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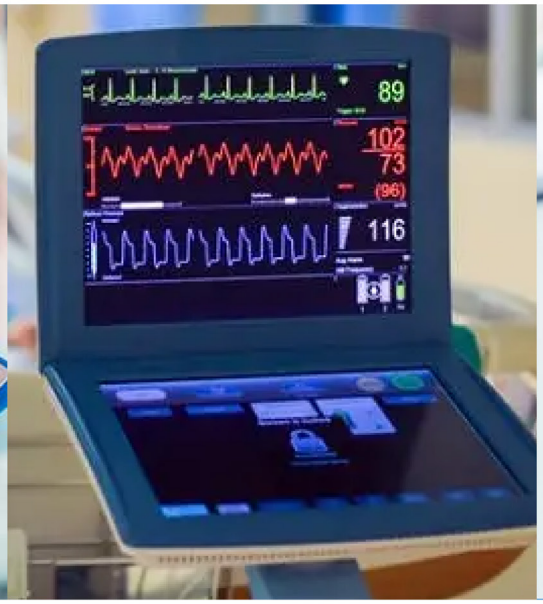

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EDITORIAL

Dear Coleagues,

We are proud to publish the this thirdh issue of ICJIM in 2023. The quality of the our journal is increasing day by day. We published this issue of our journal with two original articles, a review, and two case reports. In our journal, we receive articles from medicine and health-related fields. In near future, we want to contribute to international literature at an increasing level and to increase the success bar of our journal by entering valuable international indexes such as SCI-Expanded, Pubmed. ESCI, and Scopus. We would like to thank the authors who sent their scientific articles to our journal and everyone who contributed to the publication of the issue.

Sincerely

Prof. Dr. Aydın ÇİFCİ

Editor in Chief

The Intercontinental Journal of
Internal Medicine

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Original Article

Evaluation of antioxidant activity in without persistent ST-segment elevation

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ABSTRACT

Aims: Coronary artery disease is the most common cause of mortality and morbidity worldwide. Oxidative stress is involved in the pathogenesis of many diseases, including atherosclerosis. Thiols are important antioxidants for the elimination of reactive oxygen radicals and oxidative stress. In this study, we aimed to compare patients suffering from without persistent ST-segment elevation (NSTMI) and volunteers with normal coronary arteries in terms of antioxidants.

Methods: The study included 105 patients diagnosed with NSTMI and 51 controls. Plasma total thiol, native thiol, and disulfide levels were measured.

Results: Baseline demographic characteristics were similar between the groups. The ejection fraction was lower in the patient group. In terms of biochemical and hematologic parameters, glucose, AST, ALT, white blood cell count, and troponin were higher in the patient group, while other parameters were similar. Plasma native thiol (344.32 ± 81.28 µmol/L versus 403.62 ± 62.36 µmol/L, $p < 0.0001$) and total thiol (382.90 ± 91.13 µmol/L versus 444.17 ± 65.53 µmol/L, $p < 0.0001$) levels were lower in NSTMI patients compared to control patients, while disulfide (19.29± 3.19 versus 20.27± 8.10, $p = 0.77$) levels were similar between the groups.

Conclusion: In this study, we found that native thiol and total thiol levels, which are antioxidant markers, were lower in patients with NSTMI compared with the control group. Our study shows that antioxidant activity is affected in NSTMI, and antioxidant levels are decreased..

Keywords: Without persistent ST-segment elevation, thiol, antioxidant

INTRODUCTION

Cardiovascular disease also has a significant impact on global health. According to the World Health Organization, deaths from cardiovascular disease (CVD) represent 29% of all deaths, and deaths from CVD are increasing despite all advances in diagnosis and treatment.1 Ischemic heart disease is mostly caused by atherosclerotic plaques. Epicardial arterial stenoses that restrict coronary blood flow create an imbalance between myocardial oxygen supply and demand. Various pathological mechanisms are responsible for the formation of atherosclerosis and are seen as endothelial dysfunction, lipid penetration and deposition in the vascular intima, exaggerated adaptive immune responses, vascular smooth muscle cell proliferation, and remodeling of the extracellular matrix.[2]

Recent studies increasingly suggest that oxidative stress is also involved in the mechanism of atherosclerosis development.3-5 When oxidant stress occurs, it is thought to be involved in almost all steps of atherosclerotic plaque formation, including thrombus formation.[6,7]

Oxidant and antioxidant systems work together in a balance in the body. However, if this balance is disrupted in favor of oxidant substances, oxidative stress occurs. Free radicals formed due to increased oxidative stress play a role in the development and progression of atherosclerosis and facilitate the emergence of various CVS diseases.[8,9] Thiol groups are an antioxidant cascade that plays a vital role in the elimination of reactive oxygen species.[10,11] The components of antioxidants in this group that provide homeostasis are total thiol, natural thiol, disulfide, and organic compounds containing a sulfhydryl (-SH) group that react with oxidant molecules and neutralize them.[11,12]

Studies have shown that there is a relationship between antioxidant system levels and coronary artery disease (CAD).[8,10,11] In this study, we aimed to investigate antioxidant levels in patients suffering from without persistent ST-segment elevation (NSTMI).

METHODS

Study Population

The study was initiated with the approval of the Kayseri City Hospital Clinical Researches Ethics Committee (Date: 12.03.2020, Decision No: 20). The study included patients admitted to the Cardiology Intensive Care Unit (CICU) of our hospital between April 2020 and November 2020. This study is a single-center and prospective study. The patients included in the study were 105 patients diagnosed with NONSTMI according to the European Society of Cardiology (ESC) criteria.[13] The control group consisted of 51 patients with similar baseline characteristics. The control group was selected from those who underwent coronary angiography and were found to have normal coronary arteries. The medical history of all participants, including cardiovascular risk factors and medications, was obtained and recorded. All patients underwent routine physical examinations and transthoracic echocardiography.

All patients underwent coronary angiography as an invasive emergency strategy and continued with percutaneous coronary intervention (PCI) when necessary. All patients received medical treatment regimens during hospitalization according to the current guidelines of the ESC.[13]

We excluded patients with previous coronary artery bypass grafting (CABG) or percutaneous coronary intervention (PCI), a history of acute coronary syndrome in the last 3 months, hematologic disease, malignancy, chronic renal failure or liver disease, and ongoing infection or chronic disease. Patients with inflammatory diseases, autoimmune diseases, or those taking vitamin supplements were also excluded. All patients gave written informed consent before study participation. The research protocol for this study, which complies with the Declaration of Helsinki, was approved by the local research ethics committee.

Laboratory Analysis

For laboratory examination, blood samples were collected from all patients between 8:00 a.m. and 10:00 a.m. following a 12-hour fast after CICU admission. Antecubital venous blood samples were transferred into tryptophan-EDTA based anticoagulated tubes. Blood samples were used to measure basic blood variables (a comprehensive metabolic panel and complete blood count) and thiol levels. All routine biochemical tests were also performed on an autoanalyzer (Roche Diagnostic Modular Systems, Tokyo, Japan). Hematological parameters were analyzed with a Sysmex K-1000 automated analyzer within 30 minutes of sample collection.

