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Primary mediastinal large B-cell lymphoma and pregnancy: a challenging clinical scenario

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Abstract

A 26-weeks pregnant woman presented with progressively worsening dyspnoea and poor general conditions. Using low-dose radiation multi-imaging techniques and thoracic biopsy a primary mediastinal large B cell was diagnosed. A multidisciplinary approach identified the correct hemodynamic management, the best therapeutic strategy and the timing for delivery.

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Case Report

A 33-year-old nulliparous woman, at 26 weeks of gestation, presented to our emergency room complaining of dyspnoea, cough and weight loss that were progressively worsening in the previous two weeks. Upon arrival she was tachypnoeic and the physical examination was remarkable for pale skin and bilateral jugular distention.

The electrocardiogram showed sinus tachycardia at 111 bpm, normal atrio-ventricular and intraventricular conduction and diffuse negative T-waves.

Laboratory tests showed normal total white cells count, mild thrombocytosis and low haemoglobin level. Lactic dehydrogenase was markedly elevated at 1126 units/l (133-225). No alteration in renal and hepatic function was evident. Evaluation of the peripheral blood smear was performed and there was no evidence of immature cells.

Transthoracic echocardiography (TTE) (Figure 1, Videos 1 to 3) revealed a voluminous mass causing compression of the roof and anterior wall of the right atrium. The mass was infiltrating the inferior vena cava, the outflow tract of the right ventricle up to the trunk of the pulmonary artery and part of the ascending aorta. The left ventricle had normal dimensions and systolic function with no alterations in regional wall motion. The right ventricle showed normal contractility of the free wall; however, hypokinesia and reduced dimensions of the outflow tract were evident. Flow acceleration with an average gradient of 6 mmHg was documented at the level of right lower pulmonary vein, depicting a moderate stenosis. Mild circumferential pericardial effusion was present and the visceral pericardium at the level of the free wall of the right ventricle appeared thickened and with an irregular profile.

Contrast-enhanced thoracic computed tomography (CT) confirmed the presence of the huge mediastinal solid mass with dimensions of 13x16x18cm (Figure 2). Compression and consequent atelectasis of the middle and upper right pulmonary lobes was evident and infiltration of the superior and inferior vena cava, pulmonary artery, pulmonary vein and pericardium was present. The mass extended toward the aortic arch and supra-aortic trunks; signs of outflow obstruction were not yet visible. Contrast enhancement of the mass was inhomogeneous, consistent with the presence of a central necrotic area. Lastly, the CT showed mediastinal lymphadenopathy with multiple lymph nodes enlargement.

Thoraco-abdominal magnetic resonance confirmed the presence of the mass in the right hemithorax, indissociable from the pericardium and the compression and infiltration of adjacent structures.

Gynaecological evaluation and prenatal ultrasound were performed and demonstrated regular foetal heartbeat and normal movements.

