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An aberrant case of rapidly progressing lung adenocarcinoma in a Ukrainian refugee

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A 65-year-old Ukrainian female refugee with a low-differentiated adenocarcinoma of the right (R) lung (diagnosed 1.5 years earlier) reported to the Emergency Department with shortness of breath, fever, and a wet cough. A thoracotomy was performed during a previous hospitalization in Ukraine. Microscopic examination, performed at that time, confirmed low- differentiated G3 lung adenocarcinoma, and immunogenetic tests detected the ALK+ tyrosine kinase gene rearrangements. The patient had received several courses of treatment with ALK inhibitors — crizotinib and alectinib. Due to cancer progression, therapy with another ALK blocker, brigatinib (17185), had been initiated in the third line. On admission to the Department of Pulmonology and Oncology, physical examination showed tachycardia, tachypnoea and a decrease in the alveolar murmur over the R lung and the upper parts of the left lung. Laboratory tests results initially revealed significantly elevated markers of inflammation (leukocytosis with the left shift: leukocytes — 60.750 cells/µl, neutrophils — 58.660 cells/µl), elevated C-reactive protein (218 mg/l, ULN = 5 mg/l) and procalcitonin (4.72 ng/ml, ULN <5 ng/ml). A chest computed tomography angiography showed the practically complete airlessness of the right lung (Figure 1A), the present pathological nodular lesion in the R lung (adjacent to the bifurcation of the pulmonary trunk, surrounding the branches of the R pulmonary artery, infiltrating the R upper lobe artery, segmental arteries to the 3R segment and peripheral branches of the subsegmental arteries to the R middle lobe) obstructing the bronchi of the R

lung (Figure 1B). Impression of the nodular mass on the superior vena cava and the R atrium was visible. A pathological soft-tissue mass visualized in the lumen of the left atrium (LA) of approximately 63 × 32 mm (right-left × anterior-posterior), protruding through the mitral valve into the left ventricle (Figure 1B), compressing the left ventricular outflow tract (LVOT) and the aortic valve. Massive mediastinal, cervical and supraclavicular lymphadenopathy and pathological effusion in both pleural cavities and in the pericardium were found. Right-sided pneumonia was diagnosed, secondary to the underlying disease, and broad-spectrum intravenous empirical antibiotic therapy (amoxicillin+clavulanate, ciprofloxacin) improved the patient's condition.

Transthoracic echocardiography revealed a tumor filling almost the entire LA (Figure 1C–E), originating from the R superior pulmonary vein. 4-chamber view (color Doppler) showed stenotic mitral flow (Figure 1F). The disease was identified as T4N3M1 stage IV. The patient was disqualified from cardiac surgery by Heart Team due to a very advanced stage of cancer. Brigatinib treatment was continued. She was discharged for further outpatient care and died a month later.

Lung adenocarcinoma with *ALK* gene rearrangement is a specific molecular subtype of lung adenocarcinoma [1], characterized by a high ability to give distant metastases, including that to heart cavities. Mechanisms by which LA involvement occurs may be direct invasion of the primary tumor, involvement of lymph nodes, or the least common- pulmonary venous transfer of the original lesion [2]. The condition requires surgery, which, however, may involve the risk of neoplastic dissemination, hemorrhage and a higher probability of infection [3, 4]. The decision on the best therapeutic approach should be made by a multidisciplinary team, regarding especially life expectancy. Lung cancer resection can be performed simultaneously with cardiac surgery, but in advanced cases, heart surgery takes precedence over the lung one [5]. If cardiac surgery is not possible, conservative preparatory treatment with highly selective ALK inhibitors such as alectinib, crizotinib and brigatinib is recommended.

