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Case report

Sudden Cardiac Death. TdP (Torsade de pointes) in a Hematology Oncology Patient: a Clinical Case

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Abstract

Cardiotoxicity is a term that includes various undesirable cardiovascular events during chemotherapy in hematological cancer patients. Cardiotoxicity can occur both during chemotherapy and at different times after its completion. In clinical practice, oncohematologists often face the manifestation of cardiac arrhythmias and conduction disturbances in patients. Acute drug toxicity is often a drug-induced heart rhythm disorder.

The purpose of the report: to discuss the diagnostic features of sudden cardiac death using 24-hour ECG monitoring in a hematological oncology patient

This work examines a clinical case of a patient who underwent inpatient treatment of the underlying disease - acute leukemia. Against the background of chemotherapy treatment, drugs of the anthracycline group, cytostatics, anthrypotic drugs and the broad-spectrum antibiotic were used to treat the underlying disease and its complications. All of these drugs have cardiotoxicity. As a result, a young man with no history of structural heart disease experienced an episode of sudden cardiac death, life-threatening heart rhythm disturbance TdP (Torsade de pointes). The timely installation of Holter made it possible to document the episode of the patient's sudden cardiac death.

Prolongation of the QTc interval as a predictor of life-threatening cardiac arrhythmias, diagnostic importance of ECG monitoring in cardiac arrhythmias in patients with hematologic oncology.

Keywords: TdP - Torsade de pointes, cardiotoxicity, sudden cardiac death, Holter ECG monitoring, hematology oncology.

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Introduction

The use of a multicomponent chemotherapy program in the treatment often leads to the development of cardiotoxicity. [4] Sometimes it forces to interrupt a more effective treatment regimen and return to it only after treatment of cardiovascular pathology, and sometimes to abandon the continuation of antitumor therapy. Currently, in clinical cardiology, a serious medical problem is the cardiotoxicity of drugs, which can lead to an extension of the QT interval. The most common medications (LP) that can lengthen the QT interval include: antiarrhythmic, class IA III, antibacterial (groups of macrolides and fluoroquinolones), anticancer drugs, cytostatics (Doxirubicin, Daunorubicin) [4], a number of antidepressants, psychotropic and sedatives, antihistamines, antifungal drugs (Amphotericin, Voriconazole (vfend)), diuretic and hypolipidemic drugs [3]. Prolongation of the QT interval is often manifested by episodes of loss of consciousness and often ends with ventricular fibrillation, which is the direct cause of sudden cardiac death (Figure 1). Cardiovascular pathologies often occur among middle-aged, elderly patients, in young patients it is extremely rare. In patients with no pronounced structural pathology of the heart, sudden cardiac death (SCD), as a rule, occurs due to the development of polymorphic ventricular tachycardia (VT) or VT of the torsades de pointes type (Figure 2).

The purpose of the report. This paper presents a description of a clinical case of QT prolongation syndrome of the acquired form, the cause of which is the use of an unfavorable combination of drugs. The identification of the acquired form of QT and its description is of great interest for the clinical practice of doctors from the point of view of the etiology of serious cardiac arrhythmias and conduction disorders in patients with no history of pathology of the cardiovascular system.

A clinical case of an oncogematol patient, a manifestation of cardiotoxicity after chemotherapy (CT), and treatment of complications led to TdP (torsades de pointes) life-threatening cardiac arrhythmia, sudden cardiac death occurred. The Holter study made it possible to record all the moments of cardiac arrhythmia, measurement of the QTc interval. The importance lies in the fact that the diagnosis of complex rhythm disorders is not always possible to detect in time, and this may not have a favorable outcome for patients with hematology.

A clinical case

Patient K. is a male born in 1996, height 174 cm, weight 62 kg, was on inpatient treatment from 12.10.2016 to 29.05.2017 in the oncohematology department of National Scientific Oncology Center, Astana, Kazakhstan.

Since October 2016, the patient has noted weakness, dizziness, febrile temperature in the evenings, shortness of breath and enlargement of the cervical lymph nodes. In the conditions of the NNOC, in the Department of Hematology, the patient was diagnosed with acute lymphoblastic leukemia (variant B III) on the basis of laboratory tests, a general blood test, myelograms, bone marrow immunophenotyping, molecular cytogenetic examination (FISH diagnostics). Before the disease, the patient had no complaints about his health, he was not registered at the dispensary.