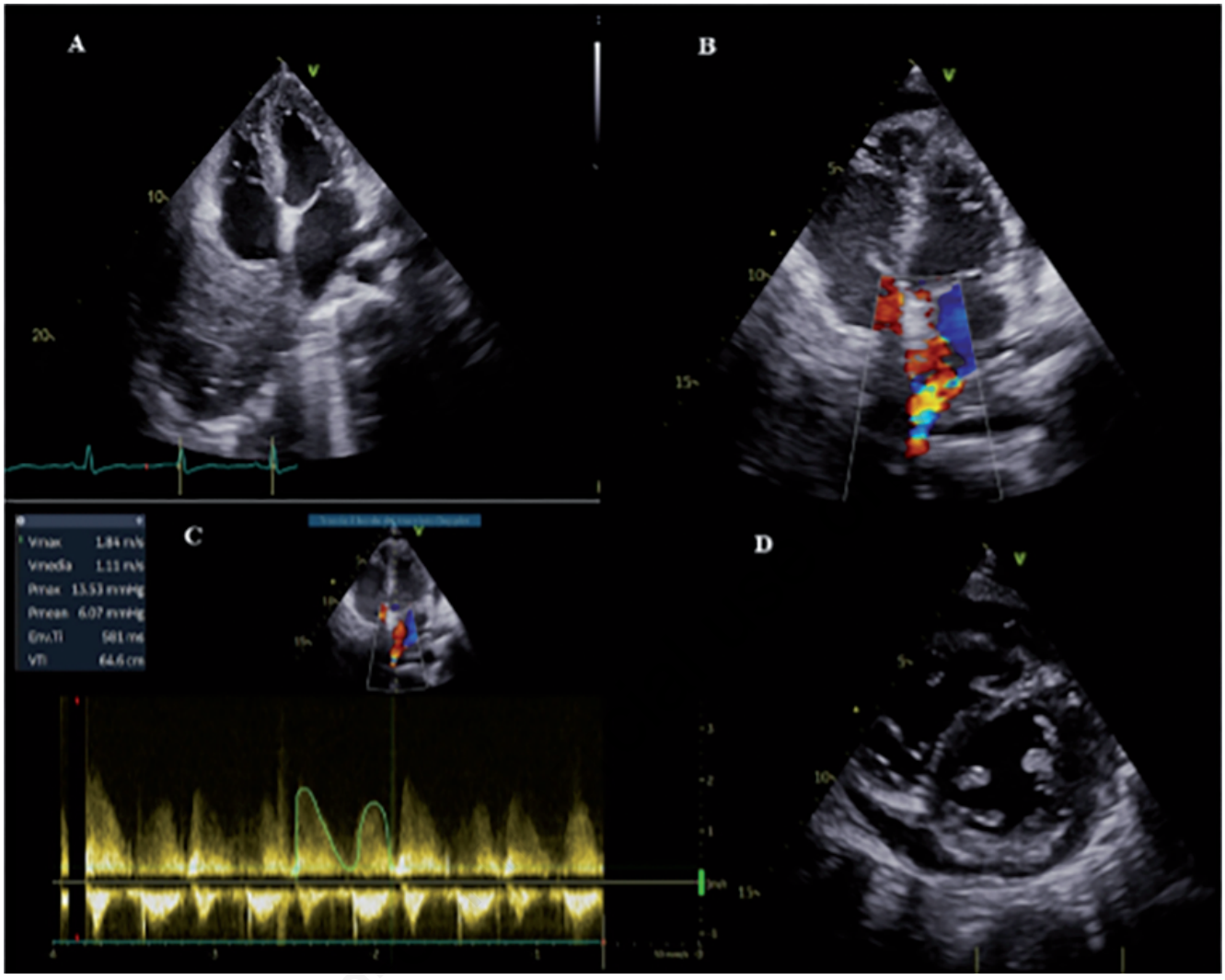

Figure 1. Echocardiography. A) Apical 4-chamber view with a pathological tissue surrounding right atrium. B,C) Accelerated Doppler inflow of right upper pulmonary vein. D) Pericardial effusion and inhomogeneity of visceral layer.

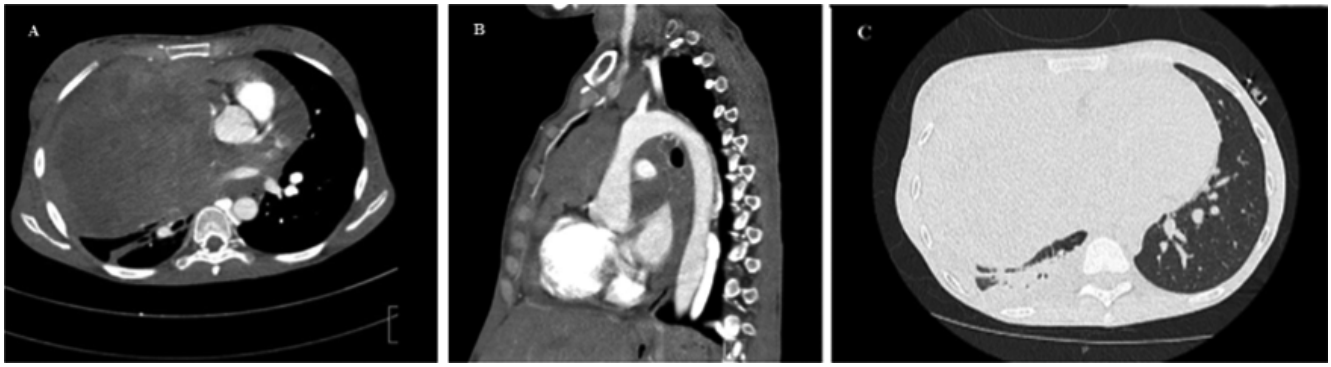

Figure 2. CT scan. A,B) Voluminous mass enveloped the right posterolateral area of the heart, the superior vena cava, some branches of pulmonary artery and veins, supra-aortic trunks and aorta. C) Complete atelectasis of middle and upper right lung lobes.

