

Case report

Electrocardiographic changes in lung cancer. Be careful not to misdiagnose: acute coronary event?, meta?, inflammation?

Katarzyna Styczkiewicz^{1,2}, Agnieszka Kostkiewicz³, Michał Górecki², Mateusz A. Iwański¹

¹ Institute of Medical Sciences, College of Medical Sciences, University of Rzeszow, Rzeszow, Poland

² Subcarpathian Oncological Center, University Clinical Hospital of Frederic Chopin, Rzeszow Poland

³ Clinical Department of Radiology, Provincial Hospital No. 2, Rzeszow, Poland

Correspondence:

Mateusz A. Iwański
Institute of Medical Sciences,
College of Medical Sciences,
University of Rzeszow
Al. mjr. W. Kopisto 2a,
35-310 Rzeszow, Poland
phone: +48 17 872 11 45
e-mail: iwanskimateusz747@gmail.com

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ABSTRACT

In cancer patients changes in the electrocardiogram (ECG) may indicate various causes. The presented case concerns a patient with advanced left lung cancer who presented deep inversion of T waves during ongoing chemotherapy. We excluded acute coronary syndrome, acute pulmonary embolism, and myocarditis. Subsequently, we suspected metastases to the myocardium; therefore, we performed cardiac magnetic resonance imaging, which however did not confirm that. The cardiac magnetic resonance imaging showed residual post-inflammatory changes in the left lung. We publish this case to show that the inflammatory process of lung segments adjacent to the heart may cause temporal myocardial oedema, resulting in ECG changes that may mimic acute coronary events.

Key words: electrocardiogram, lung cancer, myocardial oedema

INTRODUCTION

The electrocardiogram (ECG) is a useful tool for monitoring cancer treatment safety because as a common and available tool can quickly identify changes that indicate on cancer therapy-related cardiovascular toxicity [1].

Cancer patients who undergo surgery, chemotherapy, or radiation therapy are at risk of developing cardiac arrhythmias, in particular atrial fibrillation (AF) [2, 3]. The risk of AF is higher in patients over 65 years of age and/or with preexisting cardiovascular diseases (CVD). The prevalence of AF is particularly high in patients with lung cancer being usually at older age and with preexisting CVD [4]. It has also been shown that in patients with advanced cancer and concomitant CVD, QT intervals on ECG may be prolonged, which can cause serious ventricular arrhythmias, such as torsade de pointes or ventricular fibrillation, thus constituting a direct threat to life [5].

Acute coronary syndrome (ACS) in cancer patients is a frequent complication during or after oncological treatment and remains an important cause of mortality in these patients [6]. The most common types of cancer associated with ACS are lung cancer, prostate cancer, and breast cancer, according to the largest published registry on treatments and outcomes of acute myocardial infarction. Lung cancer was also associated with the highest rates of in-hospital mortality and major adverse cardiovascular complications [7]. Similarly to patients without cancer, ACS is diagnosed based on clinical symptoms, 12-lead ECG, and serial