We measured the levels of thiol groups and thiol/disulfide homeostasis as described by Erel et al.14 thiol samples were centrifuged at 1500 g for 10 minutes. We stored plasma at -80°C and processed all samples simultaneously. We detected serum natural thiol and total thiol levels spectrophotometrically. First, we measured serum natural thiol levels after a reaction with 5, 5'-dithiobis-2-nitrobenzoic acid (DTNB) without any treatment. Secondly, to measure total thiol levels, we reduced dynamic disulfide bonds in serum samples using sodium borohydride (NaBH4) to form free functional thiol groups. Then, we used formaldehyde to eradicate unused NaBH4 and measured total thiol groups, including both reduced and natural ones, following reaction with DTNB. We calculated the number of dynamic disulfide bonds by determining half the difference between total thiol and natural thiol.

Transthoracic Echocardiography

We performed transthoracic echocardiography on each participant in the CICU and the control group. We performed all measurements using a machine (Vivid 5, GE Medical System, Horten, Norway) with a 3.5 MHz transducer. We performed 2D echocardiographic measurements to assess left ventricular ejection fraction and valvular pathologies. We used Simpson's method and color Doppler echocardiography to assess ejection fraction and valvular pathologies in the apical 4-chamber view, respectively.

Statistical Analysis

All analyses were performed using SPSS V21.0 for Windows (version 21.0; SPSS, Chicago, Illinois). All data are presented as mean ± standard deviation unless otherwise stated. The Kolmogorov-Smirnov test was used to analyze the distribution pattern. A comparison of parametric values between two groups was performed using the independent samples t-test. A comparison of nonparametric values between the two groups was performed using the Mann-Whitney U test. The distribution of continuous variables between groups was performed with one-way ANOVA. Variability between groups was measured via the LSD test. Categorical variables were compared with the chi-square test. A P value < 0.05 was considered significant.

RESULTS

Baseline clinical and demographic characteristics of the study groups are presented in Table 1. There were no statistically significant differences between the patient and control groups in terms of age, smoking status, diabetes, and hypertension (p> 0.05). Systolic-diastolic blood pressures and basal heart rates were similar. In terms of echocardiography, EF was significantly lower in the patient group (p < 0001).

In laboratory analysis, leukocyte (WBC), AST, ALT, and glucose levels were significantly higher in the patient group, while there was no significant difference between the groups in terms of other biochemical and hematologic values (Table 2).

Table 1: Basal characteristic, biochemical, and hematological parameters between groups

	NONSTMI (n=105)	CONTROL GROUP (n=51)	p
Age	61.2±11.4	63.1 ±9.9	.541
Hypertension, n (%)	49 (%47)	23 (%45)	.644
Diabetes mellitus, n (%)	32 (%30)	14 (%27)	.625
Hyperlipidemia, n (%)	42 (%40)	19 (%37)	.925
Smoking, n (%)	48 (%46)	25 (%25)	.764
Systolic blood pressure (mmHg)	129.5±16.2	135.1±18.1	.622
Diastolic blood pressure (mmHg)	71.3±13.8	74.2±14.6	.329
Heart rate	88.1±12.4	76.3±10.5	.572
LVEF (%)	49.2±7.5	66±10.24	.0001*

Data are expressed as the mean ± standard deviation for normally distributed data.
NONSTMI: Without persistent ST-segment elevation, LVEF: Left ventricular ejection fractions, *p <0.05

When plasma thiol groups were evaluated, plasma native thiol (344.32 ± 81.28 µmol/L versus 403.62 ± 62.36 µmol/L, p < 0.0001) and total thiol (382.90 ± 91.13 µmol/L versus 444.17 ± 65.53 µmol/L, p < 0. 0001) levels were significantly lower in the patient group, whereas there was no significant difference between the groups in terms of disulfide levels (19.29 ± 3.19 versus 20.27 ± 8.10, p = 0.77). Troponin I level (0.006 - 27 mg/dL, P < .001) was higher in the patient group (Table 2).

Table 2. Relationship between thiol and disulfide between groups

Variables	NONSTMI (n=105)	CONTROL GROUP (n= 51)	p
Native thiol (µmol / L)	344.32 ± 81.28	403.62 ± 62.36	.0001*
Total thiol (µmol / L)	382.90±91.13	444.17 ± 65.53	.0001*
Disulfide	19.29± 3.19	20.27 ± 8.10	.77
Glycose (mg/dl)	155.2±72.4	128,8±55.7	.0001*
GFR (mg/dk/1.732)	92±21.54	95.2±22.3	.342
AST (U/L)	41.4±16.2	27.2±1.9	.0001*
ALT (U/L)	32.1±13.1	24.4±12.6	.001*
Total cholesterol (mg/dl)	191±26.8	188±52.1	.467
Triglyceride (mg/dl)	171.54±66.7	169.5±81.3	.625
HDL (mg/dl)	39.5±12.1	42.1±14.5	.875
LDL(mg/dl)	121±42.1	119.2±41.9	.345
HBA1C (%)	7.5±3.1	7.6±1.8	.117
WBC (103/ µL)	13.1±3.6	9.1 ±3.6	.0001*
Hemogram (mg/dL)	14±2.1	14.2±1.5	.325
Platelets (103/ µL)	265.6±81.5	271.5±79.5	.673
Troponin I (mg/dL)	35	0.01	.001*

Data are expressed as the mean ± standard deviation for normally distributed data. LDL: Low density lipoprotein, HDL: High density lipoprotein, WBC: White blood cell, AST: Aspartate amino transferase, ALT: Alanine amino transferase, NONSTMI: Without persistent ST-segment elevation
*p <0.05

CONCLUSION

To the best of our knowledge, this is the first study to investigate thiol/disulfide homeostasis as a marker of oxidative stress in NONSTMI patients, and it was shown to be decreased in this patient group.

The balance between oxidants and antioxidants is important for the healthy functioning of the body. Oxidants (reactive oxygen species (ROS)), which are products of cellular metabolism, can occur in the intracellular or extracellular environment.[15-17] Antioxidant defense systems such as superoxide enzymes (dismutase, glutathione peroxidase, catalase) and non-enzyme molecules (albumin, bilirubin, glutathione) are needed to maintain the oxidant-antioxidant balance.[18,19] When oxidants are produced in large amounts or cannot be eliminated by antioxidants, cells are exposed to active ROS.[18,20-22] Oxidative stress causes damage in many cells, including endothelial cells, and this is considered as the first stage of atherosclerosis.[23,24]

Thiols are sulfur analogs of alcohols, and disulfides are structures containing adjacent pairs of sulfur atoms.[25,26] The role of thiol/disulfide balance in antioxidant reactions is crucial. In addition, thiols, which are the main components of intracellular and extracellular damage protection mechanisms, are non-enzymatic antioxidants. Plasma thiol groups reduce oxidative damage in the pathophysiology of inflammatory processes in diseases such as CAD, rheumatoid arthritis, and diabetes mellitus.[27,28] In our study, thiol and disulfide values and ratios, which are members of the antioxidant system, were significantly lower in NOSTMI patients. This finding suggests that the antioxidant system was utilized in the patient group, and therefore its level decreased.

Studies demonstrating the relationship between plasma thiol levels, the thiol/disulfide ratio, and CAD are limited in the literature. Altıparmak et al.10 showed that the disulfide/thiol ratio did not change significantly, but decreased native thiol levels were associated with the presence and severity of CAD.8 found that native thiol, total thiol, and disulfide levels were lower in AMI patients compared to controls.[29] suggested that thiol disulfide volume at admission was independently associated with the development of contrast-induced nephropathy (CIN) after PCI in patients with acute coronary syndrome. In our study, it was confirmed that native thiol, total thiol, and disulfide levels were decreased in patients admitted with a diagnosis of NONSTMI. These results suggest that the levels of thiol groups can be used as markers to evaluate NONSTMI. Further studies with a more significant number of patients are needed to confirm the results obtained.

