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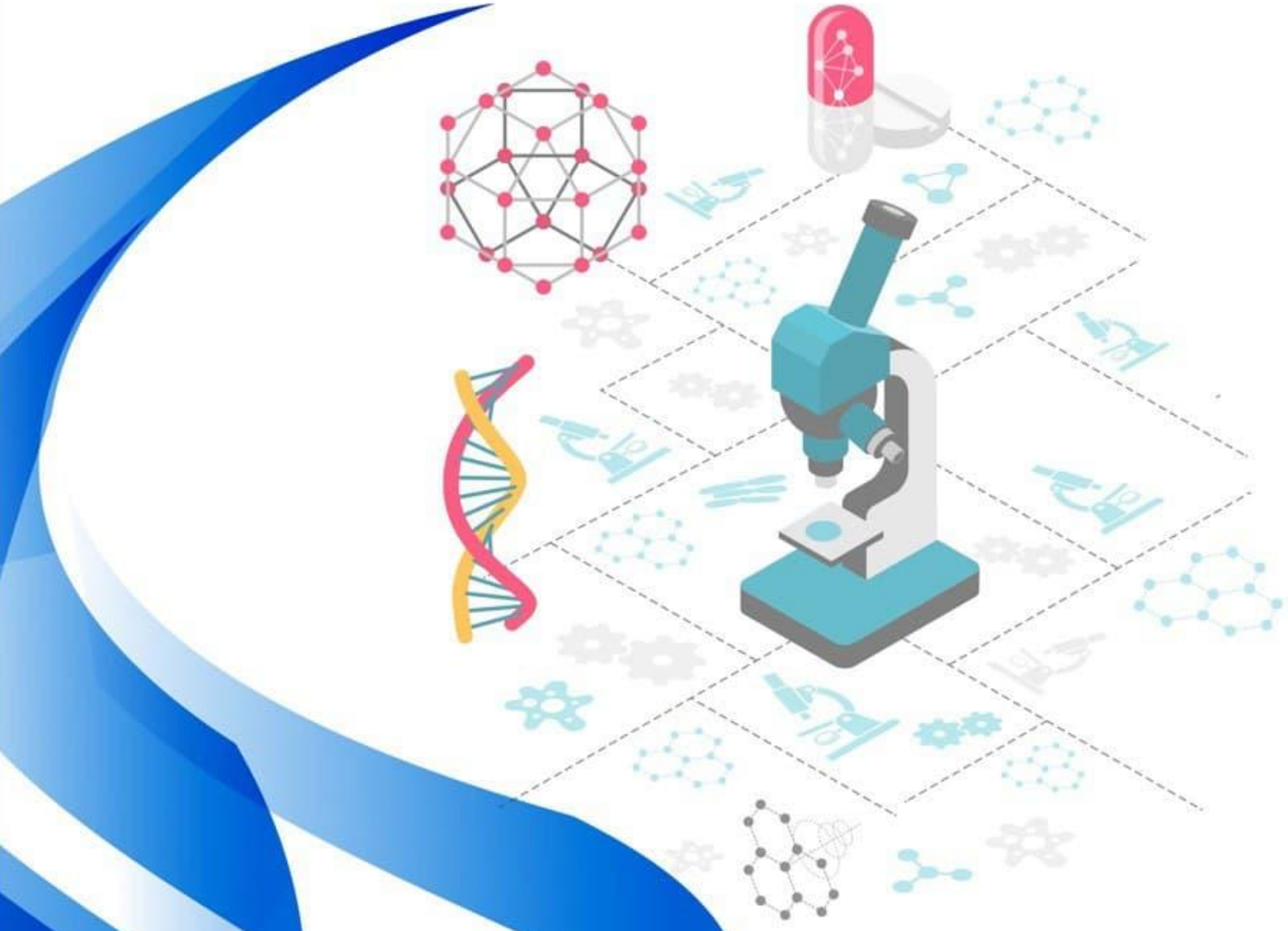

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CARDIAC ARRHYTHMIA AFTER CHEMOTHERAPY WITH CISPLATIN AND CYTARABINE. CLINICAL OBSERVATION

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Abstract. Acute cardiotoxicity of antitumor drugs can be manifested by various cardiac arrhythmias and conduction disturbances for up to 2 weeks. after their application. We present a clinical observation of a patient with Hodgkin's lymphoma treated with cisplatin and cytarabine. The next day after the end of chemotherapy, the first atrial fibrillation was noted.