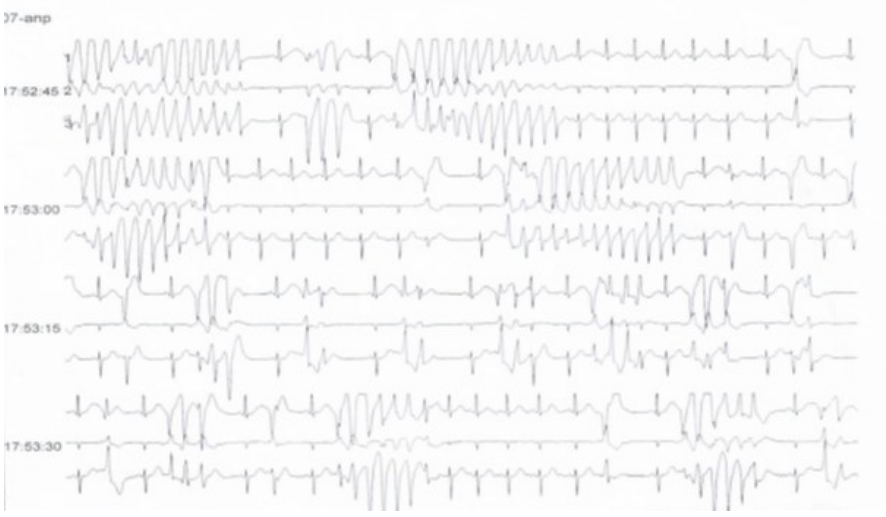

Figure 1 - Ventricular tachycardia on pointe shoes

According to the treatment protocol, the patient was fully examined before the start of chemotherapy. The examination of the cardiovascular system necessarily includes ECG, ECHOCG. 1st ECG result from 13.10.2016: sinus rhythm, correct with a heart rate of 86 beats per minute, normal EOS. ECHOCG from 13.10.2016: the chambers of the heart are not enlarged in size. The global, local contractile function of the myocardium was satisfactory, the pericardium was without features, and no structural pathology of the valvular apparatus of the heart was revealed.

During the entire period of treatment, the V course of chemotherapy was carried out, the beginning of CT from 14.10.2016 to 29.05.2017 according to the ALL-2013 KZ protocol, which includes the following drugs: synthetic glucocorticosteroid (Dexamethasone), cytosatic drugs (Cyclophosmamide, Citrarbine, Mercaptopurine), anthracycline antibiotics, cytostastics (Doxorubicin, Daunorubicin).

Against the background of myelotoxic agranulocytosis, infectious complications developed in the form of febrile neutropenia, gram-positive sepsis (Staphylococcus Aureus) and probable invasive pulmonary aspergillosis. The patient was additionally prescribed the following medications: broad-spectrum antibiotic Vancomycin, antimycotic therapy with Amphotericin, followed by transfer to Voriconazole (Vfend).

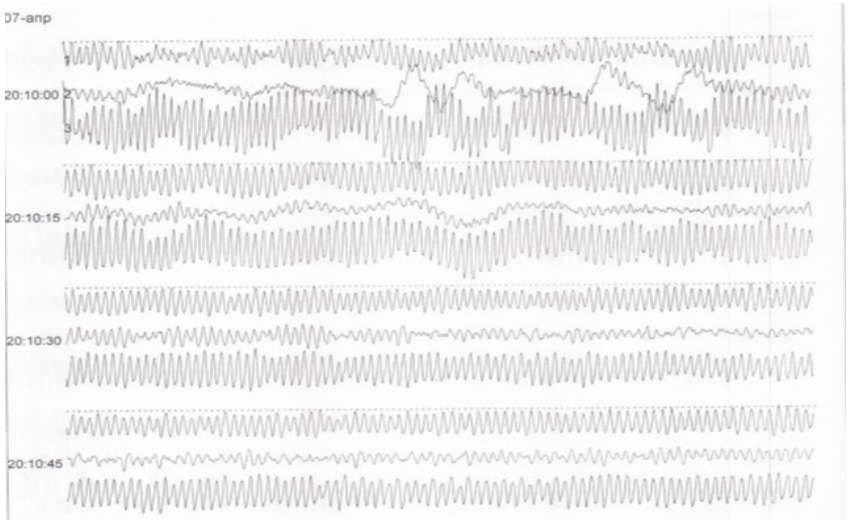

Figure 2 - Ventricular fibrillation with a heart rate of 330 beats per minute. Sudden cardiac death of the patient

