived MPCs (rexlemestrocel-L) is effective in the treatment of chronic heart failure due to LV systolic dysfunction.[14]

The Assessment of Patiromer for the Management of Hyperkalemia in Individuals Taking Renin-Angiotensin Aldosterone System Inhibitor (RAASi) Drugs for the Treatment of Heart Failure (DIAMOND) (Phase 3)

The aim of this study was to determine whether patiromer treatment of subjects who developed hyperkalemia while receiving RAASi drugs would enable the continued use of RAASi drugs in accordance with HF treatment guidelines and thus reduce the occurrence of the composite endpoint of cardiovascular (CV) death and CV hospitalization events compared to placebo treatment.[14]

Evaluation of Autologous Bone Marrow Mononuclear Cells Using CadiAMP™ Cell Therapy in Patients with Heart Failure After Myocardial Infarction (Phase 3)

This is the first study using the patient's own stem cells in the treatment of patients with systolic dysfunction secondary to ischemic heart disease. Mononuclear cells from the bone marrow are processed on a cell processing platform and administered into the heart with a special method.[14]

Evaluation of the Efficacy and Safety of Human Bone Marrow Derived Stem Cells (CEP-41750) in the Treatment of Chronic Heart Failure (Phase 3)

The primary aim of this study was to determine whether transendocardial administration of human bone marrow-derived stem cells (CEP-41750) is effective in the treatment of chronic heart failure due to LV systolic dysfunction.[14]

Oral Treprostinil in Individuals with Pulmonary Hypertension (PH) Associated with Heart Failure with Preserved Ejection Fraction (HFpEF) (Phase 3)

This study is planned to provide long-term, open-label data on the effect of ongoing long-term oral treprostinil therapy for the treatment of pulmonary hypertension (PH) associated with heart failure with preserved ejection fraction (HFpEF).[14]

FIGARO-DKD Study (Phase 3)

This study examines the cardiovascular and renal effects of finerenone in patients with mild to moderate kidney disease and type 2 diabetes.[17]

CONCLUSION

HF is a chronic disease in which many different mechanisms, humoral systems, and vasoactive agents are involved in its pathophysiology, and despite effective control, the desired efficacy has not yet been achieved with current therapies, and therefore it is difficult to fight. Although much progress has been made in terms of treatment options in the historical process, the discovery of new mechanisms and new drugs effective on these mechanisms enables many new studies in this field. However, it is very difficult to be aware of the many clinical trials in this field and to keep track of them all.

For this reason, we thought that it would be useful to share with our clinicians working in this field by collecting promising studies evaluating new generation drugs that are

still ongoing in this field and whose results will be published soon, as well as treatment options whose benefits have been shown by studies and whose use is supported by current guidelines. It is of vital importance for clinicians to be able to follow these current studies closely, to be familiar with their results, and to know in which indications they are approved and in which patients their use is beneficial in the management of patients with HF.

ETHICAL DECLARATIONS

Referee Evaluation Process

Externally peer-reviewed.

Conflict of Interest Statement

The authors have no conflicts of interest to declare.

Financial Disclosure

The authors declared that this study has received no financial support.

Author Contributions

All of the authors declare that they have all participated in the design, execution, and analysis of the paper, and that they have approved the final version.

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Case Report

Obesity and diabetes, the pandemic of our time: the difficult to manage complication of diabetes, diabetic foot

Artuner Varlıbaş[1], Şeyma Kılıç[2], Muhammet Numan İbiloğlu[2], Aydın Çifci[1]

[1]Department of Internal Medicine, Faculty of Medicine, Kırıkkale University, Kırıkkale, Turkiye
[2]Medical Student (Phase IV), Faculty of Medicine, Kırıkkale University, Kırıkkale, Turkiye

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Corresponding Author: Artuner Varlıbaş, artunervarlibas@gmail.com

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ABSTRACT

Overweight and obesity are major problems worldwide, affecting more than half of the adult population. With wrong eating habits, the rise of fast-food culture and sedentary lifestyles, obesity continues to spread almost all over the world. In addition to the many physical problems obesity causes, it also significantly affects mental health. One of the most feared conditions caused by obesity is type 2 diabetes, a systemic disease that negatively affects every part of the body. In addition to the many problems it causes, diabetes causes foot problems in one out of every 6-7 patients throughout their lives, some of which may lead to limb loss and even death. The average life expectancy of patients with diabetic foot is significantly shortened. Treatment of these patients is also very costly. In this case report, we tried to explain the relationship between obesity and diabetes and diabetic foot problems that can lead to serious financial and moral losses.

Keywords: Obesity, diabetes, diabetic foot

INTRODUCTION

Obesity is an abnormal and excessive increase in adipose tissues in the body to the extent that it impairs health. Obesity is considered obesity when the amount of fat exceeds 25% of total body weight in men and 30% in women.[1] Although the prevalence is increasing in both sexes and in all age groups, it is more common in older women and men.[2] Obesity is associated with heart disease, hypertension, hyperlipidemia and various cancers.[3] A common disease associated with obesity is diabetes.[4] Approximately 90% of individuals with type 2 diabetes are overweight or obese, accounting for 90% to 95% of diabetes cases in the world today.[5] There is overwhelming evidence that an increase in body-mass index (BMI), visceral adiposity and body weight predicts the future development of type 2 diabetes mellitus (DM).[6] DM is a chronic metabolic disease characterized by high plasma glucose levels that over time cause serious complications in the heart, vascular structures, eyes, kidneys and nerves.[7]

Neuropathy and loss of sensation in the hands and feet are also common symptoms of diabetes. Patients with loss of sensation may not realize when they are injured. Diabetic foot is a long-term complication of diabetes, with approximately 15-25% of all diabetic patients experiencing this complication at some stage in their lives.[8] Neurological, vascular, and biomechanical factors contribute to diabetic foot ulceration. Approximately 50% to 60% of ulcers become infected, and about 20% of moderate to severe infections lead to lower extremity amputations. The 5-year mortality rate for individuals with a diabetic foot ulcer is approximately 30%, exceeding 70% for those with a major amputation.[9,10] Patients with diabetic foot are typically 50-60 years old and most have had diabetes for at least 10 years. Uncontrolled diabetes, if left untreated, can lead to major deformities of the foot.[11] In more advanced cases, amputation of the foot may be necessary. If recognized in time, diabetic foot can be prevented with blood glucose regulation before deformation develops. In this case report, we wanted to draw attention to the importance of the issue by presenting a case of diabetic foot that was not recognized in the early period and prolonged the process, delayed treatment and ultimately developed necrosis.