Keywords: chemotherapy, acute cardiotoxicity, cardiac arrhythmias.

From time to time, every practicing oncologist (or hematologist) is faced with the appearance of a heart rhythm and / or conduction disturbance in his patient. The decision on the choice of effective treatment for these disorders and the need for further supportive therapy may directly depend on their suspected etiology [1-10]. Rhythm and conduction disturbances in cancer patients are detected more often than in the general population of patients of the same age or with similar comorbidities of the cardiovascular system [10-17]. This is true not only for oncological diseases in which the myocardium or pericardium is directly affected, or compression and / or displacement of the mediastinal organs occurs, i.e. diseases that cause direct damage to the heart and blood vessels, in which heart rhythm disturbances can be expected [16-28]. The occurrence of arrhythmias or heart blocks in a cancer patient may be, for example, associated with electrolyte disturbances (hyperkalemia and hypocalcemia in the development of rapid tumor lysis syndrome, hypercalcemia in bone lesions, hypokalemia and hypomagnesemia during infusion therapy with unbalanced solutions, etc.) or repeated thromboembolism of the pulmonary artery. Heart rhythm disturbances often occur when patients develop critical conditions (for example, severe respiratory failure, sepsis, renal failure, etc.). However, acute drug toxicity of

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anticancer drugs can also contribute to the development of rhythm and conduction disorders [29-31].

Clinical observation

A 19-year-old patient, who was hospitalized for Hodgkin's lymphoma, was admitted to the intensive care unit (ICU) on November 30, 2011 due to a first attack of atrial fibrillation.

Sick of Hodgkin's lymphoma for 3 years; in 2008–2009 received 8 courses of chemotherapy according to the BEACOPP-14 scheme and mediastinal irradiation (SOD 44 Gy).

In connection with the first early relapse, from November 26 to 29, 2011, DHAP chemotherapy was performed: cisplatin 170 mg as a daily infusion on the 1st day, cytarabine 3400 mg 2 times on the 2nd day and dexamethasone 40 mg per day from the 1st to the 4th day of treatment (with subsequent gradual dose reduction). In addition to anticancer drugs, he also received ondansetron, omeprazole and allopurinol these days. As a water-salt load on the day of cisplatin administration, I received intravenously 2800 ml of crystalloid solutions; in the following days, infusion therapy was not carried out. The patient's natural nutrition and fluid intake during the treatment period were not limited.

Neither before nor immediately after chemotherapy, the patient had no significant deviations from the normal values of biochemical blood parameters, normocoagulation persisted, and the hemoglobin level was 143–151 g/l. Blood pressure and pulse, determined by the attending physician daily, remained within the normal range. There were no peripheral edema, respiratory or heart failure.

The patient felt interruptions in the work of the heart early in the morning on November 30, 2011. During the day, the state of health did not worsen; interruptions in the work of the heart persisted, however, the patient did not note any decrease in exercise tolerance. In the afternoon, after recording a control ECG in the functional diagnostics department and consulting a therapist who diagnosed atrial fibrillation

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(AF), he was admitted to the ICU to restore sinus rhythm. Upon admission, the level of potassium in the blood was 3.5 mmol/l, magnesium - 0.85 mmol/l.

30 minutes after admission to the ICU, while maintaining AF, an increase in the frequency of ventricular contraction up to 130–140 per minute (on the monitor) was noted. To reduce the frequency of ventricular contraction, 5 mg of verapamil (Isoptin) was administered intravenously as a bolus for 2 minutes; after 5 minutes (with a frequency of ventricular contractions of about 100 per minute), 2.5 mg of the drug was re-introduced. Immediately after repeated administration of verapamil, the patient developed a decrease in ventricular contractions (up to 25-35 per minute) against the background of ongoing AF. Bradycardia due to refractoriness of the atrioventricular node, which was provoked by verapamil, was accompanied by hypotension and drowsiness. The patient was fitted with a temporary endocardial (intraventricular) pacemaker with a ventricular rate of 70 bpm. Against the background of the imposed rhythm, hemodynamics stabilized, drowsiness disappeared. After 10 minutes of electrical stimulation, sinus rhythm spontaneously recovered with a frequency of 97 beats/min; AF did not recur during the next 16 hours of observation in the ICU.

