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## **Multi-organ long-term complications after Hodgkin lymphoma's radiotherapy and chemotherapy**

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**Multi-organ long-term complications after Hodgkin lymphoma's  
radiotherapy and chemotherapy**

Wielonarządowe powikłania odległe po radioterapii i chemioterapii chłoniaka Hodgkina

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**Abstract**

Forty-nine-year-old woman with a history of long-term complications after radiotherapy and chemotherapy including coronary artery disease and pulmonary fibrosis was admitted to our center. Further complications — pulmonary hypertension, heart failure, and multiple heart valves insufficiency — were diagnosed. Here we present images from diagnostic procedures that allowed us to visualize those disturbances.

Key words: coronary artery disease, pulmonary fibrosis, pulmonary hypertension, mitral valve insufficiency, heart failure

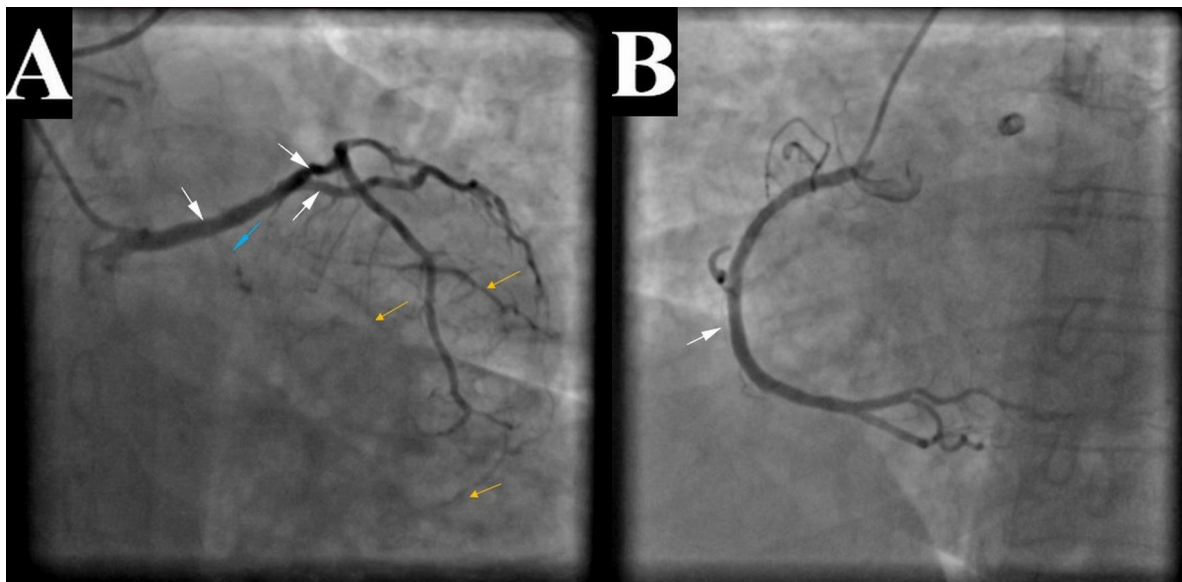
**Introduction**

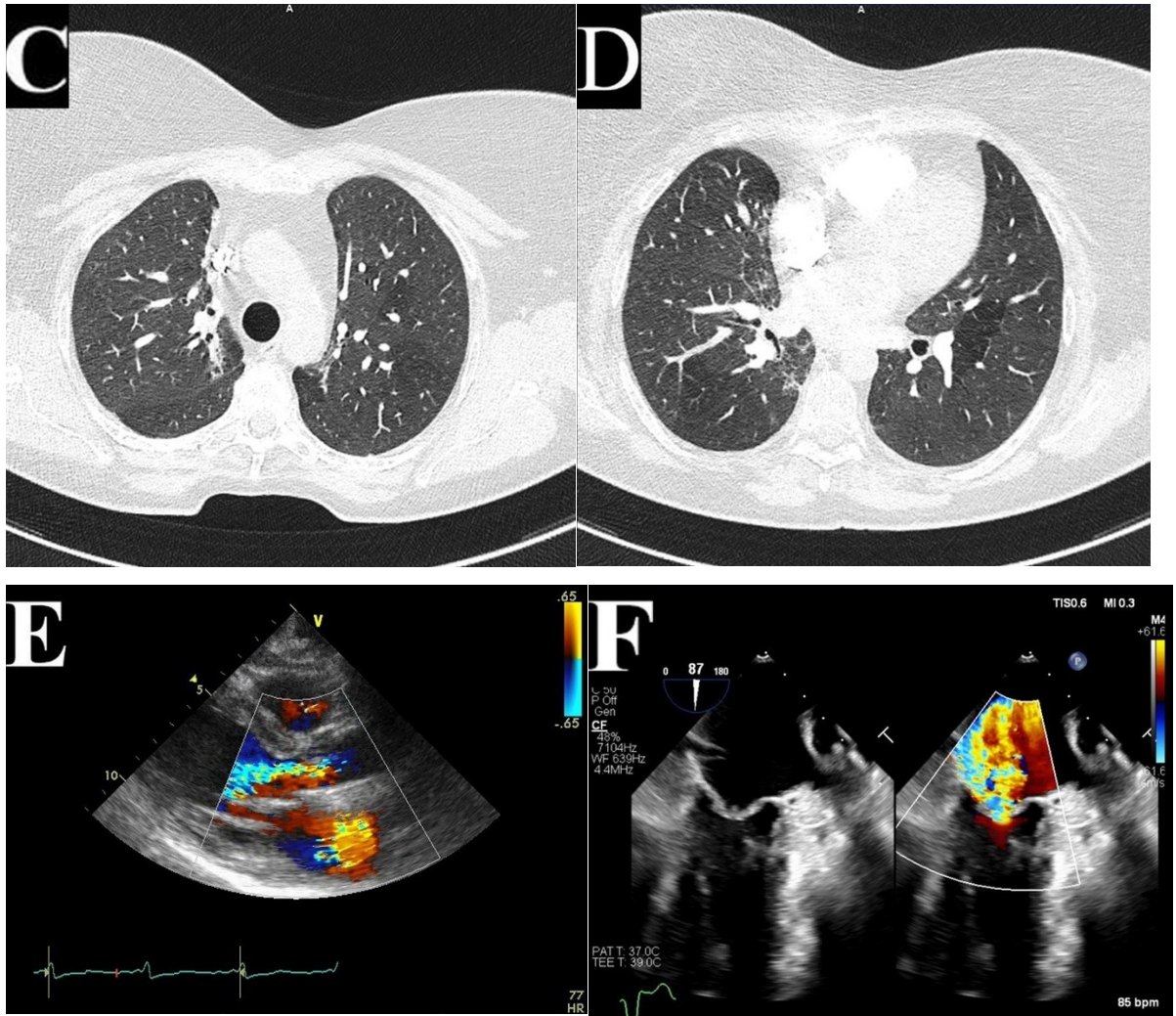
Radiotherapy and chemotherapy are lifesaving in various cases of neoplasms but can cause lifelong complications. Current approaches aim to make these therapies more neoplasm-targeted, but complications are still a big problem and a challenge.

## Case presentation

We describe the case of a 49-year-old woman, who received chemo- and radiotherapy for Hodgkin lymphoma 26 years ago (because of such a distance in time the medical record containing information about the total dose of radiation and irradiation site as well as the type of chemotherapy is not available). She was admitted to our department because of dyspnea, chest pain, and reduced exercise tolerance, which had been the reason for multiple prior hospitalizations.

The patient had undergone many diagnostic and treatment coronary angiographies with angioplasties and implantations of 6 stents in each major epicardial artery because of coronary artery disease (Figure 1A–B). At the age of 42, she survived four consecutive non-ST segment elevation myocardial infarctions in a period of 6 weeks. In chest computed tomography imaging pulmonary fibrosis was identified (Figure 1C–D). It is also worth mentioning two malignant melanomas of the skin were removed. The patient was also diagnosed with type 2 diabetes mellitus, obesity, hypercholesterolemia, hyperuricemia, hypothyroidism, liver steatosis, and chronic kidney disease.





