

Anesthesia for major oncological surgery in pregnant patient in the second trimester: case report

Abstract

Background: Li-Fraumeni syndrome (LFS) is a rare inherited cancer susceptibility disorder with a broad spectrum of tumors in both children and adults. Patients with LFS have a lifetime risk of cancer, and the most common tumors found include soft tissue sarcoma, breast cancer, brain tumors, osteosarcoma, leukemia, and adrenocortical carcinoma. Non-obstetric surgery may be necessary in any trimester of pregnancy, which brings the unique challenges of caring for two patients simultaneously. The case report involved a patient who presented with head and neck tumor and breast tumor during three pregnancies and underwent surgery in the 2nd trimester of the 3rd pregnancy.

Case report: The patient's history began in 2015 during the 3rd trimester of the 1st pregnancy, with a dental abscess and biopsy revealing chondroblastic osteosarcoma of the jaw, awaiting the end of the pregnancy to begin treatment. Two months after birth, right hemimandibulectomy with temporomandibular disarticulation. During the 2nd pregnancy, ductal breast cancer developed, progressing to miscarriage. Chemotherapy and left radical mastectomy with right segmental mastectomy. In the 14th week of the 3rd pregnancy, recurrence with chondroblastic osteosarcoma of the right maxilla, resection indicated in the 2nd trimester, and right partial maxillectomy was performed under multimodal general anesthesia, without compromising the fetus.

Conclusion: Non-elective surgeries should never be denied to pregnant patients, although it is recommended to postpone elective cases until 6 weeks after delivery. Consultations with obstetrics, neonatology, anesthesiology and surgery teams are essential for the care of the patient, regardless of the type of surgery. This meeting was held with the various teams and family members, resulting in a successful outcome after the right subtotal maxillary surgery, with a viable fetus and birth a few weeks after surgery.

Keywords: Pregnancy, head and neck surgery, non-obstetric surgery, osteosarcoma.

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Isabela Moreira Silva,¹ Luiz Eduardo Imbelloni,² Anna Lúcia Calaça Rivoli,³ Sylvio Valença de Lemos Neto,⁴ Ana Cristina Pinho,⁵ Livia Don Fonseca,³ Maria Eugênia Carvalho¹

¹3rd Year Resident of Anesthesiology, CET-SBA INCA, Brazil

²Anesthesiologist at various Hospitals, Brazil.

³Anesthesiologist at the National Cancer Institute (INCA), Brazil

⁴Head of the Anesthesiology Service of the National Cancer Institute (INCA), Anesthesiologist, Responsible for the CET-SBA of the National Cancer Institute, Brazil

⁵INCA Anesthesiologist, Responsible for the CET-SBA of the National Cancer Institute, Brazil

Correspondence: Dr. Luiz Eduardo Imbelloni, Anesthesiologist at various hospitals, Rio de Janeiro, Brazil, Email dr.luiz.imbelloni@gmail.com

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Introduction

In a recent systematic review and meta-analysis on the effects of general anesthesia during pregnancy on neurocognitive development of the fetus, it was shown that practically all commonly used general anesthetics harm brain development in multiple animal species, both for exposure before and after birth.¹ Any type of non-obstetric surgery may be necessary in any trimester of pregnancy, which is a great challenge to care for two patients simultaneously. Non-elective surgery should never be denied to pregnant patients, although postponing elective cases until 6 weeks postpartum is recommended.² Li-Fraumeni syndrome (LFS) is a hereditary tumor that exhibits autosomal dominant inheritance.³ LFS develops in individuals with a germline pathogenic variant of the cancer suppressor gene, individuals with the TP53 pathogenic variant.³ The core tumors of LFS such as breast cancer, osteosarcoma, soft tissue sarcoma, brain tumor, and adrenocortical cancer constitute many cases; however, various types of cancer such as hematologic malignancy, epithelial cancer, and pediatric cancers such as neuroblastoma can also develop.³ In 2015, the patient presented a nodulation of the right gingival ridge with three months of evolution diagnosed as an abscess at the end of the 3rd period of the 1st pregnancy. One year after diagnosis of breast cancer during the 1st period of the 2nd pregnancy, evolving to miscarriage, LFS was diagnosed. In 2022, during the beginning of the

3rd pregnancy, a right mandibular tumor was diagnosed, and resection was indicated in the 2nd trimester of pregnancy with predicted difficult airway by Mallampati IV, limited mouth opening and significant mass in the right maxilla, which was successfully performed and without compromising the unborn child.