Article information

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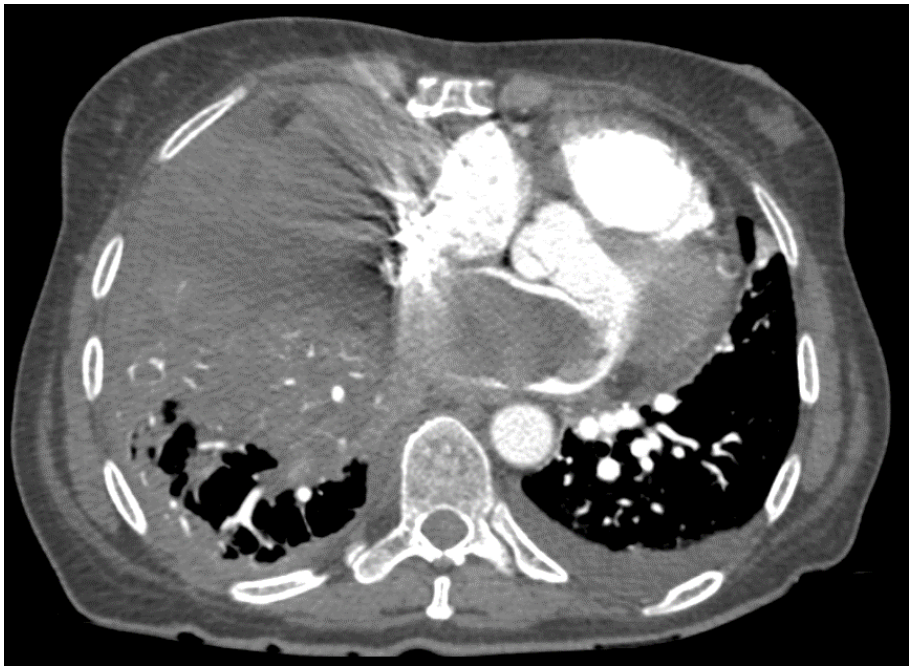