**Figure 1.** Hodgkin lymphoma’s treatment complications: **A.** Coronary angiogram showing good long-term patency of the stents implanted in left main coronary/left anterior descending and diagonal branch (indicated with white arrows). Chronic total occlusion of the proximal circumflex branch is indicated with a blue arrow — retrograde filling of the distal marginal branches can also be appreciated (indicated with yellow arrows); **B.** Coronary angiogram showing proper long-term effect with minimal restenosis in-stent implanted in mid-right coronary artery (indicated with white arrow); **C.** Chest computed tomography imaging: pulmonary reconstruction 1 mm, bilaterally paramediastinal consolidation and fibrous changes of the lung parenchyma after radiotherapy, slightly pulling oblique interlobar fissures; **D.** Chest computed tomography imaging: pulmonary reconstruction 1 mm, paramediastinal consolidation and fibrous changes of the right lung’s parenchyma after radiotherapy; **E.** Transthoracic echocardiogram in the parasternal long axis showing moderate aortic insufficiency; **F.** Severe insufficiency of the mitral valve visible in the mid-esophageal 2-chamber view of transesophageal echocardiogram

Performed coronarography showed no hemodynamically significant stenoses, but the pulmonary catheterization revealed pulmonary hypertension with high pulmonary capillary wedge pressure, indicating left heart disease as its etiology. The transthoracic echocardiography revealed III stage diastolic dysfunction of the left ventricle and the patient was therefore diagnosed with heart failure with preserved systolic function (N24-N-terminal pro-brain natriuretic peptide level was 265 pg/mL, reference range; < 125.0 pg/mL). Combined moderate mitral insufficiency with moderate mitral stenosis, with thickened and calcified leaflets and mitral annulus together with combined moderate aortic insufficiency with mild stenosis were found (Figure 1E). Despite valvular defects, the heart chambers' sizes were normal, which can be attributed to fibrotic pericardium. In the exercise stress, echocardiography mitral gradient increased from 6 mm Hg to 9 mm Hg with little effort was observed.

The transesophageal echocardiography assessment re-classified valvular defects as more advanced with severe mitral insufficiency (Figure 1F) and moderate aortic stenosis. Pulmonary tests showed features of pulmonary restriction, increased airway resistance, and decreased diffuse capacity. The patient was, therefore, qualified for aortic and mitral valves replacement with the aortic annuloplasty.

## **Discussion**

Radiation pulmonary fibrosis results from pneumocytes' destruction and relief of cytokines inducing migration of the inflammatory cells responsible for acute pneumonitis. The latter promotes excessive collagen synthesis, enhanced by transforming-growth factor  $\beta$  [1]. Our patient also received chemotherapy, which increases the risk of Radiation-Induced Lung Injury [1]. Arteries, especially of the smallest radius, exposed to radiation develop stenosis, occlusion and wall thickening [2], which can partially explain our patient's pulmonary hypertension, which also left heart disease contributed. It is worth mentioning radiotherapy is also one of the risk factors for vessel fracture [3]. Coronary artery disease associated with radiotherapy (the amount of radiation is the risk factor) is frequently dispersed and affects mainly arteries' initial parts [4], probably caused by endothelial damage and cytokines stimulating inflammation and fibrosis [2]. Among the radiotherapy-cured Hodgkin's lymphoma patients it is the second most frequent reason for death and morbidity [4]. Radiotherapy of the thorax is the risk factor for left ventricular concentric remodeling [5], which can explain our patient's heart failure and decreased exercise tolerance.

## Conclusions

To conclude radiotherapy and chemotherapy can cause various types of complications, which affect many organs. This case report showed the complexity of such complications and the necessity to use varied diagnostic devices to fully visualize all pathologies. The aim was to make this work educational in the field of cardio-oncology.

## Conflict of interest

The authors declare no conflict of interest.

## Funding

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## Streszczenie

Do ośrodka przyjęto 49-letnią kobietę z historią odległych powikłań po radioterapii i chemioterapii, włącznie z chorobą wieńcową i zwłóknieniem płuc. Zostały zdiagnozowane kolejne powikłania — nadciśnienie płucne, niewydolność serca i niedomykalność wielu zastawek serca. W tekście zaprezentowano zdjęcia z procedur diagnostycznych, które pozwoliły na zwizualizowanie tych nieprawidłowości.

Słowa kluczowe: choroba wieńcowa, zwłóknienie płuc, nadciśnienie płucne, niedomykalność zastawki mitralnej, niewydolność serca

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