CASE

A 53-year-old man, 158 cm, 75 kg (BMI: 30 kg/m^2), who worked as a furniture painter, was admitted to the emergency department when his blood glucose level was measured as 389 mg/dl the previous evening. Normally, his blood glucose level was around 140-150 mg/dl. The patient had type 2 DM for 7 years. His compliance to treatment was poor. He had complaints of burning, weakness and numbness in his feet for 3-4 years. He did not think that these complaints were due to his diabetes because he worked standing all the time. The patient was asked about a foot wound observed in the system query. Wounds started to appear on the soles of the feet 2-3 weeks ago. The patient did not pay much attention to this and neglected it. The wounds healed and recurred from time to time; diabetic ulcers formed on the soles of the 1st, 3rd and 4th toes, and necrosis formed on the tip of the 5th toe of the left foot. The patient was treated at an external center for this, but there was no improvement and his blood sugar remained high, so she came to the emergency department with concern. He also had hypertension, benign prostatic hypertrophy, lumbar disc herniation and coronary artery disease. He underwent coronary angiography followed by coronary by-pass and surgery for lumbar disc herniation. On physical examination, the patient had nystagmus and Tinnel test was positive. Neurologic examination revealed deep sensory loss and visual field defects. Vital signs were normal. Postprandial blood glucose 421 mg/dl, glycated hemoglobin (HbA1c) 9.1%, urea: 76 mg/dl (N: 17-43), serum creatinine: 1.69 mg/dl (0.7-1.2), eGFR: 51 ml/min/1.73 m^2, C-reactive protein 12.1 mg/dl (N: 0-5), albumin: 3.1 g/dl (N: 3.5-5.2), pH: 7.27 (7.35-7.45) and had mild metabolic acidosis. There was no significant pathology in other investigations. There were no findings suggestive of dehydration. There was no growth in urine culture and ketones were negative in complete urinalysis. He was using subcutaneous insulin 3 times a day, acetylsalicylic acid, ACE inhibitor, calcium channel blocker, cilostazol, pentoxifylline. She was hospitalized in the ward because of high blood glucose levels. She was treated and followed up until his blood sugar was regulated in our hospital. Daily dressings and debridement were performed for the wounds on the patient's foot and intravenous antibiotics (ceftriaxone) were administered. The patient's condition stabilized and basal-bolus insulin treatment, moxifloxacin, GLP-1 agonists were recommended in the discharge regimen and oral medications were continued. During the follow-up, the patient's active infection improved, the ulcers on the 1st, 2nd and 4th toes started to heal and the dry gangrene on the distal end of the 5th toe of the left foot was limited. An outpatient clinic visit was recommended for the distal end of the 5th toe of the left foot to be evaluated for amputation by orthopedics. The patient was discharged after the necessary information was given, treatment was organized and the patient was advised to come for follow-up (Figure).