The endocardial electrode was removed, and the patient was transferred for further treatment to the Department of Hemoblastosis Chemotherapy. Prevention of arrhythmias was not carried out. During the next few weeks of inpatient treatment, including the period of cytopenia, which proceeded with infectious complications, AF did not recur.

Discussion

In the presented observation, the first paroxysm of AF occurred in a patient in the absence of the main etiological factors for the development of this type of heart rhythm disturbance, which include old age, arterial hypertension, acquired heart defects, heart failure, coronary heart disease, pulmonary embolism, chronic obstructive diseases lungs, thyrotoxicosis and electrolyte disturbances [1]. We believe

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that the most likely cause of AF in this patient was acute cardiotoxicity of anticancer therapy. It is known that acute cardiotoxicity of antitumor drugs can be manifested by disturbances in the processes of ventricular repolarization, prolongation of the QT interval, supraventricular and ventricular arrhythmias, acute coronary syndrome, pericarditis, myocarditis and occurs up to 2 weeks after the use of a chemotherapy drug [2].

Atrial fibrillation is often detected in cancer patients: ceteris paribus, the frequency of this arrhythmia in cancer patients is 3 times higher than in patients without malignant neoplasms [3]. An important role in the development of AF in cancer patients, even in the absence of "traditional" risk factors, seems to be played by chronic inflammation [4]: the level of one of the markers of systemic inflammation, C-reactive protein, is usually elevated both in malignant neoplasms and in patients with with FP [5]. However, the presence of chronic inflammation is nothing more than a predisposing factor in the development of AF in cancer patients. At the same time, it has been shown that AF can be induced by the administration of a number of anticancer drugs: anthracyclines, ifosfamide, gemcitabine, melphalan, cisplatin, docetaxel, fluorouracil, etoposide, and even high doses of dexamethasone [6, 7].

Bradycardia and various heart blocks in patients with malignant neoplasms can be caused by many factors. Heart blocks often occur as a result of cardiomyofibrosis that develops after mediastinal irradiation. Of the drugs used to treat oncohematological diseases, sinus bradycardia is most often caused by thalidomide (according to some reports, up to 55% of cases!) [8]. Cytarabine can also cause severe bradycardia [9], which responds to the introduction of atropine with an increase in heart rate.

Heart rhythm or conduction disturbances in patients with malignant neoplasms rarely become a reason for special research or discussion by oncologists or cardiologists. However, back in the early 1980s, when conducting round-the-clock

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(Holter) ECG monitoring, several studies showed that rhythm or conduction disturbances in cancer patients are a frequent pathology. For example, in a study by M.R. Hersh et al. Rhythm disturbances were detected in more than 60% of the examined patients even before the start of anticancer treatment [10]. Studies on 24-hour ECG monitoring have raised another problem: a standard ECG study does not reveal arrhythmias in the vast majority of patients. So, in the already cited work of M.R. Hersh et al. in a standard examination (ECG in 12 leads for 1 min), arrhythmias were not detected in 84% of patients. If studies, including domestic ones, are still carried out on the diagnosis, prognostic significance, prevention and treatment of arrhythmias in operated oncological patients, then cardiac arrhythmias or conduction disturbances in patients receiving antitumor drug treatment become the subject of controlled studies very rarely. Meanwhile, in drug antitumor therapy, the patient, in addition to all the factors already available to him that contribute to the appearance of arrhythmia or conduction of the heart, receives others (in the form of several antitumor drugs, accompanying treatment, a period of cytopenia, infectious complications, tumor lysis syndrome, etc.).