ETHICAL DECLARATIONS

Ethics Committee Approval: The study was initiated with the approval of the Kayseri City Hospital Clinical Researches Ethics Committee (Date: 12.03.2020, Decision No: 20).

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.

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Original Article

Review of Q fever cases in and around Yozgat province

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ABSTRACT

Aims: Q fever is a prevalent disease, especially encountered in endemic areas, and presents itself with non-specific symptoms such as fever, arthralgia and widespread body pain, and cough. It can have various acute or chronic presentations. However, significantly rapid recovery is achieved with early diagnosis and treatment. Our study aimed to raise awareness about this disease, which seems simple but requires clinical suspicion, and support the treatment approach.

Methods: 92 individuals who applied to our hospital between 2017 and 2022 and were diagnosed with Q fever by microbiological tests were included in the study. These patients' symptoms, blood hemogram, AST, ALT, ALP, CRP values and their response to treatment were taken from patient files and analyzed.

Results: 92 patients were serologically diagnosed with Q fever. Of these, 44 (48.2%) were male, and 48 (51.8%) were female. 29 (31.5%) had afever, 32 (34.8%) had joint pain, 13 (14.1%) had a cough, and 44 (47.8%) had widespread body pain. Pneumonia developed in 18 (19.6%) patients and hepatitis in 16 (17%). Tetracycline was started in 74 patients as first-line therapy and replaced with quinolone in one patient because of intolerance. First-line quinolone therapy was used in 18 pneumonia patients.

Conclusion: First-line quinolone treatments were effective.

Keywords: Q fever case, Yozgat, endemic area

INTRODUCTION

Q-fever is a febrile bacterial infection caused by *Coxiella burnetii*. It is encountered both as sporadic cases and endemic in the world. It is transmitted from mammals such as goats, sheep, and cattle by birds and arthropods such as ticks. Birth leftovers are considered the most important source of transmission of bacteria to pastures and soils because they contain high amounts of bacteria. Q-fever is accepted as an occupational disease caused by close contact with farm animals. It can also rarely occur in laboratory workers. Transmission to humans through contact with fluids such as urine, feces, birth leftovers, milk of infected animals, inhalation and oral intake is common.[1-5]

The disease incubation period is 14-39 days, with an average of 20 days. Patients are usually asymptomatic, but some also apply with nonspecific complaints such as fever, widespread pain, arthralgia and cough. Clinical presentations in the acute or chronic picture include febrile disease, pneumonia, endocarditis, hepatitis, and osteomyelitis. It may also appear in different forms in infants, pregnant and malignant patients.[1,2,6,7]

Making a diagnosis is challenging due to the lack of specific symptoms. Serologic tests are used in the diagnosis. The Indirect Fluorescent Antibody (IFA) test is accepted as the reference method. For a definitive diagnosis, either a 4-time increase should be observed between phase-2 IgG antibody titers of acute and convalescent serums or seroconversion should occur in phase-2 antibody titers of double serum samples taken at a 14-day interval. Phase-2 IgM antibodies are formed rapidly, reaching a maximum value on the 14th day and remaining in the blood for 10-12 weeks. IFA may be negative early, and PCR may be necessary. It can be isolated from culture under high biosafety laboratory conditions.[7-9]

All symptomatic patients should be treated. It is crucial to start the treatment at an early stage. The recommended treatment in adults is first-line doxycycline, administered 2x100mg for 14 days. Chloramphenicol and rifampin can be used as well. Although studies have shown the efficacy of quinolones, further clinical experience is needed. There is insufficient data on their efficacy in the treatment of pneumonia. Trimethoprim-sulfamethoxazole can be used in pregnant women. On the other hand, individuals with endocarditis need a longer duration with combined treatment.[8,9] Our study aimed to examine the complaints of Q-fever cases frequently seen in our region, underline the symptoms that should be paid attention to for early diagnosis and evaluate the treatment using the data at hand.[8-10]

METHODS

The study was designed as a retrospective cross-sectional study. Data were collected after getting the approval of the local ethics committee. The files of 92 individuals admitted

to our hospital between 2017-2022 and were found positive for Q-fever by IFA test were reviewed. Age, gender, initial complaints and serum ALT, AST, ALP and CRP values of the patients were recorded.

Statistical Analysis

Categorical measurements were given as numbers and percentages, and continuous measurements as mean and standard deviation (median and min-max where necessary). The Chi-Square test was employed to test the significance of the difference between means and to evaluate the data obtained by counting.

RESULTS

The number of individuals in the study was 92; 44 (48.2%) were male, and 48 (51.8%) were female. The minimum and maximum ages of the individuals were 16 and 77, and the mean age was 49.00±15.40. The mean age of males and females was 48.25±15.05 and 49.68±15.80, respectively.

Of 92 patients, 29 (31.5%) had a fever, 32 (34.8%) had arthralgia, 13 (14.1%) had a cough, and 44 (47.8%) had widespread pain (**Table 1**). 18 patients (19.6%) were treated with a diagnosis of pneumonia. Of these 18 patients, only 1 had disseminated pneumonia and achieved complete recovery with treatment. 1 patient was treated with quinolone therapy due to tetracycline allergenicity; the remaining 73 patients received tetracycline therapy.

16 patients had elevated liver enzymes and were followed up for hepatitis. In all patients, the values decreased to the normal range with treatment. Regarding patients with concomitant elevated liver enzymes, ALP (30-120) was approximately 1.5 times higher than the reference value in 6 patients, and GGT (0-38) was 1-1.5 times higher than the reference value in 5 patients.

Acute phase reactant CRP (0-6) was elevated in 39 patients (54.16%) and decreased to the normal range during follow-up.

DISCUSSION

In a large-scale study with the participation of 29 European countries, 1,069 people diagnosed with Q-fever were followed. Spain, Romania and Bulgaria reported the highest cases in Europe.[11] The United States reported 193 Q-fever cases in 2017. In most of these countries, Q-fever has been recognized as a nationally notifiable disease.[12] In our country, the first outbreak was identified with 21 cases in Aksaray in 1947.[13,14] Subsequently, a series of studies were carried out on *C. burnetti*, aiming to draw attention to endemic regions and individuals in the risk group. In 2006, a study conducted on 92 individuals in the Aydın region examined seropositivity in groups with occupational exposure and found it to be high.[15] In a study conducted in the Hatay region among veterinarians and slaughterhouse workers, seroprevalence was found to be high in the risk group, drawing attention to conducting research in endemic regions.[16] The study of Kılıç et al.[17] in Ankara investigated the seroprevalence in veterinarians and animal lovers and emphasized the importance of raising awareness in these risk groups. A prevalence study was conducted in Ankara by taking 601 serum samples from blood donors to see the prevalence in the whole community, not only in the risk group. Seropositivity was higher in males than females, and 87% of seropositive donors had contact with farm animals. The study by Çelebi et al.[2] showed that Ankara is an endemic region.[18] In the study by Kılıç et al.[19] the highest seropositivity was observed in the Central Anatolia region.

Although it can occur at any age, the associatiom-n of the disease with increasing age was shown. It is higher in males than females, which can be explained by occupational exposure. The cases can be seen at any time of the year; however, they are mostly reported in spring and early summer.[20-22] A higher seroprevalence was reported among women in a study conducted in Elazığ. This difference could be explained by the fact that domestic animal husbandry is more common in that part of Turkey, and women are more engaged in this work.[23] In our study, 44 (48.2%) of 92 individuals were male, and 48 (51,8%) were female, and no statistically significant difference was found according to gender.