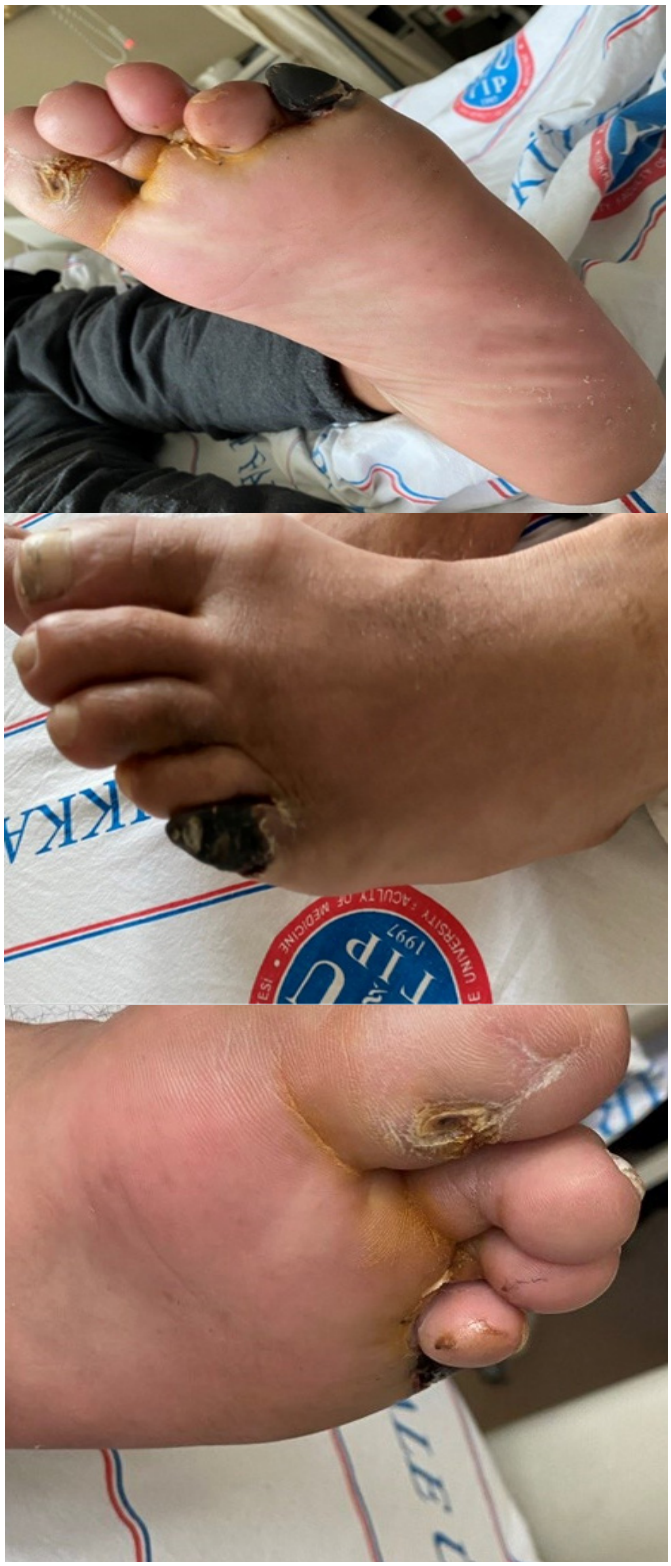

Figure. Images of patient with diabetic foot: Wagner 5 ulcer and demarcation line on the 5th finger

DISCUSSION

Obesity and diabetes are frequently seen together.[1-3,8] Diabetic patients may experience polyuria, dry mouth, polydipsia, weakness-fatigue, polyphagia, delayed healing of wounds, and paresthesia in the hands and feet due to irregular blood sugar levels.[10-12] Diabetes that develops as a result of obesity causes inflammation in the vascular structures of the kidney in the long term, impairing blood

flow to the kidney and glomerular filtration.[13] Prolonged high plasma glucose levels may cause retinopathy in the eye, macular edema by increasing the permeability of the arteries in the eye, and cataract development by increasing end products in the polyol pathway.

DM can also damage peripheral nerves, leading to complaints such as loss of sensation, burning, severe pain and numbness. These symptoms usually start at the fingertips of the hands and feet. These patients are slow to recognize when they are injured or when necrosis begins. Traumatic wounds on the feet are among these. This condition, called diabetic foot, develops due to different etiological reasons. There is consensus that the most important cause is polyneuropathy. In industrialized societies, the main cause of polyneuropathy is diabetes.[8]

With timely diagnosis and treatment, it is possible to prevent both obesity and related diabetes. Early diagnosis is very important to improve the patient's quality of life and minimize the risk of complications. When diagnosed early, lifestyle changes can prevent obesity and diabetes-related complications. Weight loss is clearly beneficial in reducing the risk of developing diabetes. In the Diabetes Prevention Program, an average weight loss of 5.5% over 2.8 years was shown to reduce the risk of prediabetes converting to diabetes by 58%.[11] Medical and surgical treatments can be applied if lifestyle changes are not sufficient or if the diagnosis is late. GLP1 agonists that reduce appetite and regulate blood glucose can be used. GLP1 agonists may be protective for diabetes and obesity. The choice of medication should be made taking into account the patient's clinical condition and compliance with the treatment. Various surgical methods can also be applied if the patient has a condition that prevents the use of medication or if the patient's compliance with the treatment is insufficient. However, surgical methods also bring risks such as venous thromboembolism, sepsis and dysfunction. Therefore, the patient should be recognized and treated before reaching this point.[11-15]

CONCLUSION

Foot problems may occur in diabetic patients due to many reasons. The patient in this case report complained of loss of sensation in his foot and inability to recognize small stones in his shoe. Although the patient had a serious foot problem, he was admitted to the emergency room due to excessive elevation of blood glucose. The severity of the wound on detailed physical examination was recognized early by the clinicians and optimal treatment of the patient was provided both in terms of blood glucose regulation and diabetes-related foot problem without amputation. Lifestyle changes, preventive measures and early diagnosis and treatment of complications that may develop in diabetic patients are important. Thus, it is possible to prevent problems before they grow and to prevent more serious negative situations. This is important for diabetic patients, who are so common, to live as healthy a life as possible.

ETHICAL DECLARATIONS

Informed Consent

The patient signed and free and informed consent form.

Referee Evaluation Process

Externally peer-reviewed.

Conflict of Interest Statement

The authors have no conflicts of interest to declare.

Financial Disclosure

The authors declared that this study has received no financial support.

Author Contributions

All of the authors declare that they have all participated in the design, execution, and analysis of the paper, and that they have approved the final version.

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Case Report

A case of myeloid sarcoma with duodenal involvement presenting with extrahepatic cholestasis

Mehmet Ali Erdoğan

Division of Gastroenterology, Department of Internal Medicine, Faculty of Medicine, İnonu University, Malatya, Turkiye

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Corresponding Author: Mehmet Ali Erdoğan, mehmet_ali_erdogan@hotmail.com

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ABSTRACT

Myeloid sarcoma (MS) is a hematologic malignancy composed of myeloblasts or immature myeloid cells presenting in the extramedullary region. MS frequently involves bone, soft tissue, skin, lymph nodes, as well as the genitourinary and gastrointestinal systems. We wanted to present a case of MS presenting with duodenal involvement. A 22-year-old male patient presented with abdominal pain and jaundice. Laboratory values of total bilirubin: 2.4 mg/dl, direct bilirubin: 1.85 mg/dl, GGT: 347 U/L. Endoscopic retrograde cholangiopancreatography (ERCP) showed dilated choledochal dilatation with migrated stent and stenosis at the distal end. The existing stent was removed, and a 10 FR 12 cm biliary plastic stent was placed proximal to the stenosis. Since hyperemic, erosive lesions were observed in the mouth of oddi and duodenum; biopsies were taken from that region. The biopsy result was reported as primary duodenal myeloid sarcoma. MS should be considered in gastrointestinal lesions.

