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Pulmonary artery stenosis due to embryonal carcinoma with primary mediastinal location

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Abstract

A 29-year old man was admitted to the intensive care unit after losing consciousness. On physical examination, a loud systolic murmur over the heart was found. Echocardiography revealed narrowing of pulmonary artery with high pressure gradient. Computed tomography of the chest revealed the presence of large tumour localised in the upper anterior mediastinum. Due to the risk of total closure of the pulmonary artery, interventional mediastinotomy was performed and diagnosis of carcinoma embryonale was established. Subsequent chemotherapy (BEP regimen) has brought regression of tumour and significant improvement in haemodynamic parameters (relief of pressure gradient in pulmonary artery). During the second surgery, the resection of all accessible tumour mass together with marginal resection of the right upper lobe was performed. No signs of cardiac or great vessels infiltration was found. Histopathologic examination revealed the necrotic masses and neoplastic foci diagnosed as teratoma immaturum. In a four-month follow-up the patient's condition remained good. The patient is still under the care of both oncological and cardiological specialists. Thus far he has not required further chemotherapy. Holter ECG monitoring revealed no arrhythmia, but the patient is still treated with mexiletine. The patient is planning to return to work.

Key words: pulmonary artery stenosis, embryonal carcinoma, mixed germ cell tumour, primary mediastinal location, mexiletine

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Streszczenie

Mężczyzna (29-letni) został przyjęty na oddział intensywnej terapii pneumonologiczno-kardiologicznej po utracie przytomności. W badaniu przedmiotowym stwierdzono głośny szmer skurczowy nad sercem, a w badaniu echokardiograficznym zwężenie pnia tętnicy płucnej do 6–7 mm, z istotnym gradientem ciśnień oraz cechy podwyższonego ciśnienia w prawej komorze. W tomografii komputerowej klatki piersiowej uwidoczniono masę guzowatą zlokalizowaną w przednim, górnym śródpiersiu. Z powodu ryzyka całkowitego zamknięcia pnia płucnego przeprowadzono interwencyjną mediastinotomię i uzyskano rozpoznanie nowotworu zarodkowego o rzadkiej — śródpiersiowej lokalizacji. Chemioterapia według schematu BEP, doprowadziła do regresji guza, i znacznej poprawy hemodynamicznej (ustąpienie cech ucisku guza na pień płucny). Podczas torakotomii resekowano pozostałe masy guza. Nie stwierdzono naciekania serca i dużych naczyń przez nowotwór. W badaniu histopatologicznym stwierdzono obszary martwicy i naciek nowotworowy o utkaniu niedojrzałego potworniaka. Podczas czteromiesięcznej obserwacji stan chorego pozostawał dobry. Pacjent nadal jest objęty opieką onkologiczną i kardiologiczną. Jak dotychczas nie wymagał kolejnego leczenia cytostatycznego. W kontrolnych zapisach holterowskich EKG nie obserwowano zaburzeń rytmu, ale chory nadal otrzymuje meksyletynę jako leczenie antyarytmiczne. Pacjent planuje powrót do pracy.

Słowa kluczowe: nowotworowe zwężenie pnia płucnego, nowotwór zarodkowy, mieszana postać guza z komórek rozrodczych, pierwotna lokalizacja śródpiersiowa, meksyletyna

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Introduction

Germ cell tumours with mediastinal location constitute barely 1–6% of all mediastinal tumours [1]. They are diagnosed mainly in young people, more frequently in men [1]. The disease generally manifests itself in dyspnoea, chest pain and cough. The current paper presents a patient in whom one of the first symptoms was a life-threatening cardiac complication. The origins of the symptoms were established owing to echocardiography.

Case report

A 29-year old male (R.G.) was admitted to the Cardiopulmonary Intensive Care Unit of the National Tuberculosis and Lung Diseases Research Institute due to a sudden loss of consciousness during physical effort (defecation).

Two months prior to hospitalisation, the patient suffered from nocturnal sweat and strength reduction, but the ailments were not intensive and he has not paid attention to them. After a month, the ailments became slightly more intensive, dry cough and swollen submandibular glands appeared. The patient ignored these symptoms as well. But when after the two following weeks fever and little dyspnoea occurred, the patient consulted his family doctor, who suspecting pulmonary infection, ordered him to perform chest X-ray examination. Yet for the symptoms persisted, while waiting for the results of X-ray examination, the patient was referred to the local Hospital Emergency Ward, where (the patient's chest X-ray result still remaining unknown) diagnosis of infection of the airways was sustained, antibiotic was introduced and the patient was dismissed from the hospital. After a few days, the patient received X-ray image, which showed mediastinal widening. After consulting the family doctor, he was referred to the National Tuberculosis and Lung Diseases Research Institute for further diagnosis.