Similar to the study by Derrick et al.[24], the common complaints of the patients in our study were fever, widespread pain, arthralgia and cough. The reason for the lower frequency of fever complaints was thought to be that the patients presented after the acute febrile period had passed or that other febrile diseases were initially considered in patients applying with fever, and this period may have passed.[25] 16 patients had elevated liver enzymes and were followed up with hepatitis. Although only two of these patients had a later recovery, all patients responded to the treatment.

In the study by Coşkunlar et al.[26] in Ankara, 47% of 106 patients with atypical pneumonia were serologically positive for Q-fever. However, it is difficult to evaluate the role of *C. burnetii* in the aetiology of atypical pneumonia since the number of studies on *C. burnetti* as the causative agent in patients diagnosed with pneumonia is not sufficient. In our study, 18 (19.6%) individuals were followed up with pneumonia. However, a prospective study on all pneumonia patients is needed to evaluate its role in atypical pneumonia.

In our study, tetracycline, the first-line treatment, was initiated in 74 individuals; quinolone treatment was preferred in one patient due to tetracycline intolerance. In addition, the treatment of 18 individuals diagnosed with pneumonia was started with quinolone, the first-line treatment. Raoult et al.[27] emphasized the insufficiency of data on the studies involving the role of quinolones in Q-fever treatment. Our study supports that quinolones are as effective and sufficient as tetracyclines regarding the results of the group that developed pneumonia. Although resistance to tetracyclines was not mentioned, the results show that quinolones may be an alternative first-line treatment to tetracyclines in future. The rapid clinical recovery of pneumonia patients and the absence of intensive care unit hospitalization and mortality may be attributed to the use of quinolones.

Q-fever should be suspected in the following patient groups because the diagnosis in these patients is only possible with clinical suspicion: patients with unexplained hepatitis, patients with unexplained ALP or GGT elevations, patients with elevated acute phase reactants such as CRP, and patients with a history of travel to or from endemic areas.[28-30]

CONCLUSION

Q-fever is a disease prevalent in the community, especially in endemic regions; contrary to popular belief, it is difficult to diagnose as it presents nonspecific symptoms.

Early diagnosis provides a significant and rapid recovery. Therefore, awareness should be raised for early diagnosis and treatment; internal medicine and surgical branch physicians should be informed about its different clinical presentations, such as hepatitis, osteomyelitis and pneumonia, especially in endemic regions. Furthermore, it should be added to the infectious pathologies investigated, especially in cases of unexplained hepatitis. In addition, contrary to popular belief, quinolones are as effective as tetracyclines in the treatment.

ETHICAL DECLARATIONS

Ethics Committee Approval: The study was initiated with. the approval of the Yozgat Bozok University Medical Faculty Clinical Researches Ethics Committee (Decision No: 2017-KAEK189_2022_15_18).

Informed Consent: Written consent was obtained from the patient participating in this study.

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Review

Current approach to diabetic polyneuropathy: current diagnosis and treatment

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ABSTRACT

Diabetes mellitus and its associated neuropathy are among the leading problems affecting the quality of life negatively. Diabetic foot problems due to neuropathy cause very serious problems. Physicians may focus too much on blood sugar regulation and ignore examinations for other macro and microvascular complications of diabetes. Although it appears earlier in patients with impaired blood sugar regulation, neuropathic symptoms are seen in almost half of diabetic patients who generally exceed 10 years. With early diagnosis and treatment, the quality of life of patients increases significantly. We touched on this issue in order to raise awareness of neuropathy, which is so common.

Keywords: Diabetes mellitus, neuropathy, polyneuropathy

INTRODUCTION

Diabetes mellitus (DM) is a collective term used to describe a group of diseases that result in high blood sugar resulting from a deficiency in insulin secretion or a defect in the action or response of insulin. Globally, the number of people with diabetes has quadrupled over the past three decades, making diabetes the ninth leading cause of death.[1] Worldwide, one in every eleven adults has DM, and 90% of them have type 2 DM.[2,3] Because of many epidemiological changes such as dietary habits, urbanization and the sedentary lifestyle that comes with it, type 2 DM is increasing in every region of the world, especially in low- and middle-income countries.[4] It is estimated that type 2 DM will affect 366 million people worldwide by 2030.[5]

Most patients with type 2 DM have at least one complication.[1] Peripheral neuropathies are one of the most important chronic complications of diabetes mellitus, together with nephropathy and retinopathy. Diabetic polyneuropathy (DPN) is the most common form of a group of diabetes-related neuropathies that include focal neuropathies and autonomic neuropathy. DPN is associated with sensory changes, loss of sensation, balance disorder and pain in the distal parts of the extremities, all of which impair patients' quality of life.[7-9]

DIABETIC NEUROPATHY

Diabetic neuropathy is a clinical or subclinical disease of peripheral nerves that occurs as a result of diabetes with no other underlying cause. It can affect the somatic and/or autonomic nervous system.6It is characterized by loss of sensory function starting distally in the lower extremities, as well as pain and severe morbidity. Over time, at least 50% of diabetic individuals develop diabetic neuropathy. While controlling the blood glucose level effectively stops the progression of diabetic neuropathy in patients with type 1 diabetes mellitus, this effect is lower in patients with type 2 diabetes mellitus.[19]

The risk of diabetic neuropathy increases with the following risk factors, indicators and comorbidities:6

- Diabetes duration
- Diabetes control (hyperglycemia)
- Arterial hypertension
- Peripheral artery disease
- Mönckeberg's sclerosis
- Diabetic retinopathy and nephropathy
- Depression
- Visceral obesity
- Hyperlipidemia
- Alcohol and/or nicotine use
- Insufficient physical activity
- Demographic factors (age, height, weight)

It is known that neuropathies developing in diabetic patients are a heterogeneous group of diseases with their symptoms, neurological involvement pattern, course, risk variables, pathological changes and underlying mechanisms.[10,11] The existing heterogeneity can be divided into at least two main subgroups; typical and atypical DPN.

Typical diabetic polyneuropathy is a chronic, symmetrical sensorimotor polyneuropathy with more prominent distal involvement and is thought to be the most common type of diabetic neuropathy.[10] Diabetic sensorimotor polyneuropathy (DSPN) develops with or against the background of long-

standing hyperglycemia, associated metabolic disorders (increased polyol flux, accumulation of advanced glycation end products, oxidative stress and lipid changes), and cardiovascular risk factors.[12-14] In addition to these, it has been observed that the microvessel changes observed in diabetic nephropathy and retinopathy are also associated with the pathological changes of the nerves affected in neuropathy. Over time, patients may develop autonomic dysfunction and neuropathic pain.[10,13]

Atypical diabetic polyneuropathies differ from DSPN in many important features, such as onset, course, mode of presentation, associations, and perhaps putative mechanisms.[15-17] Atypical DPNs can occur at any time during diabetes mellitus. The onset of symptoms may be acute, subacute, or chronic, while the course is usually monophasic or may fluctuate. Pain and autonomic symptoms are typical features.[15,17]

Among the types of diabetic neuropathy, far more studies have been conducted on distal symmetrical polyneuropathy, diabetic autonomic neuropathies, and especially cardiovascular autonomic neuropathy.[20-23] Atypical DPNs have been less characterized and studied. (18) Neuropathies similar to diabetic neuropathies may develop in prediabetic patients. Diabetic neuropathies are summarized in **Table1**.[24]