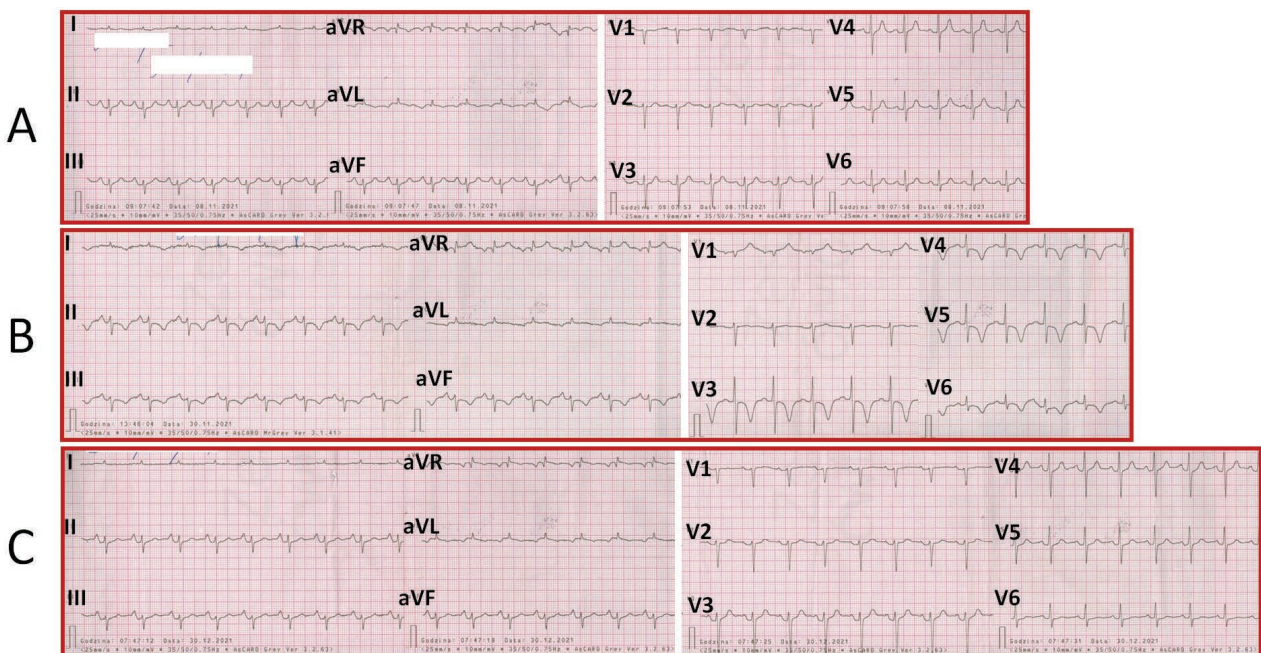
troponin levels in patients without ST-segment elevation; however, the clinical picture may be atypical [8, 9]. In rare cases, ACS may be caused by vascular compression or invasion of metastatic cardiac tumours [10].

Nevertheless, non-characteristic changes in the ECG can occasionally pose many challenges to interpretation, which makes it difficult to properly plan diagnostic and therapeutic interventions. It is important to note that the registration of nonspecific changes in T waves and ST segments on the ECG could be caused by secondary cardiac involvement, which is relatively common in lung cancer compared to other malignancies. However, this is difficult to diagnose before death since cardiac involvement can overlap with the symptoms of disseminated disease [11–13]. The only symptoms of myocardial metastases may be cardiac arrhythmias or ECG patterns indicative of acute vascular toxicities, mainly ACS (inverted T waves, ST-segment depression, or ST elevation in ECG) [14–17].

When an oncological patient presents nonspecific changes in ST-T waves, echocardiography can help establish the correct diagnosis [14]. Echocardiography increases diagnostic accuracy in patients with atypical symptoms and allows evaluation of different cardiac causes of chest pain [18].

However, in selected cases, cardiac magnetic resonance imaging (CMR) is the only method capable of making a definitive diagnosis [14, 16]. As a result of CMR, myocardial structure and function

Figure 1. A. Baseline electrocardiogram (ECG). B. ECG at the time of the inflammatory process. C. ECG after recovery from inflammation.



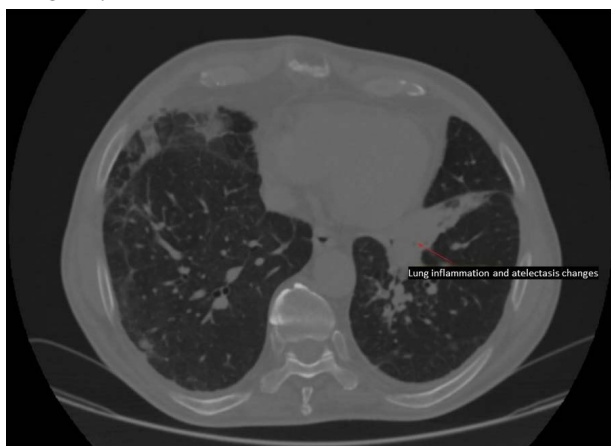
are accurately assessed, so it is possible to diagnose cardiotoxicity (ischemia, inflammation, fibrosis), infiltrative cardiomyopathy, myocarditis, pericardial disease, and pathologic cardiac masses [19].