Laboratory tests were carried out during the entire treatment, biochemical blood tests and blood electrolytes were within normal values. In the course of treatment, the patient underwent an ECG study from 05.04.2017. The ECG revealed frequent ventricular extrasystole, an episode of sustained ventricular tachycardia with a frequency of ventricular contractions (VHF) of 166 beats per minute. The patient was consulted by a cardiologist and received the conclusion "Cardiac arrhythmia: Frequent ventricular extrasitoles (paired), multiple episodes of ventricular tachycardia class 4B by Lawn. Additionally, Holter ECG monitoring (XM ECG) was recommended to the patient. During the study from 7.04.2017, in the evening, the patient lost consciousness in the department and was transferred to the onco-intensive care unit. The patient's condition deteriorated sharply, sudden cardiac death occurred due to a violation of the heart rhythm, namely ventricular tachycardia "pirouette" (torsade de pointes), which turned into ventricular fibrillation (Figure 2). Due to ventricular fibrillation lasting about 9 minutes, cardiac resuscitation was immediately performed, namely electro-pulse therapy EIT (150J), to restore the rhythm. Emergency cardioversion is recommended for life-threatening arrhythmias according to the European indication class IC [11].

During the incident, the patient underwent daily ECG monitoring (Holter), which made it possible to analyze in detail the life-threatening heart rhythm disorder "Torsade de pointes" (TdP). Holter ECG monitoring was carried out in stationary conditions with a duration of 22 h 23 min.

Table 1 - Diagnostics of "Torsade de pointes" (TdP) with the help of Holter

Heart rhythm	Sinus, sinus arhythmia
Average heart rate	77 beats per minute
Minimum heart rate	56 beats per minute
Maximum heart rate	144 beats per minute, with a sinus rhythm
Ventricular extrasystoles	A total of 3872: 2242 single, ventricular arrhythmia, 1630 episodes of ventricular tachycardia "Torsade de pointes" (TdP) were detected per day (Figure 1)
Ventricular fibrillation	1 episode of ventricular fibrillation with a heart rate of 348 beats per minute lasting 9 minutes, from 20:09 to 20:18. (sudden cardiac death) (Figures 2)
QT Interval	With an average heart rate of 77 beats per minute, the QT interval was 500 msec and the corrected Ec was 560 msec. The prolongation of the QTc interval took place of a transient nature (Figure 3)

With an average heart rate of 77 beats per minute, the QT interval was 500 msec and the corrected Ec was 560 msec. The prolongation of the QTc interval took place of a transient nature (Figure 3).

No prolongation of the QTc interval was detected on the usual standard ECG performed on the patient, and this change was detected only on the daily monitoring of the Holter ECG. Prolongation of the interval corrected by QT is a predictor of sudden cardiac death. Its lengthening against the background of pharmacotherapy in the patient manifested itself as cardiotoxicity and posed a great threat to the patient's life.

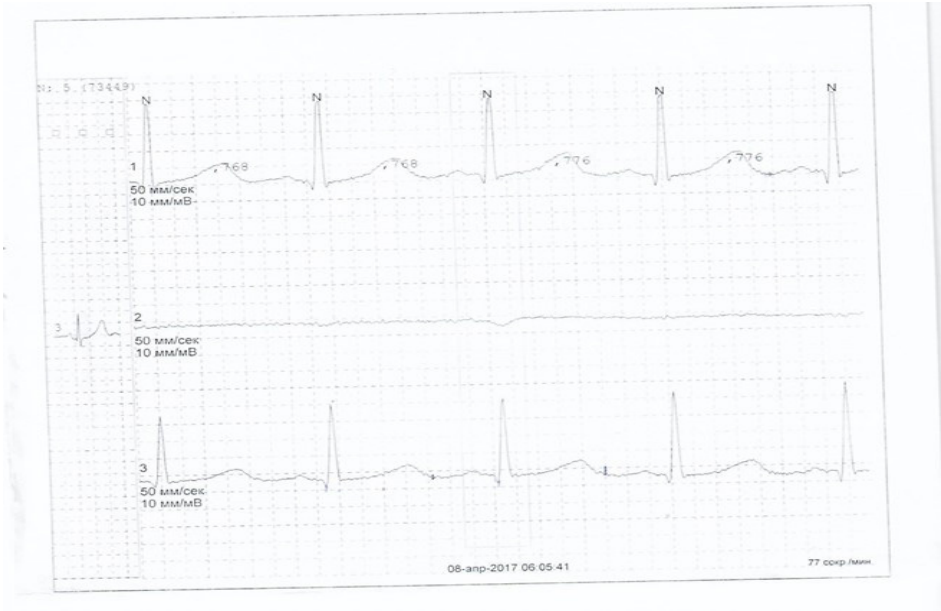

Figure 3 - Increasing the QT/QTc interval 500/560 ms

According to European recommendations, Amiodarone is on the 1st place for the treatment of life-threatening arrhythmias (Ventricular tachycardia and ventricular Fibrillation), is the drug of choice [12]. The patient received antiarrhythmic therapy according to the Cordarone 600 mg / s scheme for 2 weeks, and then 400 mg / s for 2 weeks, then 200 mg / s for 3 months.