Table 1. Classification of diabetic neuropathies (adapted from Source 24)

Diabetic Neuropathies

A. Diffuse Neuropathy
• Diabetic sensorimotor polyneuropathy
  • Mixed sensorimotor neuropathy
  • Predominant large fiber neuropathy
  • Predominant small fiber neuropathy
  • Pure small fiber neuropa**thy**
• **Autonomic neuropathy**
  • Cardiovascular autonomic neuropathy
  • Decreased heart rate variability
  • Tachycardia while resting
  • Orthostatic hypotension
  • Exercise intolerance
  • Silent myocardial ischemia
  • Sudden c**ardiac death**
• **Gastrointestinal autonomic neuropathy**
  • **E**sophageal dysmotility
  • Gastroparesis
  • Diabetic diarrhea
  • Constipation (colon atony)
  • Fecal incontinen**ce**
• **Urogenital autonomic neuropathy**
  • Neurogenic bladder
  • Sexual dysfunctio**n**
• **Sudomotor dysfunction**
  • Peripheral anhidrosis
  • Hyperhidrosis
  • **Gustator sweating**
• **Inability to recognize hypoglycemia**
• **Pupillary dysfunction**
B. Mononeuropathy (mononeuritis multiplex) (atypical forms)
• Isolated cranial nerve palsy (e.g. oculomotor nerve palsy)
• Isolated peripheral nerve palsy (e.g. ulnar, median, femoral, peroneal nerve palsy)
Mononeuritis multiplex (may resemble polyneuropathy)
 	
C. Radiculopathy or polyradiculopathy (atypical forms)
• **Radiculoplexus neuropathy**
  • **Lumbosacral polyradiculopathy**
  • **Proximal motor amyotrophy**
• **Thoracic radiculopathy**

Common Non-Diabetic Neuropathies in Diabetes
Compression neuropathies **Chronic inflammatory demyelinating polyneuropathy** **Radiculoplexus neuropathy** **Acute painful small fiber neuropathies (treatment-related)**

PATHOPHYSIOLOGY OF DIABETIC NEUROPATHY

Axons from motor neurons in the spinal cord transmit signals to the muscles, while axons from sensory neurons in the dorsal root ganglia receive signals from the skin and joints. Supporting these axons presents a unique challenge, as they are often 20,000 times longer than their corresponding cell bodies. Schwann cells provide supporting myelin for axons in the peripheral nervous system, but most sensory axons are unmyelinated, making them more susceptible to damage than motor axons.

The complex array of metabolic and vascular factors in diabetes shift the balance between nerve fiber damage and nerve fiber repair in favor of damage. This balance shift occurs in a fiber-selective pattern, preferably affecting more vulnerable distal sensory and autonomic fibers, leading to progressive loss of sensation underlying the clinical manifestations of diabetic polyneuropathy.

Studies have identified several mechanistic pathways believed to play a role in the pathophysiology of diabetic neuropathy (**Figure 1**).[26]

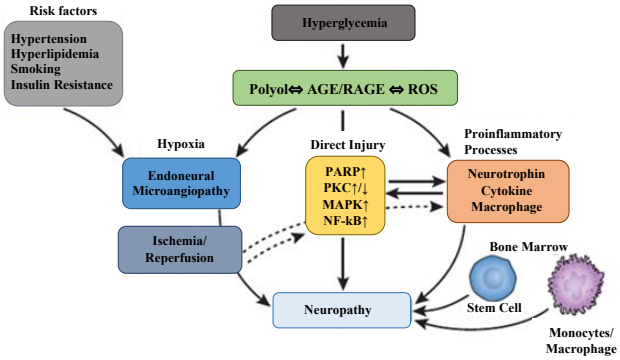

Figure 1. Summary of pathogenetic mechanisms of diabetic neuropathy (adapted from source 26)

Prolonged hyperglycemia causes downstream metabolic cascades of polyol pathway hyperactivity, enhanced glycation end products (AGE)/receptor for advanced glycation end products reactions (RAGE), and increased reactive oxygen species (ROS). Activation of poly-ADP-ribose polymerase (PARP) compromises both endoneural microvessels and neural tissues through activation of nuclear factor (NF-kB), as well as changes in protein kinase C (PKC) and an increase in mitogen-activated protein kinase (MAPK). They cause functional and structural changes in peripheral neuropathy.

Metabolic abnormalities in the nerve elicit proinflammatory reactions that induce the release of cytokines, suppression of neurotrophins and migration of macrophages and promote the development of neuropathy. There is also the possibility that other cellular components from the bone marrow may have an effect on neuropathology in diabetes. In addition, ischemia/reperfusion can accelerate nerve damage, which is partially mediated by inflammatory reactions. Risk factors represented by hypertension, hyperlipidemia, smoking and insulin resistance also contribute significantly to the development of neuropathy.[26]

NEUROPATHIC PAIN MECHANISMS

Neuropathic pain occurs as a result of permanent, maladaptive structural and functional changes in the somatosensory system after peripheral nerve injury. Experimental models of mechanical nerve injury have shown a loss of inhibition in the peripheral nervous system and central nervous system, as well as an increase in excitation and fasciculation of pain signals. However, while some individuals with diabetic neuropathy develop pain, the mechanism of the asymptomatic course of other individuals with similar neuropathy levels is not fully understood. Neurophysiological measurements, molecular pathways and pathological findings do not fully explain the presence of neuropathic pain in DM. Therefore, the current view indicates that a complex interaction of risk factors (environmental and genetic), vascular and metabolic abnormalities (glycemic flow, metabolic syndrome, vascular injury and/or dysfunction) and psychosocial factors leads to peripheral and central nervous system maladaptations. The mechanisms suggested causing painful diabetic polyneuropathy are described in **Table 2**.[27]

Table 2.Mechanisms of painful diabetic peripheral neuropathy
Minor fiber damage
Autonomic dysfunction and vascular changes
Inflammation and immune system changes
Methylglyoxal
Ion channel dysfunctions
Central sensitization

CLINICAL AND DIAGNOSTIC METHODS

The earliest manifestations of diabetic polyneuropathy probably reflect the gradual loss of integrity of both large myelinated and small myelinated and unmyelinated nerve fibers.[28] Function, symptoms and examination findings according to the affected fiber are summarized in **Table 3**.[31]

Table 3. Affected fiber, function, symptoms and examination findings		
	Large Myelinated Nerve Fibers	**Small Myelinated Nerve Fibers**
• Function • Symptoms • Examination (clinically diagnostic	• Pressure, balance • Hypokinesis (abirritation), tingling, poor balance • Ankle reflexes: decreased/absent • Vibration perception: decreased/absent • 10 g monofilament: reduced/absent Proprioception: decreased /absent	• Nociceptive, protective feeling • Pain: burning, electric shock, stabbing • Thermal (cold/hot) discrimination: reduced/absent Pinprick sensation: decreased / absent

The main symptoms of diabetic polyneuropathy include negative symptoms such as numbness and loss of balance (related to nerve fiber loss or dysfunction) and positive symptoms such as tingling and pain (related to abnormal function of nerve fibers that remain unaffected). Symptoms begin distally in the toes and feet, and positive symptoms often worsen at night. Up to half of patients with diabetic polyneuropathy may be asymptomatic, but physical examination reveals mild to moderately severe sensory loss. Decreased or absent ankle reflexes occur early in the disease, while more diffuse reflex loss is a late finding.[28]

With the progression of the disease, loss of sensation increases and when it comes to the middle of the distal lower extremity, loss of sensation appears in the hands. This gradual evolution causes the typical "sock-glove" sensory loss. Diabetic polyneuropathy often begins insidiously and can lead to foot ulcers and muscle and joint disease. Distal motor axonal loss causes atrophy of the intrinsic foot muscles and an imbalance between the strength of the finger extensors and flexors. This leads to chronic metatarsal-phalangeal flexion (claw toe deformity) that shifts weight to the metatarsal heads. This weight shift results in the formation of calluses, which can crack, become infected, and ulcerate.[28]

Early recognition and appropriate management of neuropathy in patients with diabetes is important:[29]

1. Diabetic neuropathy is a diagnosis of exclusion. Non-diabetic neuropathies may be present and treatable in patients with diabetes.
2. Up to 50% of diabetic peripheral neuropathy may be asymptomatic. If not recognized and preventive foot care applied, patients are at risk of injury.
3. Recognition and treatment of autonomic neuropathy can improve symptoms, reduce sequelae, and improve quality of life.