CASE REPORT

A 62-year-old male patient with advanced left lung squamous cell carcinoma (cT4N2M1) has been attending the oncology department in September 2021. He had a history of lung tuberculosis and was a heavy smoker for 40 years with no previous cardiac history. Since May 2021 the patient has experienced increased weakness, dyspnea, nonspecific chest pain, and hemoptysis. Chest tomography (CT) showed a large tumor in the left hilum, infiltrating the left main bronchus, adhering to the pulmonary truncus and ascending aorta with bilateral metastases. The baseline ECG (fig. 1A) revealed a sinus rhythm of 95/min with a shallow T inversion in the aVL lead.

The patient was eligible for palliative treatment with the cisplatin and vinorelbine scheme. One month after starting chemotherapy, the control ECG revealed deep inversion of T waves in leads II, III, aVF, V₃-V₆ with accompanying ST segment depression (fig. 1B) and no relevant changes in the reported symptoms except increased weakness. Blood pressure was 85/66 mmHg at a level similar to that in the past. Laboratory tests revealed moderate anemia, increased d-dimer 2069 ng/mL (N: 0-500), increased N-terminal pro-B-type natriuretic peptide 5230 pg/mL (N: < 125) and negative troponin 21.68 ng/L (N: < 45). Echocardiography showed a mildly reduced left ventricle ejection fraction of 45%. The patient was referred for CT and acute pulmonary embolism (APE) was excluded. In proximity to the heart, inflammatory changes of the lung with atelectasis were observed (fig. 2).

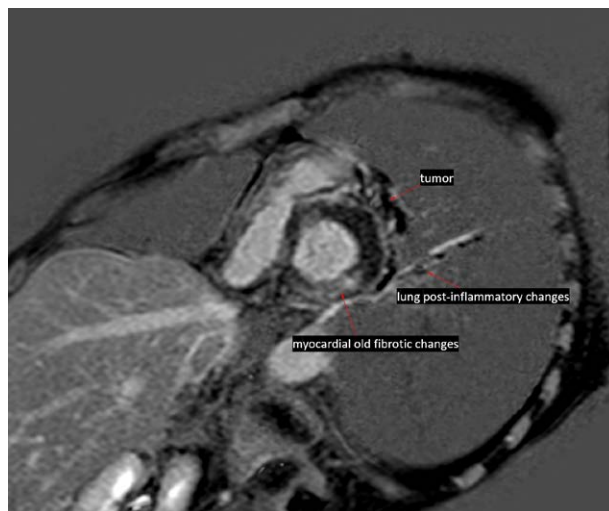
Figure 2. Chest tomography showing lung inflammatory and atelectasis changes adjacent to the heart.



The patient also underwent coronary angiography, which excluded significant changes in the coronary arteries.

In December 2021 before the fourth cycle of chemotherapy, the ECG returned to the initial state without inversion of the T waves (fig. 1C). CMR performed at that time revealed no cardiac involvement of the anterior myocardial wall close to the tumour. Residual post-inflammatory changes of the left lung and old fibrotic changes of the inferior myocardial wall were present (fig. 3).

Figure 3. Cardiac magnetic resonance imaging: phase-sensitive inversion recovery reconstruction with a breath-holding late gadolinium enhancement sequence showing post-inflammatory changes in the left lung, normal myocardium adjacent to the tumour and inflamed lung tissue, old fibrotic changes in the inferior wall of the left ventricle (not related to recent inflammation).



DISCUSSION

ACS is a relatively common cardiac event in patients with lung cancer [7]. The patient's chest pain, abnormal ECG, history of nicotine addiction, and cisplatin treatment were indicative of ACS in our case. However, during invasive diagnostic procedures, coronary angiography excluded ACS.

Another possible cause of abnormal ECG in our patient could be APE. The clinical picture of APE is often uncharacteristic and can mimic ACS leading to misdiagnosis. In the study Kukla et al. ECG changes suggestive of myocardial ischaemia, namely inverted T waves in III, aVF and V₂-V_{4r}, ST-segment depression or elevation in III, V_{1r}, V₂-V_{4r}, were observed in 208 (71.2%) patients with APE. The most common ECG abnormalities were inverted T waves in III and aVF (48.6%), inverted T waves in V₂-V₄ (41.8%) and ST-segment depression in V₄-V₆ (26.4%) [21]. Because in our case the ECG showed inversion of T waves in II, III, aVF, V₃-V₆ and ST seg-

ment depression, after exclusion of ACS, using the revised Geneva score, we evaluated the probability of APE in our patient and performed a CT scan, which, however, eliminated the possibility of APE diagnosis.