On admission to the Institute, his general condition was good. Physical examination did not show heart or pulmonary failure. During the first day of hospitalisation, thoracic CT angiography was performed, which did not reveal thrombi in the pulmonary bed. In the upper anterior mediastinum, a large tumour mass measuring 10 × 14 × 7cm was found (Fig. 1). In the evening, during effort (defecation), the patient suddenly lost consciousness, and being in a poor general condition, he was urgently transferred from the preventive ward to the Cardiopulmonary Intensive Care Unit — („R" ward).

Physical examination showed a loud systolic murmur, heard particularly along the left sternal border. The murmur was more intensive during inspiration. Systemic blood pressure was correct. Laboratory investigations revealed increased activity of LDH at the level of 938 U/l (reference values: 313–618 U/l) and elevated concentration of the following: CRP — 65.9 mg/l (reference values < 10 mg/l), D-dimers — 10650 ug/l (reference values: 68–494 ug/l) and brain natriuretic peptide (NT- proBNP) — 869.2 pg/ml (reference values < 125 pg/ml). Echocardiography showed the pulmonary artery, which was considerably pressed (up to 6–7 mm) by a big tumour. At the place of the biggest narrowing, Doppler echocardiography revealed high pressure gradient (Fig. 2). Furthermore, tricuspid valve incompetence with maximal tricuspid valve peak gradient (TVPG) amounting to about 51 mm Hg (Fig. 3) was observed. The inferior vena cava was dilated and motionless while breathing. No disorders of contractility of the left ventricle muscle, whose ejection fraction was estimated at 63%, were found. Moreover, in the mediastinum, a tumour mass was found that pressed against the wall of the right ventricle (in outflow tract) (Fig. 4). The anatomy of the right ventricle was disturbed, transverse dimension in the parasternal long axis view was 29 mm (reference value up to 27 mm).

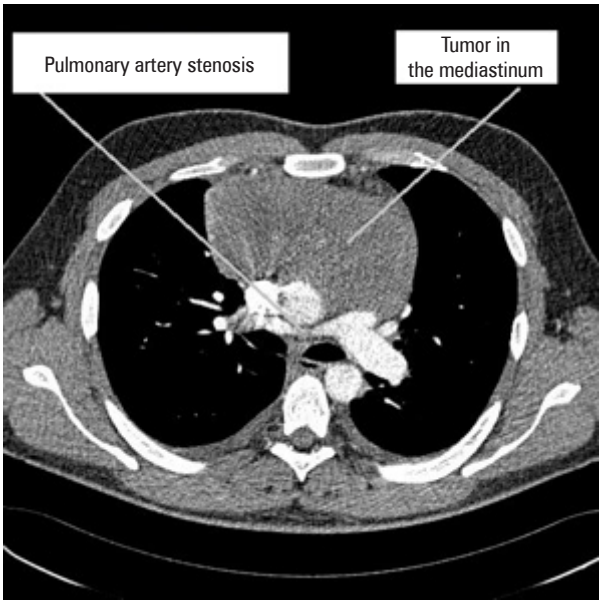

Figure 1. Computed tomography: pulmonary artery stenosis due to tumor in the mediastinum