Keywords: Myeloid sarcoma, duodenum, cholestasis

INTRODUCTION

Myeloid sarcoma (MS), also called granulocytic sarcoma, is a rare hematologic malignancy consisting of myeloblast or immature myeloid cells presenting in the extramedullary region. MS has been reported to develop in 2%-8% of adult patients with acute myeloid leukemia (AML). It can occur before, concurrently with, and after the diagnosis of AML. The diagnosis is relatively difficult because its clinical presentation is based on the symptoms of the site.[1,2] Those with isolated extramedullary involvement without bone marrow involvement are called primary MS and are observed with a rate of 2/1,000,000.[3] In addition to bone, soft tissue, skin, and lymph node involvement, MS may involve epidural tissue, mediastinum, breast, genitourinary system, and gastrointestinal system.[4]

Duodenal mucosa is frequently inflamed with duodenitis, ulcers, and mucosal inflammation of unknown cause. In addition, inflammatory bowel disease, tbc, immunologic diseases, and rare infections may be seen. The diagnosis is usually made with a biopsy taken from the lesion in this region.[3] Gastrointestinal stromal tumors, lymphoma and carcinoid tumor, especially adenocarcinoma, may be observed in the small intestine.[5] Endoscopic retrograde cholangiopancreatography (ERCP) is used in the diagnosis and treatment of pancreaticobiliary diseases. ERCP is used in cases such as tissue sampling, cholangiography, and pancreotography, removal of biliary duct stones, benign biliary strictures, malignant biliary strictures, and endoscopic papillectomy.[6]

In this article, we present a case of myeloid sarcoma with duodenal involvement who underwent ERCP for biliary obstruction one year ago.

CASE

A 22-year-old male patient presented with abdominal pain and jaundice. Physical examination revealed no additional findings except for icteric sclera. ERCP was performed one year ago due to extrahepatic cholestasis, and distal choledochal stenosis was observed. The patient who underwent stenting due to stenosis was discharged and did not come to follow-up visits. The laboratory findings of the patient one year ago are shown in Table.

In the patient's last admission, abdominal ultrasonography revealed that the gallbladder was hydropic, the common bile duct was 12 mm, and there was a stent in it. In the dynamic liver magnetic resonance (DLMR) report, a heterogeneous hypointense lesion on T1A and a heterogeneous hyperintense lesion on T2A, 4.5 cm in diameter, were observed in the head of the pancreas and surrounding the distal common bile duct. The laboratory values of the patient upon arrival are shown in Table. ERCP revealed dilatation of the common bile duct and stenosis at the distal end with a migrated stent.

Table. Laboratory values of the patient

Parameters	First Visit	New Visit	Normal Values
AST (U/L)	165	57	5-34
ALT (U/L)	325	122	0-55
ALP (U/L)	268	259	40-150
GGT (U/L)	215	347	9-64
LDH (U/L)	228	197	125-243
Total bilirubin (mg/dl)	7.75	2.41	0.2-1.2
D. Bilirubin (mg/dl)	6.7	1.85	0-1
WBC(10^9/L)	5.9	2.5	4.3-10.3
Hemoglobin (gr/dl)	12.8	13	12.2-18.1
Platelet (10^9/L)	387	281	150-400
CRP (mg/dl)	0.31	4.46	0-0.35
INR	0.97	1.38	0.8-1.2
HBsAg	Negative		
Anti-HBs	Pozitive		
Anti-HCV	Negative		
HIV	Negative		

AST: Aspartate aminotransferase, ALT: Alanine aminotransferase, ALP: Alkaline phosphatase, GGT: Gamma-glutamyl transferase, WBC: White blood count, CRP: C-reactive protein, HBsAg: Hepatitis B surface antigen, Anti-HBs: Hepatitis B surface antibody, Anti-HCV: Hepatitis C virüs antibody, HIV: Human immunodeficiency virüs

The existing stent was removed with foreign body forceps. A 10 FR 12 cm biliary plastic stent was placed proximal to the stenosis. Hyperemic, eroded, and nodular lesions were observed in the mouth of Oddi and duodenum. Moreover, a biopsy was performed (Figure). In duodenum biopsy pathology, a relatively monotonous appearance was observed in which the gland structures of the duodenum had disappeared in most areas. Additionally, atypical cells with narrow cytoplasm, oval-round nuclei, and occasionally suspicious nucleoli were observed. In immunohistochemistry, LCA, MPO, CD33, CD34, CD117, CD15, CD 99, and panCK were stained positive. Ki-67 proliferation index was determined as 80%. The biopsy result was reported as primary duodenal myeloid sarcoma.

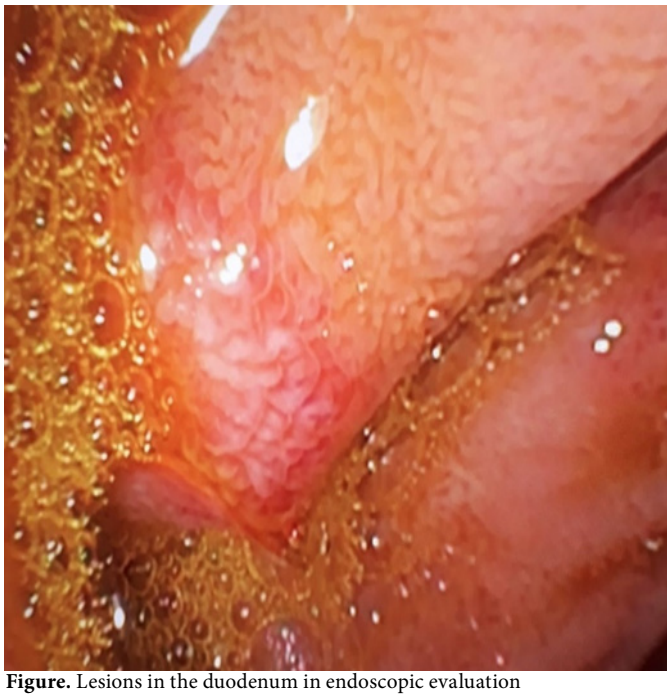

Figure. Lesions in the duodenum in endoscopic evaluation

After the diagnosis of granulocytic sarcoma, bone marrow examination was compatible with acute myeloid leukemia involvement. After AML induction therapy, a dynamic liver MRI showed the disappearance of the lesion previously diagnosed as granulocytic sarcoma.