Case report

According to Circular Letter no. 166/2018-CONEP/SECNS/MS published on June 12, 2018, by the Ministry of Health, this case report was registered on the Plataforma Brasil (CAAE: 84247424.4.0000.5274), and the Ethics Research Committee approved this case report (number 7.190.205). The patient's history began in 2015 during the 3rd trimester of her first pregnancy, with a dental abscess that did not improve with tooth extraction and antibiotic use. She was referred to the head and neck department of the National Cancer Institute (INCA), which found a vegetative lesion measuring 8 x 8 cm located on the lower right gingival margin, and the biopsy showed chondroblastic osteosarcoma of the mandible. Because she was in the final stage of pregnancy, she waited until the birth to begin treatment. Two months after birth, she underwent the right hemimandibulectomy with temporomandibular joint disarticulation, with good surgical evolution. In 2016, she complained of a nodule in her left breast. An ultrasound (US) showed a BI-RADS

5 nodule, and the biopsy revealed infiltrating ductal carcinoma. The patient was in the first trimester of her second pregnancy, which evolved to a missed abortion with uterine curettage. After recovery from the obstetric procedure, neoadjuvant chemotherapy was started with doxorubicin 60 mg/m² and cyclophosphamide 600 mg/m² for four sessions. Afterwards, a left radical mastectomy was performed with right segmental mastectomy associated with chemotherapy with trastuzumab at a dose of 8 mg/kg in the first dose and 6 mg/kg in the following doses, for a total of seven sessions. Given the different primary neoplasms in a young patient, she was referred to the medical genetics service, which diagnosed Li Fraumeni syndrome.

In 2022, she complained of new pain in her upper teeth associated with a bulging palate on the right. On examination, she had pain on palpation throughout the right hemiface, maxilla, zygomatic bone, and right preauricular region. Palpation revealed a hardened and fixed lesion in the right maxilla, and oral examination confirmed a bulging palate on the right extending to the anterior portion of the soft palate. Magnetic resonance imaging (MRI) revealed a large expansile mass affecting the right hemimaxilla, measuring 4.8x4.7x3.6 cm, with alveolar involvement of the lateral incisor and palate, maxillary sinus, and infiltration of the floor and medial wall (Figure 1). A biopsy was performed, revealing chondroblastic osteosarcoma of the right maxilla, and subtotal maxillectomy was indicated. The patient was 14 weeks into her third pregnancy. In a discussion with the obstetric team that monitored prenatal care, a surgical approach was recommended in the 2nd trimester of pregnancy, given the need for treatment to include surgery. A joint meeting was held with the entire team that cared for the patient, in the presence of the patient, her husband and relatives, to discuss the risks of miscarriage or other possible complications in any surgical procedure during pregnancy, with the second trimester being considered the period with the lowest risks in medical literature. After the agreement, the patient signed the informed consent form and authorized the use of images for later publication of the case. Female patient, 39 years old, 73 kg, 1.60 m, body mass index (BMI) 28.5, Wing II, right partial maxillaryectomy surgery. In the pre-anesthetic evaluation at the 22nd week of gestation, Mallampati IV, limited ball opening and extensive mass in the right maxilla. Laboratory tests showed hemoglobin 10.5 g/dL, hematocrit 29.3%, platelets 203,700/mm³, glucose 90 mg/dL, urea 19 mg/dL, creatinine 0.7 mg/dL, INR = 0.97, potassium 4.5 mg, sodium 140 mg. Chest X-ray without alterations and electrocardiogram with sinus rhythm, regular, without acute alterations. Using Tramadol 100 mg orally every 6 hours to control pain and ferrous sulfate 40 mg orally per day.

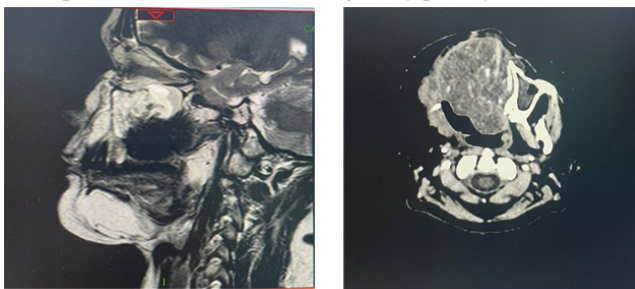


Figure 1 MRI of the second mandibular lesion on the right.