Of particular interest is the question of the frequency of arrhythmias associated with the direct proarrhythmic action of specific anticancer drugs, especially since there are quite a few publications of individual observations of such effects in these drugs. However, conducting a controlled study is associated with serious methodological problems. First of all, the presence of a tumor disease (or even the patient's knowledge of its presence), apparently, in itself can be a proarrhythmic factor. Another obstacle to conducting a controlled study on the effect of anticancer treatment on the development of cardiac arrhythmias is the polyetiology of this disease; anticancer drugs, even with a high proarrhythmic potential, can help reduce the frequency of arrhythmias if they can affect the essential cause of their occurrence (for example, reducing the tumor mass in the mediastinum or tumor infiltration of the heart). An important factor complicating the analysis of the proarrhythmic effect of a

particular anticancer drug is the combined nature of the treatment (i.e., the use of several different anticancer drugs at once) and often the simultaneous use of accompanying drugs. Despite the difficulties that arise when analyzing the causes of rhythm and conduction disturbances in a particular patient, the proarrhythmic effect of individual antitumor drugs is well documented, and in some cases reproduced experimentally. In table. Table 1 shows the most common variants of rhythm and conduction disturbances that develop in connection with the acute cardiotoxicity of some anticancer drugs.

References

1. Ellis K., Dressing T. Tachyarrhythmias. In: Cardiology. Ed. B. Griffin, E. Poplar. Moscow: Practice, 2008: 431–2. [in Russian]

2. Albini A., Pennesi G., Donatelli F. et al. Cardiotoxicity of anticancer drugs: the need for cardio-oncology and cardio-oncological prevention. J. Natl. Cancer Inst. 2010; 102: 14–25.

3. Lainscak M., Dagres N., Filippatos G.S. et al. Atrial fibrillation in chronic non-cardiac disease: where do we stand? Int. J. Cardiol. 2008; 128(3): 311–5.

4. van der Hooft C.S., Heeringa J., Brusselle G.G. et al. Corticosteroids and the risk of atrial fibrillation. Arch. Intern. Med. 2006; 166(9): 1016–20.

5. Cil T., Kaplan M.A., Altintas A. et al. Cytosine-arabinoside induced bradycardia in patient with non-Hodgkin lymphoma: a case report. Leuk. Lymphoma 2007; 48: 1247–9.

6. Ergashov B.B. A causal relationship of anticancer drugs with specific arrhythmias // Asian journal of Pharmaceutical and biological research 2021, 10(2), P. 55-65.

7. Ergashov B.B. A causal relationship of anticancer drugs with specific arrhythmias // Asian journal of Pharmaceutical and biological research 2021, 10(2), P. 55-65.

8. Ergashov B.B. Makhmudov R.B., Qayumov LK. Modern concept of clinic and diagnosis of cardiovascular complications of anticancer therapy // British Medical Journal 2021, 1, № 1.2 P. 174-180.

9. Ergashov B.B. TREATMENT AND PREVENTION OF ARRHYTHMIAS ASSOCIATED WITH ANTICANCER THERAPY // Asian journal of pharmaceutical and biological research 2021, 9 (2), P. 47-54.

10. Abdullaeva U.K. Predicting the risk of atrophic transformation in gastritis associated with chronic Helicobacter pylori // abstract of PhD dissertation on medical sciences. Tashkent. 2021. 46-p. [in Uzbek]

11. Abdullaeva U.K. Predicting the risk of atrophic transformation in chronic gastritis using serum pepsinogen // World journal of pharmaceutical research, Faculty of Pharmacy Medical University, Bulgaria, Vol. 8, Iss. 13, 2019, P. 219-228.

12. Abdullaeva U.K., Sobirova G.N., Karimov M.M., Aslonova I.J. The prevalence and possibilities of prevention of noncardial gastric cancer in the Bukhara region // American journal of medicine and medical sciences, 2020, 10(9), P. 679-681.

13. Sobirova G.N., Abdullaeva U.K., Nosirova M.S., Aslonova I.J. Evaluation of the gastrointestinal mucosa by the OLGA system in chronic atrophic gastritis // Journal of critical reviews, Kuala Lumpur, Malaysia, Vol. 7, Iss. 2, 2020, P. 409-413.

14. Karimov M.M., Sobirova G.N., Abdullaeva U.K., Aslonova I.Zh., Tulyaganova F.M. Possibilities of serological diagnosis of atrophic processes of the gastric mucosa // European Journal of Molecular & Clinical Medicine Vol. 7, Iss. 11, 2020, P. 2955-2960.