DISCUSSION

While the diagnosis of MS in the presence of AMI is relatively easy, the diagnosis of primary MS is often difficult. The misdiagnosis rate of these cases varies between 25% and 74%. The most common misdiagnosis is nonhodgin lymphoma. B-cell or T-cell lymphoma and MS have similar morphologic features, and both express some leukocyte antigens such as CD34. In addition to chloroacetate-esterase, myeloperoxidase, lysosome, and CD43, the use of other B- and T-markers, especially CD79a and CD3, is recommended for an accurate diagnosis.[2,7-9] Patients with MS may also be confused with malignant lymphoproliferative disorders, non-Hodgkin's lymphoma, histiocytic lymphoma, thymoma, myeloma, eosinophilic sarcoma, extramedullary hematopoiesis and, Ewing's sarcoma.[2] The finding of a mass on the DCMR one year ago, the normal hemogram at that time, and the disappearance of the mass on the DCMR after chemotherapy led us to believe that it might be Pirmer MS.

Small bowel involvement, estimated to be around 10%, is more common than colon involvement. In GI involvement, abdominal pain, bleeding, perforation, obstruction, intussusception, pancreatitis, bile duct obstruction, hepatic infarction, and portal hypertension may be observed.[4] It may also be confused with Crohn's disease due to terminal ileum involvement.[10]

Although gastrointestinal involvement is not common, Yamauchi et al.[11] found small small intestine involvement in 11 patients (11%) and gastric involvement in 1 patient in a study of 74 patients. Again, in a study of 26 cases of granulocytic sarcoma with extramedullary involvement, Menasce et al.[9] found only two cases, one involving the cecum and one involving the cecum and appendix. Our patient had duodenal involvement and associated cholestasis.

In previous cases, small bowel involvement may be seen as hyperemic, ulcerated areas, or inflammatory bowel disease, an intraluminal polypoid mass or an ulcerated tumorous lesion on endoscopic image.[10,12] In our patient, it was observed as patchy, nodular, and hyperemic areas.

Primary MS almost always progresses to acute non lymphoblastic leukemia (ANLL) if left untreated. Treatment of MS is the same as for ANLL, and prolonged survival has been observed.[10]

CONCLUSION

As a result, although MS is rare, it should be kept in mind in biliary obstructions and other gastrointestinal lesions.

ETHICAL DECLARATIONS

Informed Consent

All patients signed and free and informed consent form.

Referee Evaluation Process

Externally peer-reviewed.

Conflict of Interest Statement
The authors have no conflicts of interest to declare.

Financial Disclosure
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Author Contributions
All of the authors declare that they have all participated in the design, execution, and analysis of the paper, and that they have approved the final version.

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Case Report

One year follow-up and literature review of three young-age cases with high risk pulmonary thromboembolism

Sümeyra Altan Çotur, Emine Bahar Kurt, Ayşe Demirkaya
Department of Chest Diseases, Ankara Etlik City Hospital, Ankara, Turkiye

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Corresponding Author: Sümeyra Altan Çotur, altansumeyra@hotmail.com

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ABSTRACT

High-risk pulmonary thromboembolism (PTE) is an emergency clinical condition with high mortality. High-risk pulmonary thromboembolism is generally seen in immobile patients, elderly, have malignancies, and have a long-term travel history. Our aim here is to emphasize that high-risk pulmonary thromboembolism may also occur in young patients. Considering the symptoms and risk factors such as oral contraceptive use, obesity, and operation history, PTE can be detected with Pulmonary computed tomography-angiography (CTPA) or ventilation perfusion scintigraphy when necessary. It should be verified that it is not. Genetic mutation, obesity, oral contraceptive use, and previous operation history were accepted as risk factors in the young patients we treated and followed up with high-risk Pulmonary Thromboembolism presented here. After the diagnosis of pulmonary thromboembolism was made at the first stage in our patients who applied to the emergency department, the risk group was determined by taking into account the current guidelines. Three patients considered to be at high risk were evaluated for thrombolytic therapy. Two patients without contraindications were given a full dose, and one patient was given a half dose of thrombolytic. After being monitored in intensive care for the first 24 hours, they were taken to the service. Due to their young age (<45 years), their thrombophilia panel was checked. Anticoagulant treatments were started and follow-ups were planned at 3 months, 6 months, and 1 year after discharge. During the follow-up visits, CTPA, echocardiography, and lower extremity Doppler ultrasound imaging were performed.

Keywords: Pulmonary embolism, venous thromboembolism, high-risk pulmonary embolism, young-age

INTRODUCTION

Venous thromboembolism is a common term that describes two diseases, pulmonary thromboembolism (PTE) and deep vein thrombosis (DVT), with or without symptoms but often accompanying each other. Pulmonary thromboembolism is the third most common cardiovascular disease leading to acute death after coronary heart disease and stroke.[1] Another important complication is relapses, which, although rare, may result in chronic thromboembolic pulmonary hypertension (CTEPH), which is a difficult-to-treat disease that severely impairs the person's quality of life.[2] Although this disease, which has such serious complications, is preventable, prophylaxis for thrombosis is unfortunately neglected in some cases in our country and around the world.