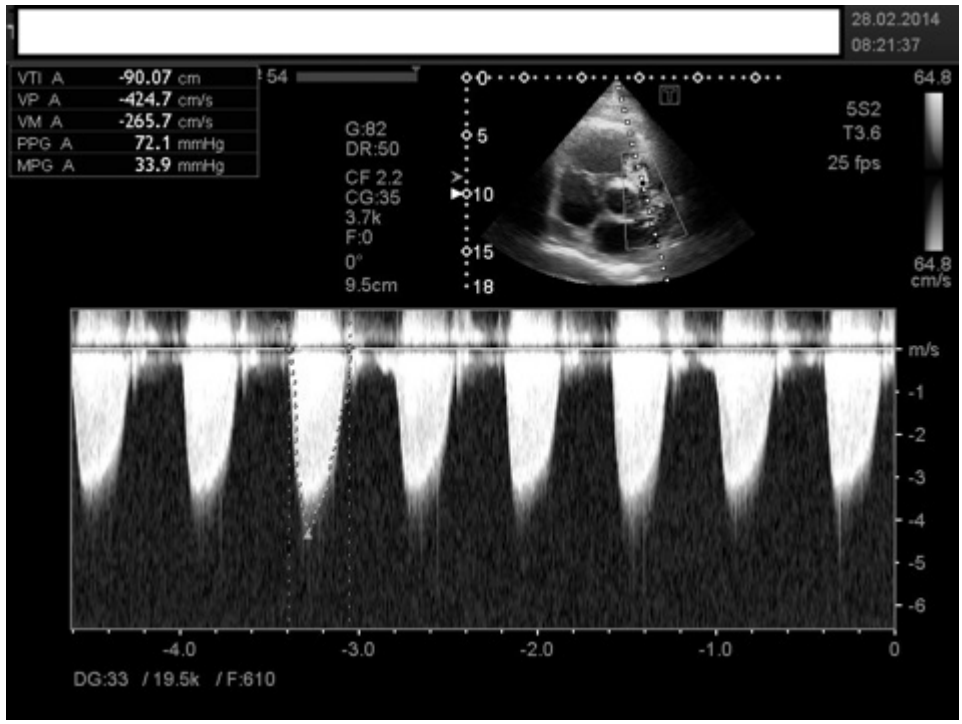

Figure 2. Echocardiography: a pressure gradient in the narrowing of pulmonary artery

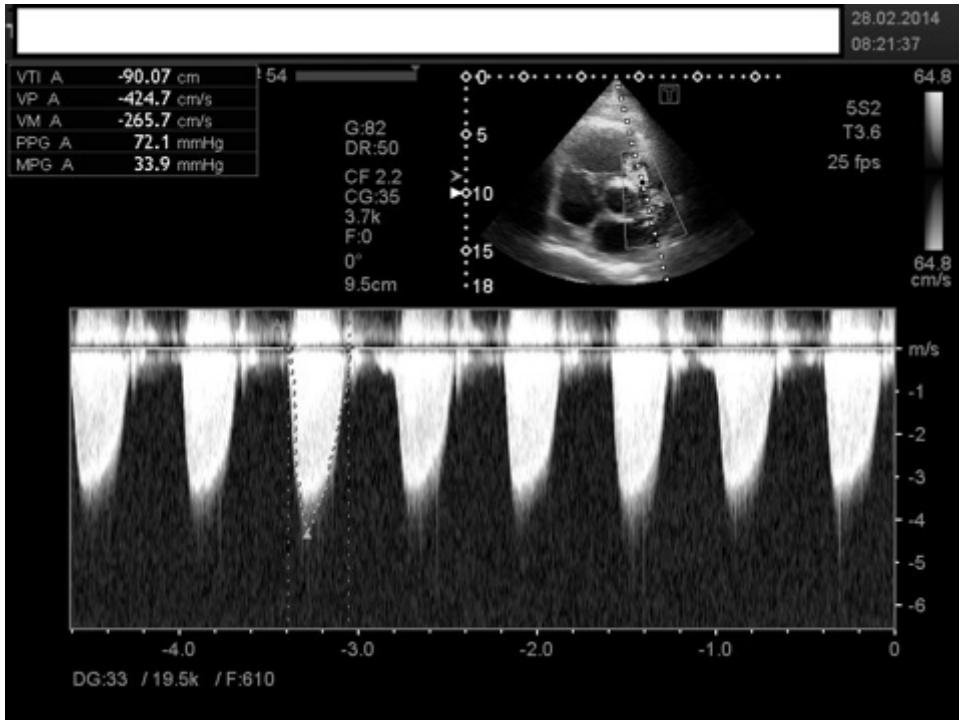

Figure 3. Echocardiography: tricuspid regurgitation

As echocardiography confirmed considerable narrowing of the pulmonary artery due to mediastinal tumour and a high risk of another loss of consciousness, a decision about urgent operation was made. On the second day of hospitalisation, an interventional right parasternal mediastinotomy was performed, revealing a large tumour, from which numerous specimens were collected. On histopathological examination, diagnosis of germ cell tumour („non-seminoma") — em-

