CASO CLÍNICO

Linfoma na Gravidez: Caso Clínico, Gestão Multidisciplinar e Abordagem Anestésica

Lymphoma in Pregnancy: Case Report, Multidisciplinary Management and Anesthetic Approach

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Afiliação

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Palavras-chave

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ABSTRACT

Lymphoma is the fourth most frequent cancer diagnosed during pregnancy, complicating about one in 6000 pregnancies. The anesthesiologist should gather patient's clinical information, from the different medical specialties, in order to arrange the best anesthetic approach.

We describe a case of a pregnant woman diagnosed with an anterior mediastinum lymphoma complicated with large volume pericardial effusion, superior vena cava syndrome, bronchial compression and pulmonary congestion, proposed to elective cesarean section. A subarachnoid block and a cesarean section in a semi-sitting position were successfully performed but continuous positive airway pressure was needed to tolerate the required surgical level of anesthesia during supine position, after blockage. The multidisciplinary management of this clinical situation was crucial. The anesthetic approach was based on the best anesthetic technique considering the pregnant woman's clinical condition, chemotherapy's possible side effects and fetal well-being.

RESUMO

O linfoma é o quarto tipo de neoplasia mais frequentemente diagnosticado durante a gravidez, complicando cerca de uma em 6000 gestações. O anestesiologista deve reunir a informação clínica do doente, relativa às diferentes especialidades médicas, de forma a definir a melhor abordagem anestésica. Descrevemos o caso de uma grávida diagnosticada com linfoma do mediastino anterior complicado com derrame pericárdico de grande volume, síndrome

da veia cava superior, compressão brônquica e congestão pulmonar, proposta para cesariana eletiva. Foi realizado com sucesso um bloqueio subaracnoideu e a cesariana em posição semi-sentada mas foi necessário pressão positiva contínua na via aérea aquando da posição supina para tolerar o nível necessário de bloqueio. A gestão multidisciplinar dessa situação clínica foi fundamental. A abordagem anestésica para este caso foi baseada na melhor técnica anestésica considerando a condição clínica da grávida, os possíveis efeitos colaterais da quimioterapia e o bem-estar do fetal.

INTRODUCTION

Lymphoma is the fourth most frequent cancer diagnosed during pregnancy, complicating about one in 6000 pregnancies.¹ Non-Hodgkin's lymphoma is less common in pregnant women, compared with Hodgkin's lymphoma. Its diagnosis in pregnancy may be associated with subtypes that are more aggressive and with a greater risk of disease spreading, such as diffuse large B-cell lymphoma (DLBCL) or peripheral T cell lymphoma. This is explained by the physiological changes during pregnancy, such as hyperdynamic circulation and increased blood flow, but also due to its later diagnosis, as the constitutional symptoms are frequently attributed to the pregnancy.^{1,2}

The clinical approach during pregnancy must be based on a multidisciplinary medical team in order to optimize maternal and fetal well-being.²

As it is a rare diagnosis, we consider this clinical report a benefit to the scientific community as it shows the multidisciplinary management, including the anesthetic approach. The anesthesiologist should gather all patient's

Autor Correspondente/Corresponding Author*: Mariana Pinto Morada: Largo do Prof. Abel Salazar, 4099-001 Porto, Portugal. E-mail: marianampinto91@gmail.com clinical information, from the different medical specialties, in order to arrange the best anesthetic technique, considering the pregnant woman's clinical condition, chemotherapy's possible side effects and the well-being of the fetus.

CASE REPORT

A 35-year-old healthy pregnant woman, at 23 weeks of gestation, arrived at the Emergency Department with a respiratory infection, progressive asthenia, facial edema and intolerance to supine position. After discussion of imagiological (computed tomography - CT scan - Fig. 1) and pathological (mediastinal mass biopsy) data, the final diagnosis of a primary DLBCL of anterior mediastinum (17x9x15 cm) was made. The patient was transferred to an intermediate care unit for management of the complications resulting from posterior deviation of mediastinal structures, which included a large volume pericardial effusion (without hemodynamic instability), superior vena cava (SVC) syndrome, pulmonary arteries compression, bronchial compression and pulmonary congestion with hypoxemic respiratory insufficiency. She initiated treatment with supplemental oxygen and non-invasive mechanical ventilation. The clinical multidisciplinary approach is represented in Fig. 2 and resumed below.