Patients with type 1 diabetes for 5 years or more and all patients with type 2 diabetes should be evaluated annually for diabetic polyneuropathy using medical history and simple clinical tests.[29] Diagnosis of diabetic polyneuropathy is primarily made clinically. Evaluation of patients includes a detailed history and physical examination focusing on cardiovascular and neurological testing, and detailed evaluation of the feet.[30]

The clinical tests used to assess small and large fiber function and protective sensation are summarized in **Table 4**:

Table 4. Evaluation tests	
Evaluated Functions	Evaluation Tests
Small fiber function	Pinprick test and sensation of temperature
Large fiber function	Vibration perception (128 Hz diapason) and 10 gr monofilament test
Protective sense	10 gr monofilament test

These tests not only screen for the presence of dysfunction but also predict the risk of future complications. Electrophysiological tests for screening or referral to a neurologist are rarely required, except when clinical features are atypical, the diagnosis is unclear, or a different etiology is suspected. Atypical features include motor involvement rather than sensory neuropathy, rapid onset, or asymmetrical presentation.[24,29]

Nerve conduction studies form part of the evaluation of diabetic polyneuropathy in atypical cases with concomitant compression neuropathy or inflammatory demyelinating neuropathy and in patients with minimal or no neurological findings. While nerve conduction studies are helpful in diagnosing patients with large fiber neuropathy, they are of limited use in diagnosing small fiber neuropathy. Small fiber function can be evaluated by skin biopsy and determination of intra-epidermal nerve fiber density, especially when results are normal. Decreased intra-epidermal nerve fiber density is

indicative of small fiber neuropathy.[30]

DIABETIC NEUROPATHY TREATMENT

Patients with diabetic neuropathy should be treated in a systematic, incremental approach, including symptomatic treatment of pain where available, including education in glycemic control and metabolic syndrome control, foot care, and safety precautions. The treatment can be examined under two separate headings as preventive care and pain treatment.[31]

A. Preventive Maintenance

Symptomatic diabetic neuropathy is usually not reversible, and treatment is aimed at slowing further progression and preventing complications such as diabetic foot ulcers, arthropathy, and falls (**Table 5**).[31]

Table 5. Preventive maintenance methods

Glycemic Control
• The role and importance of glucose control in slowing the progression of neuropathy and other microvascular complications of diabetes varies by type of diabetes. • Good glycemic control plays a role in preventing the onset and progression of polyneuropathy in patients with type 1 diabetes mellitus. • In patients with type 2 diabetes mellitus, however, glycemic control is thought to have little or no effect on neuropathy.
Risk Factor Modification
• Lifestyle changes are considered a fundamental practice to prevent the onset and progression of neuropathy, especially in individuals with prediabetes and type 2 diabetes. • Goals include achieving a normal body weight and achieving individualized glycemic, blood pressure, and lipid goals, as well as 150 minutes of moderate to vigorous aerobic activity per week.
Foot Care
• Peripheral neuropathy is one of the most important risk factors for ulcers and amputations in patients with diabetes. Foot care in patients with neuropathy is essential to help reduce the risk of complications.

B. Pain Treatment

About 15 to 20 percent of patients with diabetic neuropathy have pain in the feet, often described as burning or stabbing, as a sign of small myelinated fiber involvement. While the pain may be self-limiting and resolve within a year of onset in half of the patients, the other half have persistent pain-related symptoms. Symptomatic treatments for neuropathic pain are an important component of treatment in such patients. Pain medications are not helpful for non-painful symptoms of neuropathy, such as drowsiness.[31]

The American Academy of Neurology (AAN), the European Federation of Neurological Societies (EFNS), the Neuropathic Pain Special Interest Group of the International Society for the Study of Pain (NeuPSIG IASP), and the National Institute for Health and Care Excellence (NICE) recommend that first-line drugs for the treatment of calcium channel a2- agrees that d ligands (gabapentin and pregabalin) and antidepressants that inhibit the reuptake of serotonin-noradrenaline. Some patients may benefit from opioids or topical treatment with capsaicin or transdermal lidocaine (**Figure 2**) (**Table 6**).[32]

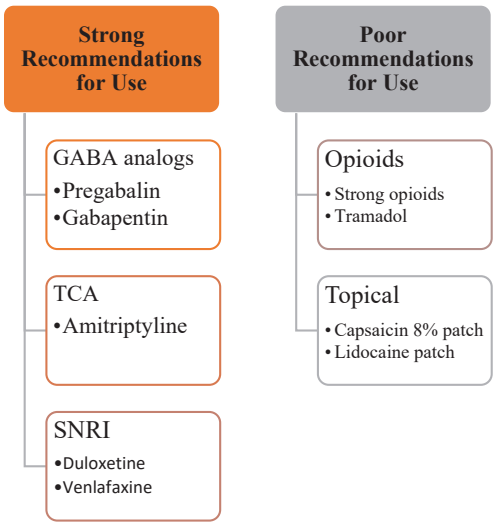

Figure 2. First-line drugs for the treatment of DNP

Table 6. Medications used in treatment DNP (adapted from source 32)

	Total Daily Dose and Dosing Regimen	Suggestions	Effewct Mechanism
Gabapentin	1200–3600 mg in three divided doses	First step, sufficient trial 3-8 weeks	Binds to voltage-gated calcium channels and reduces synaptic release of some neurotransmitters
Gabapentin, prolonged-release	1200-3600 mg, in two divided doses	First step, sufficient trial 3-8 weeks	
Pregabalin	300-600 mg in two divided doses	First step, sufficient trial 6-8 weeks	
Duloxetine	60-120 mg, once a day	First line, adequate trial 4-6 weeks	Inhibition of noradrenaline and serotonin reuptake potentialization of inhibitory pain pathways
Venlafaxine, prolonged-release	150-225 mg, once daily	First line, adequate trial 4-6 weeks	
Tricyclic c	25-150 mg, once or twice daily	First step, adequate trial 6-8 weeks	Noradrenaline and serotonin reuptake inhibition
Tramadol	200-400 mg in two or three divided doses	Second line, adequate trial 4-6 weeks	Partial μ-receptor agonist, Noradrenaline and serotonin re-uptake inhibition
Strong opioids	Individualized dosage	Third line, adequate trial 4-6 weeks	
Capsaicin 8% patch	1-4 patches to the painful area for 30-60 minutes every 3 months	Second line, (peripheral neuropathic pain)	Substance P depletion
Lidocaine patch	1-3 patches to the pain area once a day for up to 12 hours	Second line (peripheral neuropathic pain), adequate trial 3 weeks	Local anesthetic

CONCLUSION

The prevalence of obesity and diabetes is increasing all over the world. As the average human life expectancy increases, the number of years spent with diabetes also increases. Chronic complications occur in diabetic patients over the years. It is known that almost more than half of diabetic patients for more than 10 years develop diabetes-related neuropathy. Diabetic neuropathy both reduces the quality of life with the symptoms it causes and can cause many health problems, especially diabetic foot. While focusing on blood sugar regulation of patients, it is important to screen for diabetic neuropathy and other chronic complications, and to approach treatment if detected. It is very important to inform patients about the development of such complications in order to prevent more serious situations in the future.