15. Karimov M.M., Sobirova G.N., Abdullaeva U.K. Chronic gastritis and carcinogenesis issues // Herald of Pancreatic Club, 2019. Iss. 45 (4). P. 65-70. [in Russian]

16. Sobirova G.N., Abdullaeva U.K. Immunopatogenesis of chronic gastritis and its role in carcinogenesis // Journal of Biomedicine and Practice, 1 (4). P. 40-44.

17. Karimov M.M., Sobirova G.N., Abdullaeva U.K., Aslonova I.Zh., Tulyaganova F.M. Possibilities of Serological Diagnosis of Atrophic Processes of the Gastric Mucosa // Annals of the Romanian Society for Cell Biology, , Vol. 25, Issue 1, 2021, Pages. 6168 – 6174.

18. Abdullaeva U.K., Shadjanova N.S. Using the OLGA system in chronic atrophic gastritis // New day in medicine, 2020, №2, P. 9-12.

19. Abdullaeva U.K. The value of interactive teaching methods in improving the level of clinical knowledge of students // Medical education and professional development. 2019, №1 (33), P. 29-32. [in Russian]

20. Sobirova G.N., Abdullaeva U.K. Chronic gastritis and carcinogenesis issues // Central Asian Problems of Modern Science and Education. 2019, Iss. 4, №2, P. 159-172

21. Orziev Z.M., Abdullaeva U.K., Nurkhanova N.O. Study of the effectiveness of cholelitholytic therapy in patients with cholelithiasis, taking into account the type of violation of the contractility of the gallbladder // Science of the Young - Eruditio Juvenium. 2015. №4. P. 50. [in Russian]

22. Karimov M.M., Sobirova G.N., Abdullaeva U.K., Aslonova I.Zh., Tulyaganova F.M. Serological Diagnosis of Atrophic Processes of the Gastric Mucosa // The American Journal of Medical Sciences and Pharmaceutical Research, Vol. 2, Issue 12, 2020, Pages. 118-124

23. Mirzaeva D.B., Abdullaeva U.K., Boboeva R.R. The importance of interactive teaching methods in improving the level of clinical knowledge of students // Central Asian Problems of Modern Science and Education Vol. 4, Issue 2, 2019, Pages. 159-166

24. Karimov M.M., Rustamova S.T., Ismailova Zh.A., Abdullaeva U.K., Saatov Z.Z. Diagnostic efficacy of C14 breath test in Helicobacter pyloriosis // Cardiovascular therapy and prevention. 2019. Vol. 18, Issue S1, P. 85-86

25. Abdullaeva U.K., Jalolova V.Z. Study of the effectiveness of cholelitholytic therapy in patients with cholelithiasis, taking into account the type of violation of the contractility of the gallbladder // Bulletin of the Council of Young Scientists and Specialists of the Chelyabinsk Region. 2016. Vol. 5, Issue 4(15), P. 85-86 [in Russian]

26. Orziev Z.M., Abdullaeva U.K. Regional causes of extrahepatic "Subtransaminasemia" // Biology and integrative medicine 2016, №3. P. 28-40. [in Russian]

27. Abdullaeva U.K., Mirzaeva D.B. Regional prospects for metabolic therapy for stable senocardia Summary. // Bulletin of the South Kazakhstan Medical Academyю 2019. P. 74-76 [in Russian]

28. Orziev Z.M., Abdullaeva U.K., Yuldasheva D.H. Method for early prediction of the efficiency of cholelytic therapy based on dynamic control of bild pH indicators in patients with cholelystone disease // Innovative development of modern science. 2014. P.76-79 [in Russian]

29. Orziev Z.M., Abdullaeva U.K. Relationship between the effectiveness of cholelitholytic therapy and the state of contractility of the gallbladder // Bulletin of the Council of Young Scientists and Specialists of the Chelyabinsk Region. 2015. №3(10). P. 36-40. [in Russian]

30. Orziev Z.M., Abdullaeva U.K. The effectiveness of cholelitholytic therapy for cholelithiasis // Health is the basis of human potential: problems and ways to solve them. 2015. Iss. 10. №2. P. 610-612. [in Russian]

31. Shamsutdinov A.S., Abdullaeva U.K., Akhmedova N.S. Determination of the level of pepsinogens in patients with chronic h. pylori associated gastritis // ACADEMICIA: An international multidisciplinary research journal . Iss. 11. №2. P. 919-924.