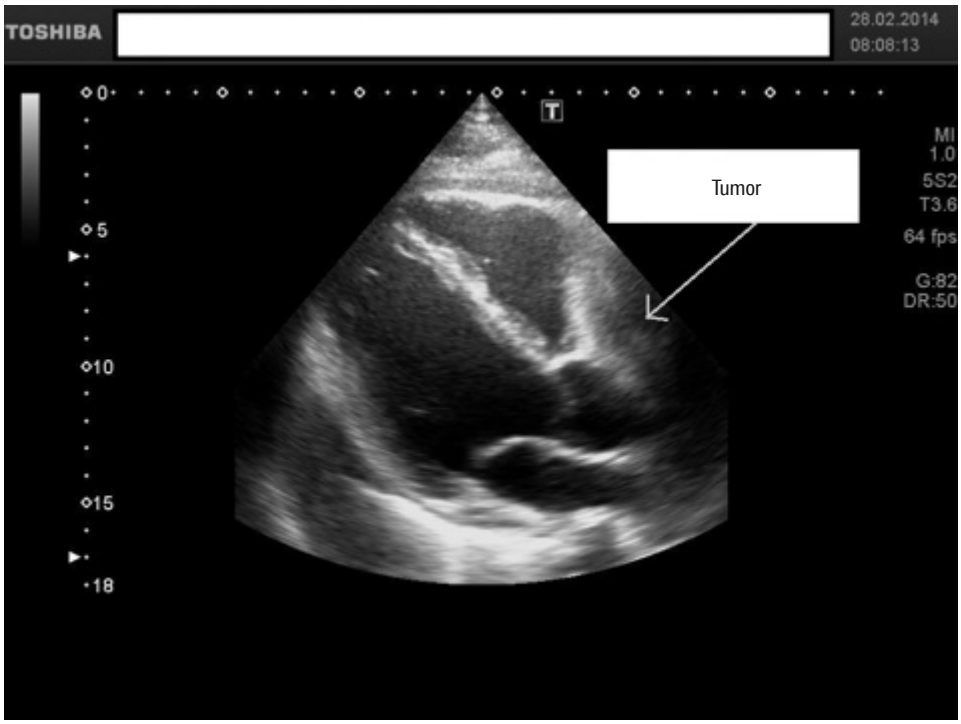

Figure 4. Echocardiography: tumor pressure on the free wall of the right ventricle

bryonal carcinoma with the features of primary medistinal location was established. Levels of tumour markers typical of embryonal carcinoma were determined as follows: AFP — 412 ng/ml (reference values: 0.0–8.0 ng/ml) and beta-hCG — 87.0 mIU/ml (reference values < 2.6 mIU/ml). No anomalies were found on ultrasonography of the testes or epididymides.

The patient was transferred to the Department of Neoplasms of Urinary System of the Maria Skłodowska-Curie Memorial Cancer Center and Institute of Oncology in Warsaw, where further increase of AFP marker up to 4000 IU/ml was observed, whereupon he was qualified for standard BEP (bleomycin, etoposide, cisplatin). During the whole therapy, primary antithrombotic prophylaxis with enoxaparine at a dose of 40 mg/day s.c. was applied. The first chemotherapy cycle was complicated by circulatory arrest in the course of ventricular tachycardia. The patient was resuscitated but owing to persisting complicated arrhythmia, he remained at the Intensive Care Unit of the Oncology Centre. Standard antiarrhythmic drugs (including amiodarone) proved ineffective, therefore the patient finally had to receive intravenous lidocaine and mexiletine. During therapy with mexiletine, no relapses of fixed ventricular tachycardia were observed.

After the IV cycle of chemotherapy, CT was performed, which showed little regression of the tumour. Echocardiography did not show pressure of the tumour against the pulmonary artery or tricuspid valve pressure gradient. AFP concentration was also gradually decreasing up to 21 ng/ml, and over the following few weeks it reached normal level (4.6 ng/ml).

As chemotherapy produced a satisfactory clinical effect, a decision about removal of the tumour was taken. Pre-operative chest magnetic resonance showed an image typical of advanced embryonal carcinoma: a tumour of 10 cm in diameter with predominance of solid elements over liquid areas. It was presumed that there was pericardium infiltration at the level of the right atrium, auricle and a free wall of the right atrium. Moreover, infiltration to a free wall of the right ventricle and the pulmonary artery at the length of 15 mm was suspected. It was presumed that the tumour firmly adhered to the great vessels: to the left brachiocephalic vein, modelling its lumen, and to the ascending aorta and aortic arch, with no evident features of infiltration. After consulting a cardiothoracic surgeon, indications for operative treatment were established. The procedure was carried out at the cardiosurgical centre, however, after thoracotomy, the thoracic surgeon who was performing the operation, did not find any infiltration in the pulmonary artery or the right ventricle. The tumour was surrendered by connective tissue and only pressed from the

outside against the said structures. Resection of the tumour and of marginal part of the upper right lung lobe was performed. Histopathological examination showed necrotic masses, including neoplastic infiltration — teratoma immaturum.