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Case Report

Levetirasetam induced acute pancreatitis : an uncommon case report

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ABSTRACT

Acute pancreatitis is an acute inflammatory event involving the pancreas and causes significant mortality and morbidity. The most common causes are gastrointestinal stones and alcohol abuse, but well-known drugs used in daily practice can also cause acute pancreatitis. In this rare case report, we aimed to present a case of levetiracetam-associated acute pancreatitis.

Keywords: Levetiracetam, acute pancreatitis, adverse effect

INTRODUCTION

Acute pancreatitis is an acute inflammatory disease of the pancreas that requires urgent intervention. It is one of the most common gastrointestinal conditions requiring hospitalization worldwide.1 Since it is a fatal condition, it is still an important subject of significant scientific studies. The etiology includes biliary causes, alcohol consumption, hypertriglyceridemia, ERCP procedure, genetic causes, drugs, autoimmune causes, hypercalcemia, infections/toxins, anatomical or physiological anomalies.[1,2] Determining the etiologic cause of acute pancreatitis is very important in terms of appropriate treatment and follow-up. There is no globally accepted curative treatment for acute pancreatitis and experimental and clinical studies are ongoing.[3-7] Preventing recurrent episodes of acute pancreatitis is important because these episodes can lead to chronic pancreatitis in the future.[8,9]

Levetiracetam is a drug used in the treatment of epilepsy and is used for focal, myoclonic or tonic-clonic seizures.[10] In the literature, very few cases of acute pancreatitis while taking levetiracetam have been reported.[11] In this rare case report, we aimed to present a case of levetiracetam-associated acute pancreatitis.

CASE REPORT

A 45-year-old male patient was admitted to the emergency department of our hospital with the complaint of girdle-like abdominal pain for several days. It was learned that he had been diagnosed with hypertension for 10 years, he was taking amlodipine 1x10 mg tablet and his blood pressure values were under control with this treatment. It was noted that he had a cerebrovascular event three weeks before presentation to the emergency department and levetiracetam 3x500 mg tablet treatment was started. There was no history of alcohol or smoking. Family history was negative except for hypertension. On physical examination, there was diffuse abdominal tenderness, no defense and rebound. Cardiac and pulmonary examinations were normal. Arterial blood pressure was 140/90 mmhg and pulse rate was 100 beats/minute. Laboratory tests revealed amylase: 528 U/L, lipase: 367 U/L, AST: 24 U/L, ALT: 9 U/L, ALP: 86 U/L, GGT: 13 U/L, total bilirubin: 0.3 mg/dL, WBC: 11×103/mm3. Triglyceride, lactate dehydrogenase and serum calcium levels were within normal limits. Upper abdominal ultrasonography revealed normal liver size and smooth contours. No dilatation was observed in the intrahepatic bile ducts. Gallbladder dimensions, wall thickness (2.6 mm) and luminal echo were normal. Choledochal diameter was 4.8 mm. Pancreas and midline structures could not be clearly evaluated due to gas distension. Abdominal CT showed contamination of the peripenacreatic fat planes. The patient was admitted to our internal medicine service with a diagnosis of acute pancreatitis and treatment was started. Etiologic causes were evaluated in a detailed manner. Biliary causes, alcohol use, hypertriglyceridemia, hypercalcemia, infectious causes, drug use, genetic causes and toxins were investigated. Levetiracetam, which was started three weeks ago, was thought to cause acute pancreatitis based on rare case reports in the literature.[11] The patient was consulted to neurology and levetiracetam was stopped and carbamazepine was started. Oral nutrition was stopped and iv hydration and

analgesia were provided. On the third day of treatment, the patient's pain decreased, amylase and lipase levels decreased, and oral intake was gradually restarted. He was discharged after one week of ward follow-up. The patient was followed up for six months under carbamazepine treatment and he did not develop acute pancreatitis during the follow-up period.

CONCLUSION

Acute pancreatitis is an important inflammatory condition of the pancreas that is life-threatening and can cause significant morbidity. Although the most common cause is gallstone disease and alcohol abuse, various drugs and toxins can also cause acute pancreatitis.[1,2] The most important step in cases of drug-induced acute pancreatitis is to exclude other common causes and to consider the possibility of drug- or toxin-induced pancreatitis. The incidence of drug-induced pancreatitis is less than 5% and the prognosis is generally good with low mortality.[12,13] In this rare case report, we utilized Naranjo adverse drug reaction probability scale for acute pancreatitis probability percent and a score of 5 was reached.[14] Thus we suggest that a probable association between levetiracetam and this pancreatic situation.

In recent years, it has been reported in the literature that liver enzyme elevation and rarely acute pancreatitis have developed more frequently with levetiracetam use. It has been suggested that these side effects may be dose-dependent or may be caused by idiosyncratic effects. However, it is not clearly known how and why this drug causes acute pancreatitis.[9] Nevertheless, in the presence of common causes of acute pancreatitis, it should be kept in mind that levetiracetam use may be a reinforcing reason for the development of acute pancreatitis.

Today, with the development of imaging and laboratory techniques, acute pancreatitis and other pancreatic pathologies can be detected more easily and increasingly. In cases of acute pancreatitis in which all other causes are excluded, drug- and toxin-related acute pancreatitis should definitely be considered. Although levetiracetam is not considered among drugs that frequently cause acute pancreatitis, it should be remembered that it may cause acute pancreatitis in rare cases.

ETHICAL DECLARATIONS

Referee Evaluation Process: Externally peer-reviewed.

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Case Report

A rare food poisoning: *clostridium botulinum*

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ABSTRACT

Botulism is a disease caused by exotoxins secreted by Clostridium botulinum; a gram-positive anaerobic, spore-forming bacterium commonly found in soil.

Keywords: Food poisoning, botulism, clostridium

INTRODUCTION

Botulism is a disease caused by exotoxins secreted by Clostridium botulinum; a gram-positive anaerobic, spore-forming bacterium commonly found in soil. It is rare but can cause neuroparalysis in skeletal and respiratory muscles at various levels in humans and animals, respiratory failure, and death in severe cases.[1,2] They secrete seven different toxins (neurotoxins A–G) with different serologic properties but similar pharmacologic effects. In humans, toxins A, B, E, and F cause poisoning.[3,4] With technological developments, especially canned vegetables made at home are the cause of botulism rather than ready-made canned food.[5] These neurotoxins, which are the most lethal toxins known, are not resistant to heat and irreversibly block the release of acetylcholine at the presynaptic and autonomic nerves' cholinergic endings at the neuromuscular junction after ingestion with food. The incubation period of botulism is between 18-38 hours, and the first finding is blurred vision and diplopia symptoms due to the involvement of the eye muscles. In the clinical evaluation of the patients, tendon reflexes are decreased, and sensory deficits are in the background. Autonomic cholinergic symptoms such as fatigue, dry mouth, blurred vision, mydriasis, heart rate and blood pressure changes (bradycardia, hypotension), unexpected color changes in the skin, sweating disorders, urinary retention, abdominal pain, nausea, vomiting, and constipation may be observed.[1,3] Toxins can be detected in serum and feces within 3 days after the ingestion of food. Production of bacteria in stool culture after the third day after exposure is the most sensitive method for diagnosis. Guillain-Barré syndrome, myasthenia gravis, poliomyelitis, drug reactions, and other chemical poisons should be considered in the differential diagnosis of botulism. Electromyography (EMG) is useful in the differential diagnosis of other diseases related to botulism.[6,7] The most important point in treatment is early diagnosis and rapid administration of antitoxin. A polyvalent antitoxin is used in treatment. In this report, we aim to present the clinical and electrophysiologic findings of a patient who developed botulism three days after consuming canned frozen peas..