Figure 1. Thoracic CT (sagittal plan): the anterior mediastinum mass with 17x9x15 cm of dimension

Obstetrics: Assessment of maternal-fetal condition during hospitalization. There were no criteria for pregnancy interruption, unless there was a worsening of clinical maternal condition and there should be no appropriate treatment delays. An elective cesarean section at 30 weeks of gestation was planned, always depending on the pregnant's clinical stability and developmental state of the fetus by then. **Haematology:** Assessment of tumor stratification revealed



Figure 2. Medical specialties involved in this patient's multidisciplinary management

an enormous curative potential, which resulted in a decision for a chemotherapy regimen with fetal protection (vincristine and prednisolone), to reduce the mediastinal mass and SVC syndrome, until delivery date. The patient was also submitted to therapeutic hypocoagulation with unfractionated heparin until 4 hours before cesarean.

Cardiology: Assessment of the large volume pericardial effusion followed by pericardiocentesis, placement of a pericardial drain and clinical and echocardiographic reevaluations.

Pneumology: Assessment of the bronchial compression by the mediastinal mass alerted for the eventual need for an endobronchial prosthesis placement.

Vascular surgery: Assessment of SVC syndrome and the possibility of placement of an endovascular prosthesis.

Psychiatry: Assessment of the patient's mental state during hospitalization by frequent psychiatric re-evaluations.

Anesthesiology and multidisciplinary discussion at 30 weeks:

The patient presented a favorable imagiological progression (substantial reduction in the mediastinal mass and significant reduction of the compressive effect on the great vessels of the mediastinum, namely SVC syndrome, already without intraluminal thrombosis). It was observed clinical stability, with better tolerance to supine position, hemodynamic stability with blood pressure of 115/70 mmHg, heart rate of 70 beats per minute and peripheral saturation of oxygen (SpO₂) of 97% without oxygen. It was decided to perform an elective cesarean section, at 30 weeks of gestation, after four pulses of chemotherapy regimen (vincristine and prednisolone) and fetal lung maturation (dexamethasone during 48 hours). Preoperative study was as follows: hemoglobin 10.6 g/dL, platelets 328x10⁹/L, normal coagulation 4 hours after heparin

suspension, creatinine 0.42 mg/dL and normal hepatic function. After discussion with all medical specialties involved in the patient's management and considering all the risks and benefits of the anesthetic techniques available, the following technique was chosen: subarachnoid block with 0.5% hyperbaric bupivacaine (8 mg) plus morphine (100 mcg), at L3-L4 intervertebral space;

i) cesarean section in a semi-sitting position with supplementary oxygen by nasal cannula;

Monitoring with American Society of Anesthesiologists standards and invasive arterial pressure was made. Premedication with endovenous metoclopramide 10 mg and pantoprazole 40 mg was given. The subarachnoid block was successfully performed with a 27G Whitacre needle. To reach the required surgical dermatome level (T4), it was necessary to decrease the elevation of the headboard, which generated some respiratory discomfort and desaturation with minimum peripheral saturation oxygen of 91%, without hypotension. This was easily solved (SpO₂ 99%) with continuous positive airway pressure of 10 cmH₂O (CPAP) and FiO₂ 100% through a facemask. Hemodynamic stability was maintained throughout all the surgical procedure. Blood loss was the expected for a cesarean delivery and adequate intravenous crystalloid fluid was administered. The patient gave birth to a female newborn with a dysmorphic syndrome that was transferred to a neonatal intensive care unit.