While patients may present with complaints of chest pain and shortness of breath, they may also present with syncope, right heart failure, severe hypoxemia, and cardiac arrest. Some cases may need mechanical ventilation (MV) and need to be monitored in intensive care. In the emergency department and intensive care units (ICU), bedside echocardiography (ECHO) is a valuable imaging method in hemodynamically unstable patients.[3] In the treatment of high-risk PTE, thrombolytic agents are a life-saving treatment option in suitable patients. Although studies are showing that patients with a high risk of bleeding, especially those over the age of seventy-five, diagnosed with high-risk PTE are treated with low-dose thrombolytic agents, it has not yet been included in the guidelines.

CASE 1

A 21-year-old female patient had a history of oral contraceptive (OCS) use due to Polycystic ovary syndrome (PCOS) and was admitted to the emergency room due to shortness of breath and chest pain. She had no hemoptysis. During her first physical examination in the emergency room, his respiratory rate was 24 breaths/min, his arterial blood pressure (TA): was 87/45 mmHg, her heart rate was 120 beats/min, and his oxygen saturation in room air (SpO_2): 85%. In the first examination, the D-dimer level was 4 mg/L, and CTPA was performed with the preliminary diagnosis of PTE. CTPA revealed a filling defect compatible with PTE in both pulmonary artery lumens and all lobar and visible segmental branches (Figure 1).

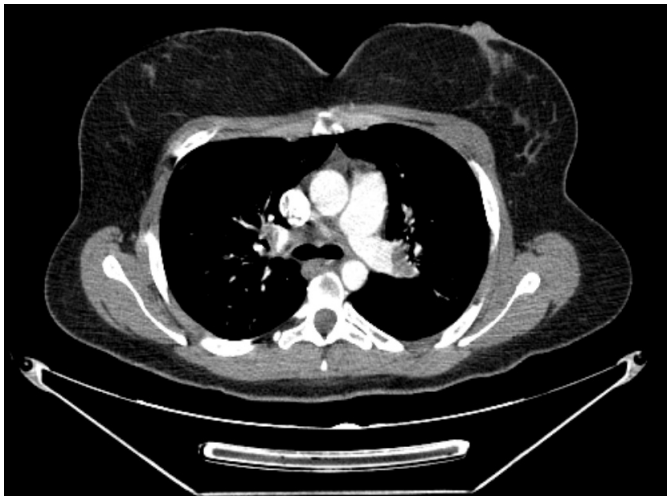

Figure 1. Emergency department admission moment BTPA

After the patient was followed up in the intensive care unit for the first 24 hours, he was taken to the service as his hemodynamics were stable. During the service follow-ups, collagen tissue markers and genetic thrombophilia panel were checked due to the young age of the patient (under 45 years of age). Anti-nuclear antibody and Anti-dense fine spotted 70 (Anti-DFS70) results were positive. Genetic tests resulted in MTHFR (methylenetetrahydrofolate reductase) heterozygous mutant and Factor 13 heterozygous mutant. Lifelong anticoagulant treatment was planned with the recommendation of the hematology department.

The patient was started on Warfarin Sodium and DVT treatment. No PTE was observed in the patient's 3rd monthly follow-up (Figure 2). DVT was continuing in lower extremity Doppler ultrasonography.

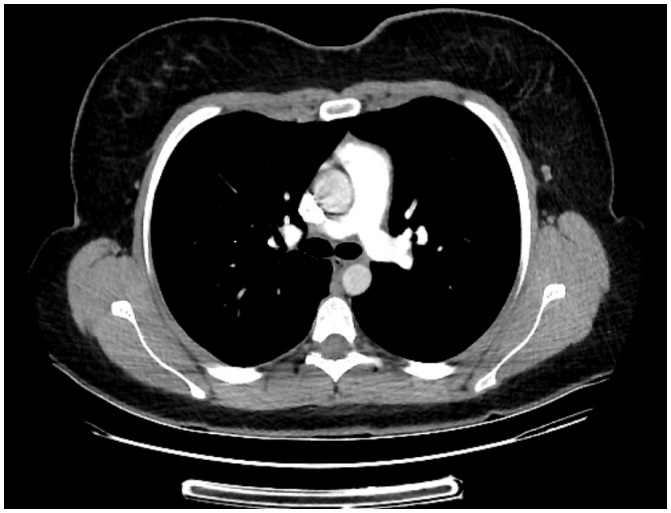

Figure 2. 3rd month BTPA

PTE was not observed at her 6th month follow-up (Figure 3). The Doppler ultrasound evaluation was noted to be suboptimal and no thrombus was detected.

The patient's radiological appearance was normal in terms of PTE at his 1-year follow-up. ECHO findings were normal, but the DVT continued in the left popliteal vein of the lower extremity in Doppler ultrasonography. Cardiovascular surgery was consulted and it was decided to continue treatment with Warfarin Sodium by ensuring the effective INR level of the patient.All follow-ups of the patient have been summarized in the table below

