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Case report

Obstacles in the treatment of coronary artery disease in patients with cancer

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Abstract Cardiovascular disease (CVD) and cancer are the two leading causes of death worldwide, accounting for over 70% of all deaths. The prevalence of CVD and cancer is increasing, and the two conditions often coexist in the same patient. The management of patients with both CVD and cancer presents a significant challenge, as treatments for one condition may increase the risk of complications in the other. Despite advances in medical therapies and interventional procedures, CVD continues to be a significant public health challenge. The prevalence of CVD among cancer patients is even higher than the general population, and they have an increased risk of CVD-related morbidity and mortality. In this report, we present a case of 59-year-old man with a history of colon cancer who presented with ACS and treated with optimal medical therapy due to high bleeding risk. Our case highlights the importance of a multidisciplinary approach to the management of ACS in cancer patients, based on the latest gudielines and evidence-based practices.

Kew words acute coronary syndrome, cancer, dual antiplatelet therapy, bleeding

Introduction

Cardiovascular disease, especially ischemic heart disease and cancer are two of the leading causes of morbidity and mortality worldwide[1]. The incidence of cancer and cardiovascular disease continues to increase globally, and there is an increasing number of patients with both malignant and cardiovascular disease(2). Management of these patients poses a specific challenge for healthcare professionals, due to drug interactions, the effects of chemotherapy and radiation therapy on the cardiovascular system, and the high risk of both bleeding and thrombotic events[3,4,5,6]. Several studies have been conducted in recent years in order to enable better understanding of complex patophysiology of these patients and to identify potential strategies for effective treatment of this specific subgroup of patients[7].

Case presentation

Male patient, 59 years old, who was without known comorbidities until February 2019, had episodes of diarrhea for which he was examined by a gastroenterologist. Two months later patient had 4 to 6 diarrheal bloody stools per day, as well as one episode of rectorrhagia. This was the reason for reevaluation by gastroenterologist, a colonoscopy was performed and patient was diagnosed with colorectal cancer (adenocarcinoma) with secondary deposits in the liver. Colon surgery was performed next month, with formation of a colostomy. He was admitted to Institute for Oncology and Radiology of Serbia (IORS) two months after the surgery due to administration of the first cycle of adjuvant chemotherapy regimen according to the FOLFOX protocol (folic acid+5FU+oxaliplatin). After 30 minutes from the beginning of administration of the second dose of chemotherapy, patient complained of chest pain with propagation to his shoulders. Therapy administration was discontinued, ECG was performed, 1mm - ST depression and negative T waves in leads I, aVL, V5 and V6 were registered. Due to the suspicion of the development of acute coronary syndrome (ACS), dual antiplatelet therapy (DAPT) (acetylsalicylic acid 300mg, Clopidogrel 300mg) was prescribed along with PPI, the patient was referred to ER and because of elevated troponin plasma levels (hs TnT 170 ng/L, cut off 14ng/L) he was admitted to the Coronary ICU. An echocardiographic examination revealed normal left ventricle size (EDD/ESD 5.5/3.6 cm), without evidence of regional wall motion abnormalities, normal left ventricular function, EF 64%, without pericardial effusion. Selective coronary angiography revealed a 90-95% stenosis of the OM branch, without angiographically significant stenosis on other coronary arteries, and PCI of OM branch was indicated as soon as possible, depending on the clinical condition and the possibility of applying long - term DAPT. After the administration of next dose of dual antiplatelet therapy (acetylsalicylic acid 100mg, Clopidogrel 75mg), rectal and colostomy bleeding occurred, and a consultation

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with a gastroenterologist was performed, but, due to active rectal bleeding, permission for the use of dual antiplatelet and anticoagulant therapy was not obtained, and the patient was treated with optimal medical therapy in the further course of hospitalization. During hospitalization, the chest pain did not recur, nor did the gastrointestinal bleeding, the maximum value of hsTnT was 408, and after the normalization of the TnT value, the patient was transferred to IORS for further treatment of the malignant disease.