A thoracic biopsy under ultrasound guidance was urgently performed and the histological examination allowed the diagnosis of primary large B-cell lymphoma of the mediastinum (PMBCL).

The clinical scenario was suggestive of a mediastinal syndrome with compression of the right bronchus and right heart and with pericardial involvement.

The patient was admitted to the Haematology Department and chemotherapy was immediately started with cyclophosphamide-hydroxydaunorubicin-oncovin-prednisone (CHOP) regimen. On the second day of chemotherapy, we observed a sudden worsening of the clinical conditions with severe respiratory distress and signs of low cardiac output and peripheral hypoperfusion. The patient presented with hypotension, elevated heart rate, increased arterial blood lactate level, low central venous oxygen saturation (45%) and elevated N-terminal prohormone; therefore, she was admitted to Intensive Care Unit (ICU). Inotropic support was started with rapid hemodynamic stabilisation and lactate clearance. Considering the compression of the right heart, a strict follow-up with TTE was performed in order to maintain an adequate volemia.

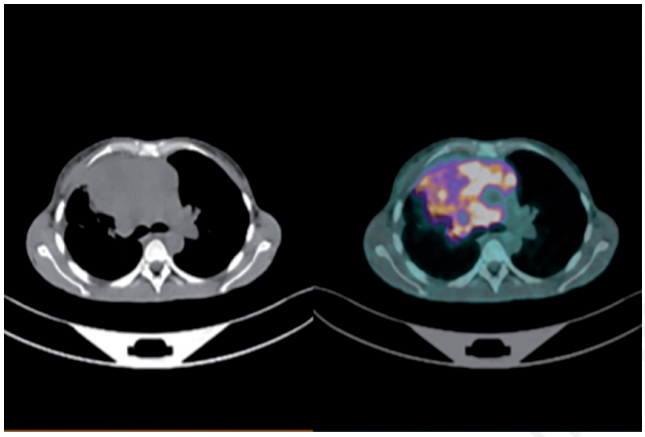

Figure 3. CT-PET: high metabolic activity in mediastinum.

Despite the massive pulmonary compression, ventilatory support was never required during the ICU stay.

At the CT scan performed after 15 days of therapy, no significant reduction in the mediastinal mass was observed. Considering the lack of response to antineoplastic therapy, the gestational age (29 weeks at that time) and the estimated weight of the foetus of 1.4 kg, a delivery with a caesarean section was performed.

TTE performed after delivery showed no differences in morphological and hemodynamic data. CT-positron emission tomography (PET) (Figure 3) was performed for staging and revealed a high metabolic activity in the mass and in mediastinal, iliac and inguinal lymph nodes.

Cardiac magnetic resonance (Figure 4 and Videos 4 and 5) confirmed the presence of the mass and the compression of the atria. A focal myocardial area of hyperintense signal at short inversion time recovery (STIR) sequence was evident in the anterior wall of the left ventricle, compatible with presence of oedema; late gadolinium enhancement (LGE) was present in the same area with a non-ischemic pattern. Diffuse pericardial thickening was visible with mild hyperintensity at STIR images and marked LGE.

The patient underwent a second cycle of chemotherapy with etoposide, prednisone, vincristine, cyclophosphamide, doxorubicin, and rituximab (EPOCH-R regimen) and was then discharged.

At 1-month follow up the patient presented in quite good general conditions; nevertheless, TTE showed only a reduction in the pericardial effusion and no improvement in the extension of the mass. After 2 months, the CT scan showed a reduction in the dimension of the mediastinal mass which was 10x7.5 cm with an improvement of the atelectasis and of the pulmonary compression.