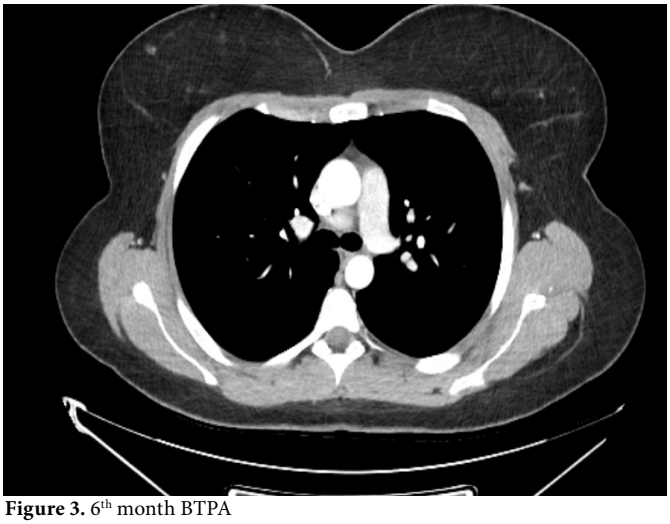

Figure 3. 6th month BTPA

CASE 2

A twenty-three-year-old female patient, who had no risk factors other than that condition, was admitted to the emergency room with a complaint of sudden shortness of breath. She had no hemoptysis. On physical examination in the emergency room, TA: 70/45 mmHg, pulse 115 beats/min, respiratory rate 20 breaths/minute, SpO_2: 94%. CTPA was performed in the emergency department due to the difference in diameter between legs and the D-dimer level being 2.9 mg/L. In the pulmonary CT angiography, it was observed that thromboembolism material was found within the lumen of the left main pulmonary artery, causing partial occlusion in the artery, and the identified embolic material extended to the right main pulmonary artery and causing partial occlusion (Figure 4).

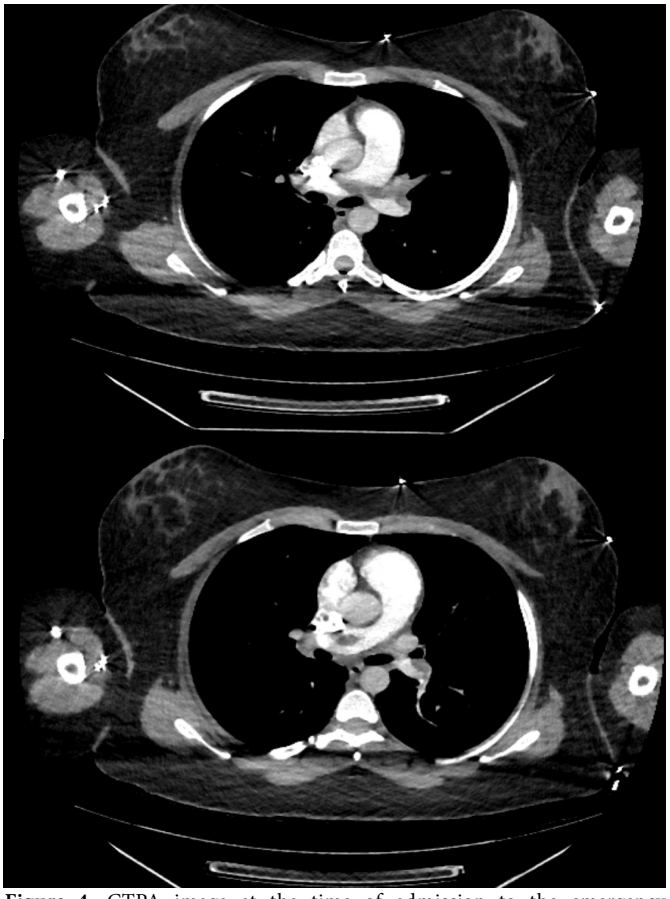

Figure 4. CTPA image at the time of admission to the emergency department

EF in bedside echo; 60% was seen as Spab: 20, and the right structures were evaluated as normal. It was planned to give full dose thrombolytics to her, whose systolic blood pressure was <90 mmHg, hemodynamically unstable, and considered high risk due to Pulmonary embolism severity index (PESI) class 3 and cardiac troponin positivity. After receiving a total of 40 mg of thrombolytic, the thrombolytic infusion was stopped due to bleeding from the vascular access. After 24 hours of follow-up in the ICU, she was taken to the service when his hemodynamics remained stable.

Lower extremity Doppler USG performed for possible DVT in the left lower extremity; the femoral vein and popliteal vein were observed to be thrombosed and DVT treatment was started. Due to her young age, a thrombophilia genetic panel was sent for genetic screening. It resulted in a factor 2 homozygous mutant. In the patient's 3rd and 6th-month follow-ups, PTE was not observed in CTPA, ECHO, and lower extremity Doppler USG was normal.

Anticoagulant treatment was terminated at the sixth-month follow-up. No pathology was detected in the patient at the first-year follow-up.All follow-ups of the patient have been summarized in the table below.

CASE 3

A twenty-seven-year-old female patient with no chronic disease and a cesarean section 2 months ago was admitted to the emergency department due to stabbing chest pain. She described chest pain radiating to the back and had hemoptysis the size of 1 teaspoon. CTPA was performed on the patient with a history of surgery and hypoxia, as PTE was suspected. CTPA revealed a filling defect extending from the left main pulmonary artery to the lingual segment and branches of the inferior lobar artery (Figure 5).

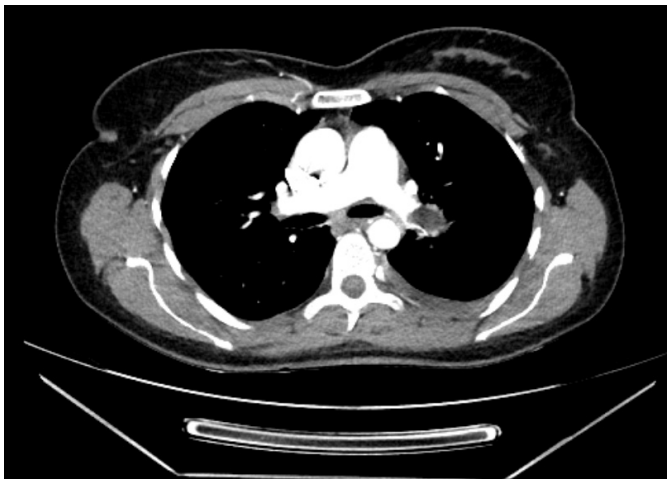

Figure 5. CTPA image at the time of admission to the emergency department

As the patient's hemodynamics were unstable, an ECHO was performed at the bedside. EF was found to be 60% spab 20 mmHg. On his physical examination: TA: 78/55 mmHg, pulse 138 beats/min, SpO2: 83%. She whose pulmonary embolism severity index (PESI) corresponded to class 3 and whose systolic blood pressure was below 90 mmHg, was classified as a high-risk patient. She was admitted to the intensive care unit. The hemodynamically unstable patient was administered a half dose of thrombolytic agent. She was monitored in the ICU for 24 hours and was transferred to the service after his vital signs improved. The Doppler USG of the lower extremities, which was examined for a possible DVT, showed no DVT.