Discussion

The use of antithrombotic therapy in cancer patients with CVD is a topic of ongoing research. The European Society of Cardiology (ESC), the European Hematology Association (EHA), the European Society for Therapeutic Radiology and Oncology (ESTRO), and the International Cardio-Oncology Society (IC-OS) have jointly developed guidelines for the management of cardio-oncology patients[8]. The guidelines emphasize the importance of assessing the cardiovascular risk of cancer patients before initiating cancer treatment and regularly monitoring the cardiovascular status of cancer survivors. According to guidelines, it is advised to perform immediate PCI in patients with cancer presenting with STEMI or high-risk NSTE-ACS with life expectancy ≥6 months, while non-invasive approach is preferred in patients with poor cancer prognosis and/or very high bleeding risk. The guidelines recommend that the choice of antithrombotic therapy should be based on the type of cancer, the stage of cancer, the type of PCI, and the patient's bleeding risk. The guidelines also recommend that the duration of DAPT should be individualized based on the patient's bleeding and ischemic risks. One key theme that emerges from the literature is the elevated risk of both thrombotic and bleeding events in cancer patients undergoing PCI for AMI. Guo et al. found that cancer patients had a higher risk of both thrombotic and ischemic events following PCI, even after controlling for other risk factors such as age, gender, and comorbidities[6]. In addition, several studies have demonstrated that cancer patients undergoing PCI are at higher risk of readmission due to bleeding and ischemic events than non-cancer patients[9,10]. One study conducted by Bharadwaj et al. evaluated the outcomes of PCI in 6.5 million patients with a current or previous diagnosis of cancer in the United States. The study found that cancer patients who underwent PCI had a higher risk of in-hospital mortality, bleeding, and stroke when compared to non-cancer patients[3]. Similarly, Nakatsuma et al. found that cancer patients had significantly higher adjusted risk for all-cause death, non-cardiac death and major bleeding when compared to non-cancer patients[11].

In addition to the challenges of balancing the risks of ischemic and bleeding events, recent studies have also highlighted the importance of recognizing the common pathophysiology underlying cancer, atrial fibrillation, atherosclerosis, and thrombosis. A state-of-the-art review by Leiva et al. explores this common pathophysiology, noting that all of these conditions are characterized by an imbalance between pro-coagulant and anti-coagulant factors that can increase the risk of both thrombotic and bleeding events. Authors note that inflammation, hypercoagulability, and oxidative stress are all key drivers of both cancer and cardiovascular disease, and suggest that targeting these pathways may be a promising approach for managing competing risks in patients with both conditions and they suggest that better understanding of this shared pathophysiology could lead to improved prevention and treatment strategies for these conditions[2].

Several studies have explored the use of dual antiplatelet therapy (DAPT) in cancer patients undergoing PCI in ACS treatment, with focus on estimation of risk for both bleeding and thrombotic events. Tsigkas et al.(12) summarized the current evidence on DAPT use in patients with malignant disease. It is noted that shorter use of DAPT (1-3 months) reduces bleeding risk, but it is recommended that prolongation of DAPT use should be considered in patients with increased risk of thrombotic events. Tang et al. noted that among cancer patients treated with PCI in ACS, bleeding and all-cause mortality rates were lower when compared to non-PCI cancer patients with ACS[1]. Another study by Hayashi et al. investigated the cardiovascular and bleeding risks in patients with inactive cancer and AMI who received primary PCI using drug-eluting stent and DAPT. The study found that inactive cancer was associated with a higher risk of both major bleeding and cardiovascular events[13]. All of the above mentioned studies highlighted the need for individualised therapeutic approach. Similarly, a commentary by Mamas and study conducted by Potts et al. emphasizes the importance of individualized treatment strategies that take into account both ischemic and bleeding risk factors[5,14].