According to available case reports, any new ECG changes in patients with lung cancer, particularly if they suggest ACS without appropriate symptoms, and are not accompanied by elevated troponin levels, can indicate cardiac metastases [10–16]. In our case, the stage and location of the tumour suggested cardiac metastases, which may occur in up to 18% of cases of squamous cell lung cancer [22]. There are some case reports of patients with lung cancer after surgical treatment in whom myocardial metastases also mimicked ACS on the ECG [23, 24]. There are three common ECG patterns that could indicate cancer infiltration of the myocardium: ST-segment elevation, negative T waves (as in our case), and right bundle branch block [22]. The high diagnostic precision of CMR in patients with suspected cardiac tumours is helpful in such cases [25]. However, the CMR performed in our patient did not confirm the presence of cardiac metastasis.

Liang et al. described a rare case of cardiovascular toxicity caused by gemcitabine/cisplatin adjuvant chemotherapy in a patient with cholangiocarcinoma who was clinically diagnosed with Wellens syndrome by electrocardiography [26]. The so-called Wellens syndrome (deep T wave inversion in V_2 – V_3 that often extends to V_1 – V_6) was initially thought to be triggered only by atherosclerotic subocclusion of the left anterior descending artery, but it was later observed in other conditions with reversible left ventricle dysfunction due to ischemic or non-ischaemic causes, including takotsubo syndrome [22]. Therefore our another hypothesis was that the inflammatory process of the lung segments adjacent to the heart caused transient swelling of the myocardium, resulting in the described ECG changes. A CMR was performed with a delay

in time, so myocardial oedema was not captured. However, after excluding other possible explanations, we hypothesise that the observed changes in the ECG similar to Wellens syndrome and their spontaneous resolution could be attributed to previously existing lung inflammation that leads to transient myocardial oedema.

CONCLUSION

We present this case to emphasise that the clinical picture of cancer patients, especially lung cancer with frequently overlapping CVD, and the changes in ECG throughout ongoing oncological therapy may often be a challenge and require increased vigilance, knowledge, and collaboration with oncologists.

Key messages

- Interpreting ECG changes in cancer is a huge challenge requiring complete knowledge of the cardiological and oncological status of the patient.
- In high-risk cardiac patients, a differential diagnosis must be performed to exclude acute coronary syndrome, acute pulmonary embolism, myocarditis, metastases to the myocardium, myocardial oedema, and the direct cytotoxic effect of oncological treatment.
- The clinical picture of the oncological patient can often be misleading, which requires increased vigilance, knowledge, and cooperation of the cardiologist with oncologists.

ORCID

Mateusz A. Iwański – ID – <https://orcid.org/0009-0002-6192-156X>

Katarzyna Styczkiewicz – ID – <https://orcid.org/0000-0003-4036-8320>

Michał Górecki – ID – <https://orcid.org/0000-0002-8694-6766>

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Authors' contributions:

Conceptualization, K.S., A.K., M.G. and M.A.I.; methodology, K.S., A.K., M.G. and M.A.I.; software, K.S., and A.K.; validation, K.S., A.K., M.G. and M.A.I.; formal analysis, K.S. and M.A.I.; investigation, K.S. and M.A.I.; resources, K.S., A.K., M.G. and M.A.I.; data curation, K.S. and M.A.I.; writing-original draft preparation, K.S. and M.A.I.; writing-review and editing, K.S. and M.A.I.; visualization, K.S. and M.A.I.; supervision, K.S.; project administration, K.S. and M.A.I. All authors have read and agreed to the published version of the manuscript.

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The authors had full access to the data and take full responsibility for its integrity. All authors have read and agreed with the content of the manuscript as written. The paper complies with the Helsinki Declaration, EU Directives and harmonized requirements for biomedical journals.