A month after the incident, a control Holter daily ECG monitoring was prescribed. With repeated Holter against the background of antiarrhythmic therapy, ventricular and supraventricular activity was not detected. The QT interval with an average heart rate of 85 beats per minute is 400 msec and QT is 480 msec.

The patient underwent V courses of CT, and doctors were able to achieve complete remission of the underlying disease, the effect of CT came on the 180th day. Subsequently, the patient was discharged in a satisfactory condition, supportive chemotherapy and follow-up with a hematologist was recommended.

Discussion

One of the important and significant tasks of cardiology is the early detection and treatment of patients with a high risk of sudden cardiac death (SCD). The most dangerous disease with the risk of developing arrhythmogenic SCD is the long QT syndrome, in which the risk of developing SCD reaches 71% [8]. According to the prospective study "International LQTs Registry", in 57% of cases SCD occurs before the age of 20 years [10]. In 2016, under the auspices of the Committee for the Development of Practical Recommendations of the European Society of Cardiology, a document was released that tells about the treatment of cancer patients with chemoradiotherapy, resulting in cardiovascular toxicity [9]. A fairly large group of chemotherapeutic drugs has a cardiotoxic effect, which can be expressed as asymptomatic changes on the ECG, as well as myocardial infarction, as well as the development of toxic cardiomyopathy with symptoms of severe heart failure [9, 10].

Antitumor antibiotics of the anthracycline group, cytostatic drugs (Daunorubicin, Doxorubicin) have side effects on the cardiovascular system. Doxorubicin is one of the drugs that can cause acute or late forms of cardiotoxicity [4, 5]. As a consequence, its doxorubicin cardiotoxicity is an arrhythmia that can develop at any time (Table 1).

The list of medicines that are used to treat oncohematological patients is long, as there is a long way to treatment. The appointment of multicomponent therapy leads to multiple complications, which in turn require correction and treatment, as well as the appointment of additional medications. Thus, when prescribing medications, it is necessary to keep in mind the possibility of increasing the risk of death of patients with an increasing probability of developing "Torsade de pointes" and to monitor the duration of the QT interval [8], and with the help of Holter it is desirable. Prolongation of this interval is often associated with cardiotoxicity and is drug-induced [10]. Paroxysms of ventricular tachycardia "Torsade de pointes" (TdP), can be clinically manifested by episodes of loss of consciousness and often end with ventricular fibrillation, which is the direct cause of sudden death [7].

The importance of this clinical case lies in the fact that it is not always possible to document ventricular fibrillation, TdP, a life-threatening cardiac arrhythmia that the patient had during the day, because doctors did not suspect a complex cardiac arrhythmia. In our clinical case, sudden cardiac death occurred due to the cardiotoxicity of drugs: anthracycline group of antibiotics and anti-fungal agents. We are sure that side effects and incompatibility of medications have led to an extension of the QT/QTc interval. The QT interval adjusted according to the Bazett formula is considered to be prolonged, lasting more than 450 ms in men and more than 470 ms in women [10].

The value of the QT interval greater than 500 ms is a fact for identifying the cause of its lengthening, since it is a predictor of ventricular arrhythmias and sudden cardiac death, therefore it is recommended to immediately cancel the drugs that cause these changes [8].

For a more accurate and detailed diagnosis of acquired prolongation of the Qt interval in oncohematological patients [5, 6, 7], it is necessary to additionally prescribe an XM ECG.

Conclusion

In the current clinical case, it was found that a drug-induced QT interval extension, which led to a sudden, serdic meeting of the patient. Patients who receive combinations of drugs that affect the duration of the QT interval With, should be warned about the need to promptly inform the attending physician about any symptoms that may be manifestations of "flutter-flicker".

Oncogematologists should be fully aware of possible cardiac arrhythmias, and close cooperation between cardiologists and hematologists will lead to better stratification of the risk of developing cardiovascular diseases, monitoring and treatment.

In order to detect asymptomatic prolongation of the QT interval and more than 500ms, it is necessary to regularly conduct an electrocardiographic examination. It is important to share cases of cardiac arrhythmia against the background of a combination of various medications in order to reduce mortality from arrhythmia in a cohort of oncohematological patients. Considering this clinical case, it should be noted that monitoring the QT/QTc interval is more important to prevent the treatment of panic attacks, maybe this is beneficial for the government, since it is a reliable source of information.