The department of obstetrics and gynecology was consulted regarding the availability of anticoagulant treatment during lactation. Treatment with low molecular weight heparin (LMWH) was decided. In the thrombophilia panel, the heterozygous mutation MTHFR-A1298c and the heterozygous mutation of factor 13 were positive. In consultation with the hematology department, it was decided that lifelong anticoagulation was not necessary.

At the patient's 3rd month follow-up, the PTE was still visible on CTPA. The results of ECHO and Doppler USG of the lower extremities were assessed as normal. The patient was treated with anticoagulants for 6 months, but then stopped coming for follow-up visits at his request. He did not receive any treatment.

The CTPA performed at the first-year follow-up examination revealed that the thrombus in the pulmonary arteries had become chronic. The patient underwent an ECHO to test for CTEPH. On ECHO, Spab: 24 mmg and right ventricles were found to be normal.Doppler USG examination of the patient's lower extremities, which was evaluated for possible DVT, did not reveal DVT. The patient, who had completed the breastfeeding period, was given medical treatment and a follow-up examination was scheduled.All follow-ups of the patient have been summarized in the table below

If we need to summarize the cases, the similar and different aspects of 3 cases, along with the findings during follow-ups, have been presented in the Table below

DISCUSSION

Pulmonary thromboembolism is a disease whose incidence, prevalence, morbidity and mortality increase with age.[4] For this reason, it is not considered in most young age patients, and the diagnosis of medium and high risk PTE in the young population becomes difficult.

In patients with pulmonary thromboembolism who do not have cardiopulmonary comorbidities, sudden dyspnea and tachypnea are the most common clinical symptoms. Pleuritic pain often accompanies dyspnea and tachypnea.[5] Our patients presented to the emergency room with complaints of sudden onset of dyspnea and chest pain, which are consistent with the most common presenting symptoms of patients diagnosed with PTE. There was tachypnea on physical examination. When risk factors were questioned, a genetic mutation causing thrombus susceptibility was detected in one of our patients. Obesity was accepted as a risk factor in two of our patients . One of our patients had a history of surgery within the last three months.

High-risk pulmonary thromboembolism may also occur in young patients . In cases where there are symptoms and risk factors that suggest PTE, it should be confirmed whether PTE is present with CTPA or V/Q scintigraphy.

High-risk pulmonary thromboembolism is an urgent and serious clinical condition with high mortality, which may present with sudden onset dyspnea, hypotension, signs of right heart failure, presyncope or syncope, and cardiac arrest, and whose treatment must be started quickly after diagnosis.[6]

Table. Summary table for 3 cases

	CASE 1	CASE 2	CASE 3
Age	21	23	27
Gender	Woman	Woman	Woman
Risk factors	Genetics, obesity	Morbid obesity	Genetics, history of previous surgery
Wells	4.5 points: medium risk	7.5 points: high risk	10 points: high risk
PESI	91: class 3	73: class 2	117: class 4
CTPA	In both pulmonary artery lumens, lobar and some segmental branches	Partial occlusion within the lumen of the left main pulmonary artery extending to the right main pulmonary artery	Filling defect extending from the left main pulmonary artery to the lingual segment and lower lobar artery branches
Is it accompanied by DVT?	Yes	Yes	No
Treatment	Alteplase 100 mg (full dose) + Lifetime anticoagulant	Alteplase 40 mg+warfarin (6 months) and diosmin+hesperidin 2*500 mg	Alteplase 50 mg (half dose)+LMWH 2*1 due to lactation; Patient not complying with treatment
Complication after treatment	None	Treatment could not be completed due to bleeding.	None
Follow-up			
3 months	PTE was not observed. DVT was ongoing	PTE was not observed. DVT was not observed.	It was observed that the appearance of PTE continued.
6 months	PTE was not observed. DVT was not observed(The evaluation was made suboptimal)	PTE was not observed. DVT was not observed.	She didn't come to check.
1 year	PTE was not observed. DVT continued	PTE was not observed. DVT was not observed.	CTPA showed that the thrombus in the pulmonary arteries had become chronic.

PESI: Pulmonary embolism severity index, CTPA: Computed tomography pulmonary angiography, DVT: Deep vein thrombosis, LMWH: Low molecular weight heparin, PTE: Pulmoner tromboemboli

High risk. Pulmonary thromboembolism is generally seen in patients who are immobile, elderly, have comorbidities, have malignancies, and have a long-term travel history.[7] However, it can also occur at young ages, as it did here. When diagnosing PTE in people under the age of forty-five, it is important to investigate the risk factors in detail, question the history of previous operations, the medications used, check genetic tests, and eliminate predisposing factors such as obesity that will require life changes.

CONCLUSION

High-risk pulmonary thromboembolism is an urgent and serious clinical condition with high mortality. However, it can also occur at young ages, as it did here. In clinically suspected patients, rapid diagnosis should be made and treated.

ETHICAL DECLARATIONS

Informed Consent

All patients signed and free and informed consent form.

Referee Evaluation Process

Externally peer-reviewed.

Conflict of Interest Statement

The authors have no conflicts of interest to declare.

Financial Disclosure

The authors declared that this study has received no financial support.

Author Contributions

All of the authors declare that they have all participated in the design, execution, and analysis of the paper, and that they have approved the final version.

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