She was referred to the surgical center without oral or intravenous medication, monitored with continuous ECG, pulse oximetry, capnography, noninvasive blood pressure, bispectral index and urinary output. Peripheral venous access was punctured with a 20G catheter in the right upper limb, prophylactic antibiotics were administered with amoxicillin plus clavulanate 1.5 g, and the right femoral vein was instilled with a 7Fr x 20cm deep venous catheter. Total intravenous

general anesthesia was initiated, with preoxygenation under a face mask with 100% oxygen, rapid sequence anesthetic induction with fentanyl 150 µg, lidocaine 120 mg, propofol 1% target-controlled continuous infusion of 2.5 µg/ml, rocuronium 80 mg, ketamine 20 mg, continuous intravenous infusion of dexmedetomidine 0.3 µg/kg/h and remifentanyl 0.2 µg/kg/min. Orotracheal intubation was performed with a McGrath video laryngoscope and a 7.5 wired orotracheal tube. Controlled bleeding showed a loss of approximately 1,000 ml, with blood transfusion guided by serial arterial blood gas analysis (Table 1) and norepinephrine infusion for 90 minutes at a maximum dose of 0.1 µg/kg/min. At the end of the surgical procedure, a tracheostomy was performed, and 4 mg of intravenous morphine was administered. After reversal of the neuromuscular blockade with 150 mg of intravenous sugamadex guided by a train of four stimuli, extubation was uneventful. The duration of anesthesia was 7:15 hours. After extubation with the patient completely awake, an abdominal ultrasound was performed, showing a live fetus, HR of 186 bpm. The patient was transferred with oxygen enrichment via tracheostomy cannula, stable without vasoactive amines to the ICU. After stability, the discharge to the ward 48 hours after the surgical procedure and discharged from the hospital on the 99th postoperative day. At the end of the third pregnancy, a cesarean section was performed, resulting in the birth of a viable fetus without any complications. The patient died in the palliative care unit at the end of the year after the surgery. At the present time, the child is 2 years old and has normal development for her age group.

Table 1 Serial blood gas analysis performed during surgery

| Parameters | GAS 1 = 0 h | GAS 2 = 2 h | GAS 3 = 4 h | GAS 4 = 6 h |
|-------------------------|-------------|-------------|-------------|-------------|
| pH | 7.38 | 7.37 | 7.31 | 7.3 |
| PCO ₂ (mmHg) | 28.2 | 29 | 31.4 | 34.7 |
| PO ₂ (mmHg) | 205 | 238 | 135 | 200 |
| Hb (g/dL) | 6.4 | 6.8 | 7.4 | 8.8 |
| Ht (%) | 19.5 | 19.6 | 21.4 | 26.5 |
| Lactate (mg/dL) | 0.3 | 0.4 | 0.6 | 0.7 |
| BIC (mEq/L) | 16.6 | 16.7 | 16.1 | 17.2 |

GAS: Serial blood gas; BIC: Bicarbonate.

Discussion

Pregnancy is associated with anatomical and physiological changes predisposing to difficult airway management, which can be expected from gestation week 20 and until 2 days postpartum.⁴ Neck pathology from tumors, previous surgery, or radiation increases the risk of failure in every aspect of airway management.^{5,6} Patients with LFS have a lifetime risk of cancer, and the most found tumors include soft tissue sarcoma, breast cancer, brain tumors, osteosarcoma, leukemia, and adrenocortical carcinoma.⁷ In 2015, a patient presented chondroblastic osteosarcoma of the right mandible and underwent maxillectomy. One year later, she was diagnosed with infiltrating ductal carcinoma of the left breast and was treated with left radical mastectomy and right segmental mastectomy associated with chemotherapy. In 2022, the chondroblastic osteosarcoma of the right maxilla recurred, and subtotal maxillectomy was indicated, which was successfully performed during the 2nd trimester of the 3rd pregnancy under general anesthesia, with no changes to the fetus assessed at the end of the surgery with US. And now, two years after birth, she is developing normally for her age group. Regarding fetal considerations, the first trimester fetal organogenesis occurs, and anesthetic agents can cause teratogenesis.⁸ The second trimester is preferred for non-elective surgeries.⁸ Patients have the lowest risk

of premature birth, and major embryonic development is complete at birth by eighth week. Virtually all topics relevant to the first and second trimesters also apply to the third trimester if labor has not yet begun, and a consultation with the obstetrician is essential.⁹ It is important to understand the physiological changes of pregnancy and the effect of drugs on the mother. In the first pregnancy, the tumor was discovered in the third trimester, and surgery was only performed after birth. In the second pregnancy, there was a spontaneous abortion. In the third pregnancy, the recurrence was discovered early on, and surgery was performed until the second trimester, in accordance with international guidelines.