Several other recent studies have also highlighted the challenges of managing ACS in patients with cancer, including both short-term and long-term outcomes. For instance, a study by Matsumoto et al. found that presence of active cancer was associated with worse short-term and long-term outcomes in patients with ACS, including higher rates of major bleeding during index hospitalization and higher rates of both major bleeding and major adverse cardiovascular events after discharge when comapred to patients with a history of cancer and those without cancer[1]. A review by Lucà et al. highlights the importance of recognizing the increased risk of ACS in patients with cancer, as well as the challenges of managing both conditions simultaneously. The authors suggest that the management of such patients should be individualized based on the patient's bleeding and ischemic risks, the type of cancer, and its treatment, choosing invasive approach in case of STEMI and high-risk NSTEMI, while the non-invasive strategy should be reserved for low-risk NSTEMI patients and in cases of stable coronary artery disease (CAD)[7]. They also emphasize the importance of a multidisciplinary approach to the management of such patients. Similarly, Potts et al. suggest that treatment of cancer patients should be individualized and done in collaboration of cardiologists and oncologists[14]. Considering these evidences from

literature, and taking into account absence of significant ECG changes suggesting the development of STEMI or high-risk NSTEMI, reccurent symptoms of myocardial ischemia, signs or symptoms of heart failure and normalisaton of cardiospecific enzymes plasma levels, as well as presence of rectal and colostomy bleeding after loading dose and first day maintenance dose of DAPT, the medical team concluded that the risk of long-term DAPT use would be unacceptably high, and a decision was made to treat the patient with individually tailored optimal medical therapy (OMT).

Given the increased risk of adverse events in cancer patients undergoing PCI, it is important to consider strategies for reducing this risk. Some studies suggested an approach aimed to precisely identify patients who are at a higher risk of bleeding or thrombotic events and tailor their treatment accordingly[16,17]. In an editorial published in JACC: Cardiovascular Interventions, Ky and Fanaroff suggest that precision medicine can help to define bleeding and ischemic risk in cancer patients undergoing PCI by taking into account patient-specific factors such as cancer type, stage, and treatment history. Also, it is noted that current bleeding and ischemic risk scores may not adequately capture the unique risk profile of cancer patients, because they are based on results of trials in which those patients are not included[4].

In conclusion, the management of ACS in cancer patients is complex and requires a multidisciplinary approach. Clinicians should carefully evaluate the risks and benefits of different treatment options, taking into account the patient's individual characteristics, cancer type and stage, bleeding and thrombotic risk and the potential interactions between antiplatelet and anticoagulant therapy and chemotherapy. The latest guidelines provide comprehensive recommendations to guide clinicians in decision-making and treatment selection, but more research is needed to better understand the optimal management of ACS in cancer patients. By collaborating with oncologists and other specialists, clinicians can improve the outcomes of these challenging patients and provide better care.

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Sažetak

Teškoće u lečenju koronarne bolesti kod pacijenata sa karcinomom

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Kardiovaskularne bolesti (KVB) i maligniteti predstavljaju dva vodeća uzroka smrti širom sveta, a odgovorni su za oko 70% svih smrtnih ishoda. Prevalencija KVB i maligniteta je u porastu, a ova dva stanja su često istovremeno prisutna kod istog pacijenta. Lečenje pacijenata sa KVB i malignitetom predstavlja veliki izazov, jer terapijski pristup lečenju jednog oboljenja može povećati rizik od nastanka komplikacija pri lečenju drugog oboljenja. Uprkos razvoju medikamentne terapije i interventnih procedura, kardiovaskularne bolesti i danas prestavljaju značajan javnozdravstveni izazov. Prevalencija KVB među pacijentima sa malignitetima je veća nego u opštoj populaciji, a u ovoj grupi pacijenata je uočen i povećana stopa morbiditeta i mortaliteta od KVB. U ovom radu prikazan je je slučaj 59- godišnjeg muškarca sa karcinomom debelog creva kod koga je došlo do razvoja AKS lečenog individualno prilagođenom medikamentom terapijom zbog visokog rizika od krvarenja. Naš slučaj naglašava važnost multidisciplinarnog pristupa u lečenju AKS kod pacijenata sa malignenetom, zasnovanog na najnovijim preporukama i dokazima iz velikih randomizovanih studija.

***Ključne reči**: akutni koronarni sindrom, karcinom, dvojna antiagregaciona terapija, krvarenje*