During a four-month follow-up the patient's condition has remained good. He is still receiving oncological and cardiological care. Thus far he has not required another chemotherapy. Holter ECG monitoring revealed no arrhythmia, but the patient is still treated with mexiletine. The patient is planning to return to work.

Discussion

Germinal cell tumours (GCT) are divided into two groups: seminomas and non-seminomas. Among non-seminomas, the following types are distinguished: carcinoma embryonale, teratoma maturum, teratoma immaturum, yolk sac tumour, chorioncarcinoma and mixed germ cell tumours (MGCT). In the described case, carcinoma embryonale was diagnosed first, and in the subsequent biopsy — teratoma immaturum. It may be supposed that from the very beginning the tumour was heterogenous, or it underwent change due to chemotherapy. Thus initial diagnosis of carcinoma embryonale was sustained.

Similarly as it was in the described case, GCT are usually diagnosed in men in the third decade of life. They are generally located in the gonad [1]. They rarely occur in the mediastinum (2–5% of cases) [1]. Other more rare extragonadal locations include: peritoneal space, lung, liver and hypophysis. Extragonadal location of non-seminoma is pertained to very poor prognosis [1].

Tumours located in the mediastinum are mostly symptomatic: patients suffer from dyspnoea, cough, chest pain [2]. In the described case, after initial period with few symptoms, the patient lost consciousness during defecation. Physical examination discovered a loud systolic murmur along the left sternal border, which was more intensive during inspiration. A loud systolic murmur diagnosed during physical examination in the chest near the left sternal border is frequently caused by valvular anomalies, however, it is difficult to clearly determine the place of stenosis without echocardiography [3]. The narrowing of the pulmonary artery alone seldom is the cause of systolic murmur or elevated pressure in the right ventricle [4–6]. It is impossible to arrive at diagnosis basing only on physical examination. In the described case, echocardiography revealed a tight narrowing of the pulmonary artery, which was not visible at CT angiography. Therefore, the necessity of easily accessible portable ultrasonography, including heart imaging, is being raised in the literature, as the examination performed even using a simple, mobile apparatus frequently allows to make initial diagnosis [7, 8]. In the described case, echocardiography allowed to diagnose elevated pressure in the right ventricle and in the part of the pulmonary artery before the narrowing. Concluding elevated pressure in the right ventricle and tricuspid valve incompetence through a narrowed pulmonary artery, due to germ cell tumour, is a matter of casuistics [9–11].

In patients in whom remission was achieved, the main treatment of non-seminomas located in the mediastinum is combined therapy: chemotherapy with following tumour resection [12]. The first-line treatment include bleomycin, etopisode and cisplatin (BEP) [1]. The first cycle of BEP regimen in the described patient was complicated by a sudden circulatory arrest in the course of ventricular trachycardia. Arrhythmia was possibly caused by a massive pressure from the outside on the right atrium and ventricle — as histopathological examination did not show their infiltration. After resuscitation and effective treatment of ventricular arrhythmia, and taking into account a young age of the patient and lack of another effective treatment, a decision was made about continuation of chemotherapy. Further treatment was complicated by pulmonary embolism, despite the use of primary anticoagulant prophylaxis with low molecular weight heparin, which was applied in accordance with the guidelines. Moreover, neutropenia with severe infectious complications occurred. Finally, the patient received 4 cycles of chemotherapy, achieving partial remission of lesions and normalisation of the concentrations of tumour markers AFP and beta hCG. Echocardiography showed regression of flow disturbance through the pulmonary artery and normalisation of pressure in the right ventricle.

However, pre-operative assessment that used magnetic resonance was still showing the possibility of affected circulatory system, thus the operation was conducted by the team of thoracic and cardiac surgeons. Finally, the tumour together with the fragment of the upper right lung lobe was removed. Histological examination did not show cardiac or vascular infiltration, and concerning the lung, infiltration did not exceed the pleura.

Irrespective of the initial achievement of the therapy, prognosis in the described case is uncertain. 5-year survivals in the group of non-seminomas with medistinal location affect

barely 45% of patients [1]. Remote metastases, particularly those to the central nervous system, are negative prognostic factors, as well as elevated initial concentration of beta hCG, as it occurred in the described case.

To conclude, it should be emphasised that sudden symptoms in the circulatory system in a young person without history, may be related to tumours with mediastinal location such as lymphoma, thymoma and sparsely — germ cell tumour [6]. In such cases echocardiography is the method of choice that allows to determine the cause of the ailment, particularly to reveal infiltration (stenosis) to the heart structures and/or to diagnose a menacing cardiac tamponade.

Conflict of interest

The authors declare no conflict of interest.

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