Discussion

The differential diagnosis in a pregnant patient presenting with progressively worsening dyspnoea may be challenging. We report an unusual case of aggressive malignant neoplasm in an immunocompetent woman during gestation. PMBCL is a subtype of diffuse large B-cell lymphoma (DLBCL) and it typically presents in

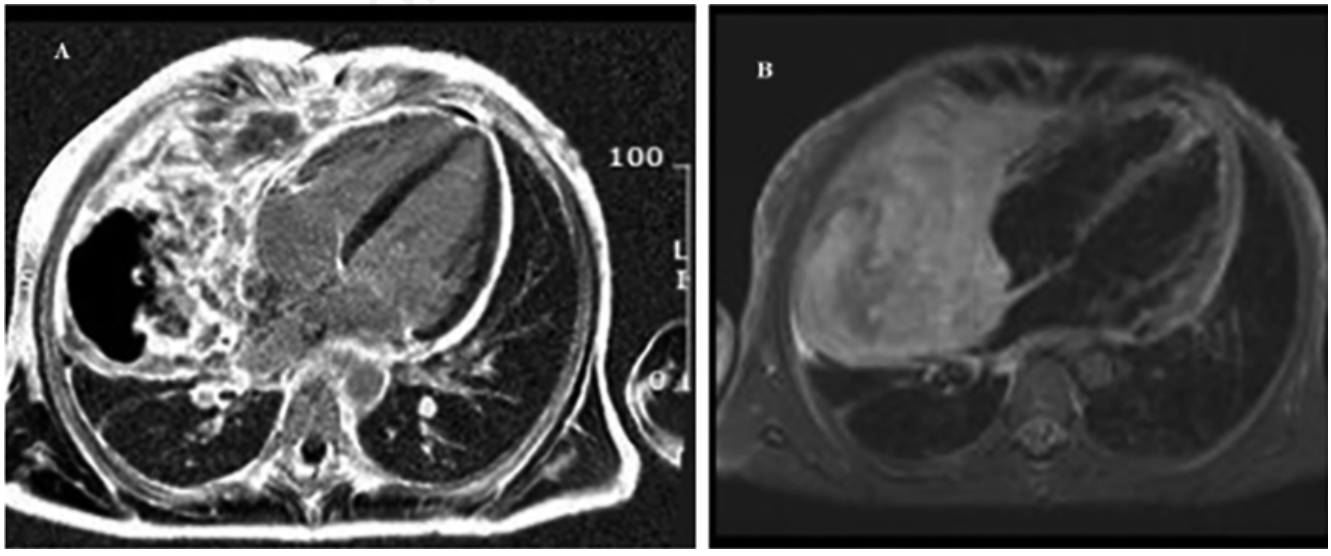

Figure 4. CMR: 4-chamber late gadolinium enhancement (A) and STIR images (B).

young women [1-3]. It accounts for 2-4% of non-Hodgkin lymphoma and for up to 10% of DLBCL. The incidence of hematopoietic malignancies complicating pregnancy is 0.02%. No clear guidelines exist on the management of these patients and the best therapeutic strategy is still a matter of debate. It is now known that from the second trimester of pregnancy, the side effects on foetal development related to CHOP chemotherapy are considerably low [4,5]. Contrarily, the negative effect of rituximab due to placental transmission are well-known. In our patient the gestational age at presentation and the severe clinical scenario did not allow an immediate delivery and a multidisciplinary evaluation was necessary to establish the best therapeutical management. A dose-adjusted chemotherapy cycle was started in order to avoid hemodynamic instability; the necrotic effect on the mass may have overlapped with cytokines and lactates' delivery caused by cardiogenic shock. Compared to the other few cases reported in literature [6,7] our patient showed a short period of hemodynamic instability which makes the decision even less straightforward.

TTE had a pivotal role both at first diagnosis and during the entire follow-up and it was fundamental to support the decision to perform second-line imaging evaluations that are often considered potentially harmful during gestation. Moreover, TTE was the modality of choice to monitor the patient during the ICU stay and the period of hemodynamic instability when other imaging techniques could not be used.

Conclusions

In our case, a careful evaluation and balance of both haematological and gynaecological aspects was essential. A multidisciplinary approach was needed to identify the best diagnostic and therapeutic strategy and the best timing for delivery. A close hemodynamic monitoring is mandatory when a mediastinal syndrome is present.

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