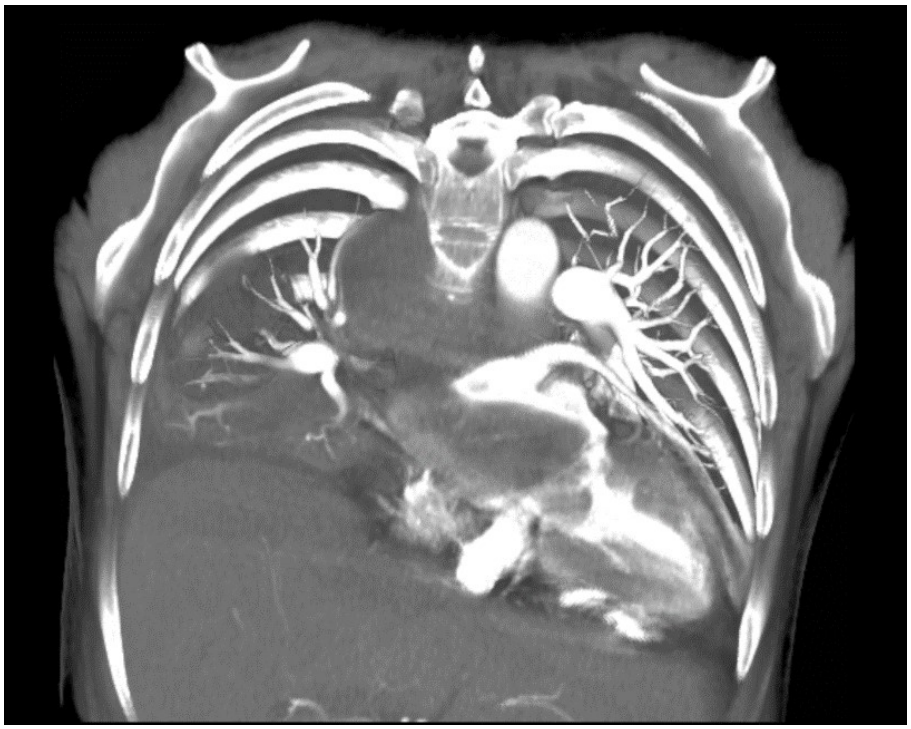

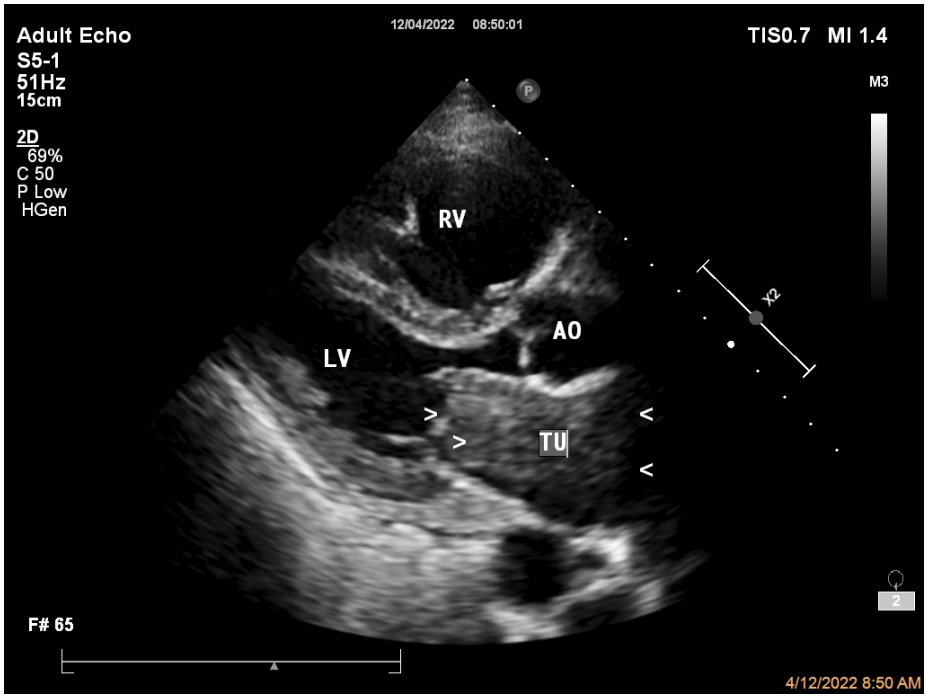
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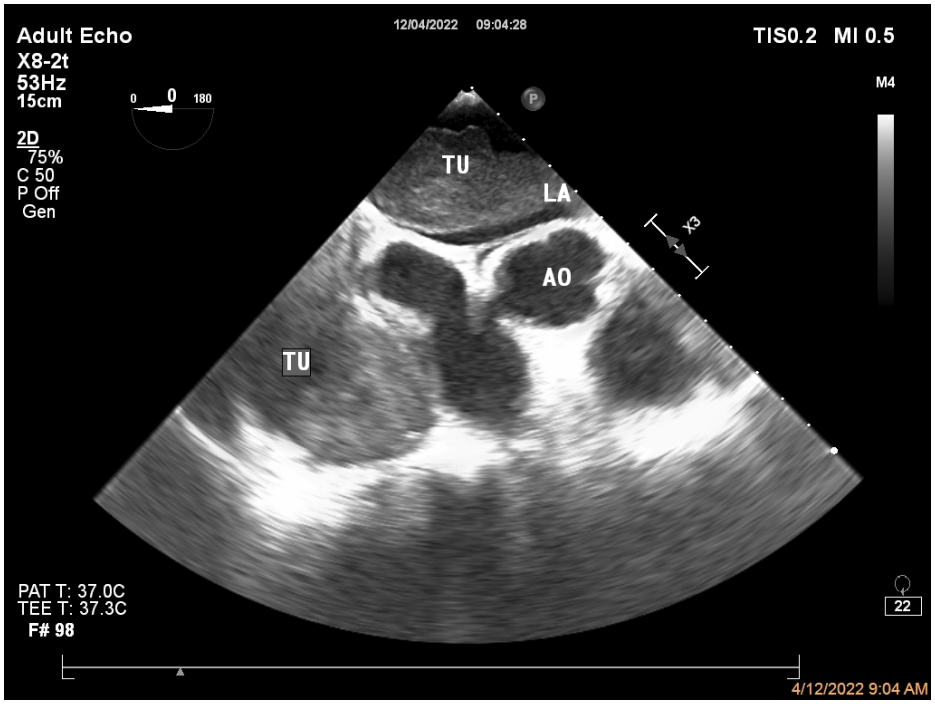
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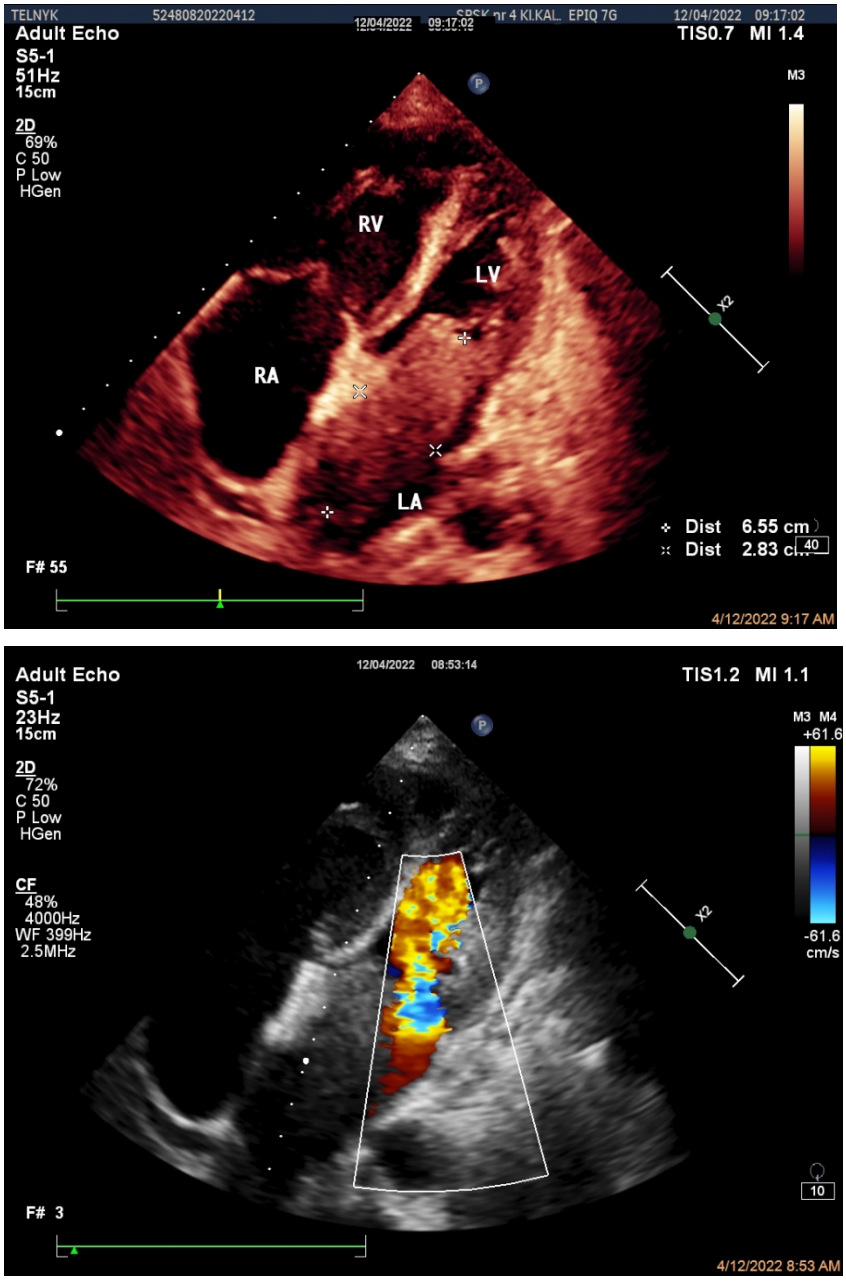

Figure 1. A. Axial projection of computed tomography (CT) in the arterial phase. Extensive mass located in the right lung filling almost the entire left atrial cavity. A small amount of fluid in both pleural cavities. **B.** CT, 3D volume rendering presenting nodule masses in the mediastinum and right lung, poor vascularization of the right lung, and a nodule mass passing from the LA to the LV. **C.** TTE, Parasternal Long Axis View, tumor mass visible in LA (arrows). **D**. TEE, Aortic Valve level , tumor visible in right lung and LA **E**. TTE, Apical 4 Chamber (A4C) View, pathological soft-tissue mass visualized in the LA (6.5 cm × 2.8 cm) , protruding through the mitral valve into the LV. **F**. TTE, Apical 4 Chamber View, colour Doppler, stenotic mitral flow due to mass protruding into the LV

Abbreviations: LA, left atrium; LV, left ventricle; LVOT, left ventricular outflow tract; RA, right atrium; RV, right ventricle; TTE, transthoracic echocardiography; TEE, transesophageal echocardiography; TU, tumor