At the post-anesthetic care unit, the puerperal woman remained hemodynamically stable, no respiratory distress was observed and there was no need of oxygen supplementation. The patient started thromboembolic prophylaxis with alternating compression stockings immediately and, 12 hours after cesarean delivery, according to Hematology indication and with bleeding losses in the normal values expected in a post-operative cesarean section, she restarted hypocoagulation with unfractionated heparin. After 14 hours, she was transferred to the Obstetrics ward.

Ten days after cesarean delivery, the patient started R-CHOP cycles and was discharged home on the same day. Three months later, after 4 cycles of R-CHOP chemotherapy, there was a good response to treatment with reduction in mediastinal mass greater than 50%.

DISCUSSION

In pregnancy, lymphoma may behave more aggressively due to the physiological changes and the drugs used in chemotherapy may have their pharmacokinetics and pharmacodynamics altered, especially in the second and third trimester.³ Anthracyclines and vinca alkaloids (e.g. vincristine) have the least fetotoxicity.⁴ Some scientific studies show that there is little effect on long-term fetal survival with chemotherapy, while others reveal harmful effects, especially in the central nervous and hematopoietic

systems, as well as intrauterine growth restriction.⁵ Maternal toxicity is mainly in the central nervous system (CNS), which can be expressed by CNS dysfunction, seizures, coma and/or peripheral neuropathy.⁶⁻⁷ In this case, clinical, analytical and echocardiographic evaluation did not show any significant maternal toxicity, only a mild anemia.

The selection of the anesthetic technique has to consider both patient condition and oncological disease. Controversial data about the relationship between the type of anesthesia and recurrence/progression of the cancer exist. Therefore, more studies are needed regarding this particular subject. One study showed that regional anesthesia seemed to reduce both perioperative immunosuppression and cancer's recurrence.8 All cases described in the literature agree with the preference for regional anesthesia rather than a general anesthesia, maintaining spontaneous ventilation and avoiding potentially airway collapse, because in a pregnant woman, there is increased risk of this complication due to the presence of the fetus and the normal respiratory physiological changes of pregnancy, (reduction of the functional residual capacity and total volume of the lung and relaxation of bronchial smooth muscle) which leads to greater compressibility of the airway from the mediastinal mass. Besides that, diaphragm relaxation reduces the normal transpleural pressure gradient and enhances the effect of extrinsic compression. 9,10 In some case reports, epidural anesthesia with small incremental doses of local anesthetics, until a sensory level of T4 was achieved, was the chosen technique. Authors advocate that a single shot subarachnoid block could result in a rapid and unpredictable hypotension (unwarranted risk in SVC syndrome) and level of block in semi-sitting position. An epidural catheter allows more gradual onset and easier treatment of sympathetic block, but titrated epidural block also carries a risk of hemodynamic instability¹¹⁻¹³ and has a higher failure rate than spinal anesthesia.14 The epidural catheter was subsequently removed due to the need for hypocoagulation in the postoperative period.¹¹ In other case reports, the anesthetic management included a combined spinal epidural anesthesia, using epidural catheter to complete the adequate level, not achieved with spinal block in semi-sitting position.^{14,15} The subarachnoid block was performed by other authors, based on the ability to manipulate the block using gravity and the denser block.9 Finally, although the treatment was successful on treating SVC syndrome and pericadium effusion, there was still a high risk of cardiovascular collapse during positive pressure ventilation.¹⁶

In this particular case, the discussion between all the medical specialties was crucial. The multidisciplinary approach is clearly presented and a quick and effective resolution of one of the complications associated with subarachnoid block is demonstrated (supine position tolerated with CPAP through a facemask). There were three main points taken into account

during these medical briefings:

- the possible side effects of vincristine during pregnancy (anemia; thrombocytopenia; leukopenia; immunosuppression; central nervous system, cardiac and renal toxicity);
- the potential respiratory complications during eventual general anesthesia, considering the bronchial mechanical compression of the mediastinal mass;
- necessary immediate hypocoagulation in the postoperative period due to the SVC thrombosis and the associated risks of neuroaxial technique.