In laboratory animals, anesthesia during pregnancy results in neuronal injury, leading to learning and memory impairments, regardless of the animal species, type of anesthetic, and time during pregnancy.¹ There are no clinical observational studies in humans to confirm this. The patient was anesthetized with several drugs described in the case report, but no laboratory studies were performed on the child until she was two years old, and it is known from family reports that the child has had normal development up to this date. Pregnancy is associated with anatomical and physiological changes that lead to potentially difficult airway management.⁴ The objective of this review was to address the published evidence on the management of anticipated difficult airways in pregnant women, with special emphasis on multidisciplinary prenatal planning, awake tracheal intubation, and other airway approaches that consider physiological and situational factors that are specific to the pregnant patient and the obstetric work environment. However, the management of patients undergoing head and neck procedures during pregnancy was not addressed. In addition to the difficulties described in the review, the patient had already undergone subtotal right maxillaryectomy, left radical mastectomy with right segmental mastectomy associated with chemotherapy, with predicted difficulty intubation, which was performed with a McGrath video laryngoscope and a 7.5 wired orotracheal tube, without difficulty. Showing that good planning results in successful intubation. In another article aiming to guide anesthetic management with clinical advice for each trimester of pregnancy, no item was observed for patients undergoing head and neck surgery during any trimester.² However, it is an important article that reports the considerations of the fetus in the 1st, 2nd and 3rd trimester of pregnancy, and the maternal considerations in each period in relation to the type of surgery. The 2nd trimester of pregnancy is considered the best period for performing the surgery, which happened with success for both the mother and the fetus in this case.⁹ Estimating the incidence of all cancers during pregnancy is a challenging task. In Brazil, it was not possible to correlate obstetric and oncological records because they were not linked. The most common malignant tumors associated with pregnancy are, in decreasing order of frequency, melanoma and breast cancer, cervical cancer, lymphomas and leukemias.¹⁰ The patient in this case presented cervical and breast cancer with a subsequent diagnosis of LFS, which is a hereditary tumor that exhibits autosomal dominant inheritance.³ LFS develops in individuals with a pathogenic germline variant of the cancer-suppressor gene, individuals with TP53 pathogenic variant. Aiming to determine the incidence of cancer associated with pregnancy in Australia in the period 1994 to 2008, with a total of 781,907 women and their 1,309,501 pregnancies, it showed that there was an increase that was only partially explained by the increase in maternal age.¹¹ Depending on the tumor entity, localization, stage and prognosis, surgery during pregnancy may be inevitable. Surgery can be performed on all non-abdominal or nongenital organs with safety if special precautions are used. Pregnant patients may have multiple complex comorbidities that may affect peripartum management and

anesthetic care. Pre-anesthetic consultation is essential and ideal for early assessment of high-risk pregnant patients. This report took place at the Cancer Hospital and showed the importance of this assessment and the need to include the topic of cancer during pregnancy in review articles and guidelines.¹²⁻¹⁴ The lack of knowledge and the rarity of cancer in pregnancy spearheaded the creation of the International Network on Cancer, Infertility and Pregnancy (INCIP) that aims to contribute to the advancement of cancer management for pregnant women and facilitate large-scale studies.¹⁵

Conclusion

Identifying cancer during pregnancy is a very challenging procedure, since the physiological changes that occur during pregnancy can delay the adequate investigation of an underlying neoplasm. Therefore, it is essential that a multidisciplinary team be involved in promptly assessing gestational age, evaluating fetal viability and growth, while defining the best maternal diagnostic strategy and the best indicated treatment. Several recommendations established in 1992 for LFS are still applicable to genetic testing in familial cancer syndromes that include children.¹⁶ The multidisciplinary approach in this patient involving obstetricians, oncologists, neonatologists, anesthesiologists, surgeons and meeting with family members is essential for the success of surgical treatment in the 2nd trimester of pregnancy, with excellent results for the patient and perfect birth a few days after surgery for resection of head and neck osteosarcoma, performed with scheduled cesarean section. Several review articles on non-obstetric anesthesia during pregnancy address patients with cancer of various etiologies and locations.

Acknowledgments

None.

Conflicts of interest

The authors declare that there are no conflicts of interest.

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