CASE REPORT

AA 33-year-old woman with no known history of any disease presented to the emergency department with nausea, vomiting, and abdominal pain for two days. No significant pathology was found as a result of the tests performed, and the patient was given symptomatic treatment and discharged. On the third day, the patient was readmitted to the emergency room with complaints of respiratory distress, dysphagia, and hoarseness. No pathology is detected in the evaluation performed by otorhinolaryngology and pulmonology specialists. No pathology was detected in the patient's investigations and cranial imaging. In the first neurological examination, consciousness was clear and cooperative, eye movements were limited to 4 directions, pupils were markedly mydriatic, direct and indirect light reflexes were -, bilateral ptosis was +, swallowing reflex was markedly decreased, speech was hypophonic, 4 extremities were mobile, no side signs were present, deep tendon reflexes were normoactive, and bilateral base skin reflexes were flexor. With the current clinical picture, the patient is hospitalized in the neurology clinic for further investigation and treatment. Electromyography (EMG) is planned for the etiology. One upper and one lower extremity were studied in the EMG, and there were no findings other than low motor CMAP (compound muscle action potential). The patient was transferred to the intensive care unit before the repetitive nerve stimulation test could be performed because the patient's respiratory failure increased. Within a few hours after transfer, the patient was electively intubated because respiratory failure did not respond adequately to non-invasive methods. Lumbar puncture (LP) was performed to

exclude acute polyneuropathy. Cerebrospinal fluid (CSF) examination revealed protein 35.19 mg/dl (reference upper limit 32), glucose 94 (concurrent serum glucose 134), and no cells.

Anti-musk (muscle-specific kinase) antibody and acetylcholine receptor antibody tests were sent to the patient to rule out myasthenia gravis (MG). Since myasthenic crises could not be ruled out, a 2-g/kg 5-day IVIG treatment was planned. The LP results and normal deep tendon reflexes ruled us out Miller Fisher's syndrome, which is a variant of Guillain-Barré syndrome with ophthalmoplegia, areflexia, and ataxia. A detailed anamnesis was obtained from the patient's relatives again for botulism disease, which was in the patient's differential diagnosis. When the patient's relative stated that the patient had consumed frozen peas 3 days before the onset of these complaints and since the clinical picture was compatible, a serum sample was taken for toxin type determination and pentavalent botulism antidote was administered. No deterioration in consciousness or significant limb weakness was observed during the daily follow-up in the intensive care unit. A few days later, a decrease in ophthalmoplegia and a decrease in the need for ventilator support were observed.

The antibody results sent to rule out myasthenia gravis (MG) were negative, and the serum sample was positive for toxin a and b. The diagnosis of botulism was confirmed. The patient received mechanical ventilator support for one week and then was extubated, and was followed up in the clinic for rehabilitation. The patient whose clinical condition improved in the follow-up was discharged with cure.

CONCLUSION

Clostridium botulinum is a gram-positive bacillus and anaerobic bacterium that can be found widely in the external environment, especially in soil. Botulism is known to be caused by the ingestion of canned foods prepared from foods such as homemade vegetables, meat, fish, and cheese under inappropriate conditions.[1-8,9] While bacterial spores are resistant to high temperatures and can be destroyed by boiling for 2-3 hours, the toxin is heat sensitive and denatures by boiling for 10 minutes.[1] It can cause disease in humans and animals with different strains and different clinical presentations. The main factor causing the disease is the neurotoxin produced by the bacteria. Neurotoxins are classified into seven types, ranging from A to G. In humans, the most common causative agents are A, B, and E. However, neurotoxins F, G, and H may also be the causative agents of the disease, albeit rarely (10). In our case, both toxin types A and B were positive, as seen in some cases. Symptoms appear 18-38 hours after the ingestion of infected food. In some patients, this period may shorten by up to 2 hours, while in others it may extend by up to 8 days.[1-11] In our case, symptoms appeared within the first 36 hours. Since the disease first affects the ocular and oropharyngeal muscles, the first findings include dry mouth, ptosis, diplopia, limitation in extraocular movements, strabismus, nystagmus, mydriasis, and nonreactive pupils. The triad consisting of extraocular muscle paralysis, pupillary dysfunction, and ptosis is considered being an indicator that the disease is severe and respiratory failure may develop.[1-2] In our patient, complaints of strong swallowing, hoarseness of voice, and visual findings, including difficulty in focusing near, diplopia, and blurred vision, started initially. In the following days, the disease progresses downward and spreads to the extremities and respiratory muscles. Most cases have signs of autonomic dysfunction, such as mydriasis, poor pupillary response to light and distance, dry mouth, constipation, and urinary retention. Mental functions and sensations remain normal.[1-13,14] Serum electrolytes, renal and liver function tests, complete blood and urine tests, electrocardiography (ECG), and cerebrospinal fluid may be completely normal in the absence of secondary complications. No abnormality was found in our patient as a result of these tests, and ECG and biochemistry tests were also found to be normal. The diagnosis of the disease is made by demonstration of botulinum toxin in the blood, demonstration of toxin and/or microorganism in stool or gastric contents, and demonstration of toxin or organism in suspected food (15). Since botulism is a very rare disease, it is a clinical condition that is very difficult to diagnose, especially if it is not included in the differential diagnosis.[8,10-14] The diagnosis can be confirmed by observation of typical symptoms and EMG findings together with the patient's anamnesis of canned food consumption and the exclusion of other diseases with similar clinical presentations. Although EMG is non-specific, the most common pathologies are low motor compound muscle action potentials (MCAP), inhibition responses in repetitive nerve stimulation, and conduction blocks in single-fiber EMG.[16] **Table 1**.

Table 1. Demonstration of CMAP amplitude decrease in all four motor nerves studied in our patient

Motor Nerve Conduction						
	Starting (ms)	Time (ms)	Amplitude (mV)	Area (microVs)	Distance (cm)	Speed (m/s)
Right median						
1 Wrist	2.9	12.7	2.5	8.0		
2 Elbow	6.9	15.4	2.4	7.7	23.0	57.5
Right ulnar						
1 Wrist	2.7	13.0	2.7	8.8		
2 Elbow	8.3	8.7	2.8	6.8	25.0	54.6
Right peroneal						
1 Wrist	3.1	8.6	2.4	5.5		
2 Fibula head	9.9	14.5	2.4	9.3	31.2	45.9
Right tibial						
1 Wrist	2.9	12.8	2.5	5.6		
2 Pop. fossa	11.0	12.1	1.9	6.1	41.0	50.6

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