CONCLUSION

This case report shows the importance of multidisciplinary management of a pregnant woman with cancer. There should always be a balance between fetal well-being and maternal prognosis. This multidisciplinary management allowed a favorable clinical evolution and the planning of a more adequate anesthetic approach, which revealed to be successful.

Ethical Disclosures

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REFERENCES

- Pereg D, Koren G, Lishner M. The treatment of Hodgkin's and non-Hodgkin's lymphoma in pregnancy. Haematologica. 2007; 92:1230-7.
- Hodby K, Fields PA. Management of lymphoma in pregnancy. Obstet Med. 2009; 2: 46–51.
- 3. Berveiller P, Mir O. Taxanes during pregnancy: probably safe, but still to be optimized. Oncology. 2012; 83:239–40. doi: 10.1159/000341820.
- Azim HA, Pavlidis N, Peccatori FA. Treatment of the pregnant mother with cancer: a systematic review on the use of cytotoxic, endocrine, targeted agents and immunotherapy during pregnancy. Part II: hematological tumors. Cancer Treat Rev. 2010; 36:110–21. doi: 10.1016/j.ctrv.2009.11.004.

- Vandenbroucke T, Verheecke M, Calsteren KV, Han S, Claes L, Amant F. Fetal outcome after prenatal exposure to chemotherapy and mechanisms of teratogenicity compared to alcohol and smoking. Expert Opin Drug Saf. 2014; 13: 1653–65. doi: 10.1517/14740338.2014.965677.
- Esposito S, Tenconi R, Preti V, Groppali E, Principi N. Chemotherapy against cancer during pregnancy: A systematic review on neonatal outcomes. Medicine. 2016; 95:38. doi: 10.1097/MD.0000000000004899.
- 7. Huettemann E, Sakka S. Anaesthesia and anti-cancer chemotherapeutic drugs. Curr Opin Anaesthesiol. 2005; 18:307–14.
- Gudaitytė J, Dvyvlys D, Šimeliūnaitė I. Anaesthetic challenges in cancer patients: current therapies and pain management. Acta Med Lituanica. 2017; 24:121–7.
- 9. Crosby E. Clinical case discussion: anesthesia for Cesarean section in a parturient with a large intrathoracic tumour.
- Hartigan PM, Ng JM, Gill R. Anesthesia in a patient with a large mediastinal mass. N Engl J Med. 2018; 379:587. doi: 10.1056/NEJMc1804797.
- Buvanendran A, Mohajer P, Pombar X, Tuman KJ. Perioperative management with epidural anesthesia for a parturient with superior vena caval obstruction. Anesth Analg. 2004; 98:1160-3.
- Kanellakos GW. Perioperative management of the pregnant patient with an anterior mediastinal mass. Anesthesiol Clin. 2012; 30:749–58. doi: 10.1016/j. anclin.2012.07.010.
- Dasan J, Littleford J, McRae K. Mediastinal tumour in a pregnant patient presenting as acute cardiorespiratory compromise. Int J Obstet Anesth. 2002; 11:52–6.
- Mahmood A, Mushambi M, Porter R, Khare M. Regional anaesthesia with extracorporeal membrane oxygenation backup for caesarean section in a parturient with neck and mediastinal masses. Int J Obstet Anesth. 2018; 35: 99-103. doi: 10.1016/j.ijoa.2018.02.009.
- Bevinaguddaiah Y, Shivanna S, Pujari VS, Chikkapillappa MA. Anesthesia for cesarean delivery in a patient with large anterior mediastinal tumor presenting as intrathoracic airway compression. Saudi J Anaesth. 2014;8:556-8. doi: 10.4103/1658-354X.140901.
- Dubey PK, Tripathi N. Anesthetic considerations in a patient with large anterior mediastinal mass. J Cardiothorac Vasc Anesth. 2019; 33:1073-5. doi: 10.1053/j. jvca.2018.03.023.