Ethical aspects. Informed consent was obtained from the patient's legal representative for the publication of medical information in a medical scientific journal in the form of a scientific article.

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Кенеттен жүрек өлімі. Гематологиялық онкологиялық науқаста TdP (Torsade de pointes): клиникалық жағдай.

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Түйіндеме

Кардиоуыттылық – бұл гематологиялық қатерлі ісікпен ауыратын науқастарда химиотерапия кезінде жүрек-қантамыр жүйесінің әртүрлі жағымсыз құбылыстарын қамтитын термин. Кардиоуыттылық химиотерапия кезінде де, оны аяқтағаннан кейін әртүрлі уақытта да болуы мүмкін. Клиникалық тәжірибеде онкогематологтар жиі науқастарда жүрек ырғағының бұзылуының және өткізгіштіктің бұзылуының көрінісімен кездеседі. Дәрілік заттардың жедел уыттылығы көбінесе дәрілік жүрек ырғағының бұзылуы болып табылады.

Хабарламаның мақсаты: Онкогематологиялық науқаста химиотерапиядан кейінгі кардиоуыттылық әсерінен болған ЭКГ мониторингін қолдану арқылы кенеттен жүрек өлімінің диагностикасын сипаттау.

Бұл жұмыста негізгі ауру – жедел лейкоздың стационарлық емінен өткен науқастың клиникалық жағдайы қарастырылады. Химиотерапияны емдеу фонында негізгі ауруды және оның асқынуларын емдеу үшін антрациклин тобының препараттары, цитостатиктер, антропотикалық препараттар және кең спектрлі антибиотик қолданылды. Бұл препараттардың барлығында кардиоуыттылық бар. Нәтижесінде, анамнезінде құрылымдық жүрек ауруы жоқ жас жігіт кенеттен жүрек өлімінің эпизодын бастан кешірді, өмірге қауіп төндіретін жүрек ырғағының бұзылуы TdP (Torsade de pointes). Холтердің дер кезінде орнатылуы науқастың кенеттен жүрек өлімінің эпизодын құжаттауға мүмкіндік берді.

QTc аралығының ұзаруы өмірге қауіп төндіретін жүрек аритмиясының предикаторы ретінде, гематологиялық онкологиясы бар науқастарда жүрек ырғағының бұзылуында ЭКГ мониторингінің диагностикалық маңызы.

Түйін сөздер: TdP - Torsade de pointes, кардиотоксикалық, кенеттен жүрек өлімі, Холтер ЭКГ мониторингі, гематологиялық онкология.

Внезапная сердечная смерть. TdP (Torsade de pointes) у пациента онкогематологии: клинический случай

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Резюме

Кардиотоксичность – это термин, который включает в себя различные нежелательные сердечно-сосудистые события на фоне химиотерапии у онкогематологических больных. Кардиотоксичность может возникать как во время химиотерапии, так и в разное время после ее окончания. В клинической практике врачи онкогематологи часто сталкиваются с проявлением у пациентов нарушения ритма и проводимости сердца. Острая лекарственная токсичность, часто является как лекарственно-индуцированное нарушение ритма сердца.

Цель сообщения: Обсудить диагностические особенности внезапной сердечной смерти с помощью суточного мониторирование ЭКГ у пациента онкогематологии на фоне кардиотоксичность в последствии химиотерапии.

В данной работе рассматривается клинический случай пациента, который проходил стационарное лечение основного заболевания – острый лейкоз. На фоне лечения химиотерапии, препараты антрациклиновой группы, цитостатики, антигрипковые препарты и антибиотик широкого спектра действия были применены для лечения основного заболевания и его осложнении. Все перечисленные препараты имеют кардиотоксичность. В результате, мужчина молодого возраста, который в анамнезе не имел структурную патологию сердца, пережил эпизод внезапной сердечной смерти, жизнеугрожающего нарушения ритма сердца TdP (Torsade de pointes). Своевременная установка Холтер, позволила зафиксировать документально эпизод внезапной сердечной смерти пациента.

Удлинение интервала QTc как предиктор жизнеугрожающих нарушения ритма сердца, диагностическая важность мониторирование ЭКГ при нарушений ритма сердца у пациентов онкогематологии.

Ключевые слова: TdP - Torsade de pointes, кардиотоксичность, внезапная сердечная смерть, Холтер мониторование ЭКГ, онкогематология.