

## Case Report: Ultrasound-Guided Neuroaxial Anesthesia in Pregnant Patient with Opioid-Allergic Achondroplasia

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### ABSTRACT

Achondroplasia is a low prevalence genetic disorder characterized by disproportionate short stature and skeletal dysplasia, caused primarily by mutations in the fibroblast growth factor receptor 3 (FGFR3) gene associated with disturbances in bone growth. It is the most common form of dwarfism characterized by rhizomelic shortening of the limbs, macrocephaly with frontal bossing and spinal alterations, which presents significant challenges in the anesthetic management of pregnant women due to anatomical and physiological alterations, such as predictors of difficult airway, thoracic restriction due to bone dysplasias, spinal deformities and the multiple physiological changes characteristic of pregnancy. Achondroplasia has an increased incidence of menstrual disorders, infertility, amenorrhea, so conception is rare.

We report the case of a 29-year-old female patient diagnosed with achondroplasia and 37 weeks of pregnancy with cephalopelvic disproportion, with a history of opioid allergy documented by provocation test, who underwent elective cesarean section. After a detailed evaluation that included a careful spinal assessment with ultrasound to ensure the feasibility of the neuroaxial block, given the frequent technical difficulties associated, an ultrasound-guided neuroaxial block was chosen as the primary anesthetic technique due to the predictors of difficult airway and opioid allergy, which was performed with adjusted doses of local anesthetics, in addition to the preoperative use of intravenous non-opioid drugs to optimize intraoperative and postoperative pain control. The procedure passed without complications, and the multidisciplinary management allowed a satisfactory maternal-fetal evolution.

**KEYWORDS:** achondroplasia, pregnancy, anesthetic management, ultrasonography, complications.

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### INTRODUCTION

Dwarfism is a condition characterized by an adult height of 148 cm or less of genetic and metabolic etiologies. 3, 4 Skeletal dysplasias represent a heterogeneous group of conditions that include about 400 different phenotypes. Their incidence in the population is one per 4,000 newborns. Among them, achondroplasia is the most prevalent, affecting 1/15-30,000 individuals 1. It is a form of disproportionate dwarfism, characterized by short stature with short limbs, macrocephaly, bulging forehead, midface hypoplasia,

micrognathia, radiculopathy and exaggerated thoracolumbar kyphosis, foramen magnum stenosis and trident hand. 2, 5, 6 It is associated with gain mutations specifically in c.1138G>A, in the fibroblast growth factor receptor 3 (FGFR3) located on chromosome 4p16.3, which inhibits the proliferation and differentiation of chondrocytes in the growth plate, generating a set of skeletal comorbidities derived from the involvement of the endochondral bone (long bones and axial skeleton). It is inherited in an autosomal dominant manner in 97% of cases. 6,8 In relation to the

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reproductive system, achondroplasia has an increased incidence of menstrual disorders, infertility, amenorrhea, uterine leiomyomatosis and early menopause. Thus conception is usually rare and difficult with risk of spontaneous abortions, polyhydramnios, preeclampsia, preterm delivery and cephalopelvic disproportion. 9,10,23 Pregnancy in women with achondroplasia is a challenge for anesthesiologists, on the one hand, the management of the airway and on the other hand, the approach to the neuroaxial plane, which are considered of a high degree of technical difficulty due to the anatomical and physiological alterations of the condition itself. 7, 11, 12

The use of ultrasound for neuroaxial anesthesia in patients with achondroplasia is beneficial due to the spinal anatomical alterations they present, since it provides greater safety and precision of the blocking technique, improving the success rate and reducing the complications associated with landmark-guided techniques. 15, 16 The incidence of opioid hypersensitivity is rare, which can only be confirmed by provocation testing, which is the diagnostic gold standard. 17 The selection of anesthetic technique in these patients should focus on carefully balancing the risks and benefits of general and neuroaxial anesthesia. This process requires an individualized assessment that considers their current clinical status, as well as the unique anatomic and physiologic characteristics of each patient. 30

Currently there are no specific guidelines to standardize the perioperative management of these patients. 34 The available evidence comes mainly from clinical case reports, which were reviewed after documenting this case. From this review, the most important aspects were taken in order to improve the anesthetic approach and promote the use of ultrasound as a tool to optimize the anesthetic technique.

### CLINICAL CASE

We present the case of a 29-year-old female patient, originally from Yucatan, Mexico, ASA 2, 108 cm tall, weight 72.5 kg, with diagnosis of pregnancy of 37 weeks of gestation due to LMP, cephalopelvic disproportion and satisfied parity,

electively scheduled for cesarean section and bilateral tubal occlusion. As important medical record, achondroplasia, G2, P0, C0, A1, without known cardiac, neurological, endocrinological and respiratory diseases. Surgical; uterine curettage instrumented in 2008 for an incomplete abortion of 12 weeks of gestation, was managed under intravenous sedation which presented with angioedema and hypotension in the perioperative period which was reversed with administration of intravenous corticosteroids and vasoactive amines, without requiring advanced management of the airway. After the event, the patient consulted with the allergology service who documented a type I hypersensitivity reaction to fentanyl and morphine in a provocation test. No other history of importance. On physical examination, patient with macrocephaly, bulging forehead, with maxillo-zygomatic retraction, large tongue, thick neck (38 cm) with excess skin in its circumference and difficulty in extension. Mallampati IV airway, steno-mentonian distance IV (10.5 cm), thyromental distance III (5 cm), Bellhouse-Dore III, Class II interincisor distance (3 cm), decreased oral opening. STOP-BANG scale score 4/8 high risk of OSA. Chest, "pectus excavatum" and redundant breasts. Spine shows moderate lumbar lordosis with dorsal kyphosis and thoracic deformity (Figure 2). Upper extremities with limitation to full extension. Preoperative evaluation with electrocardiogram and laboratory tests within normal physiological parameters, Hb 12.3, Hto 36.3%, leukocytes 6.4, platelets 245,000, PT 12.2, TTP 29.1, INR 0.98, Fibrinogen 94, Glucose 98 mg/dl, urea 23 mg/dl, creatinine 0.6, BUN 7.8 mg/dl. In the anteroposterior radiological projection of the abdomen, at the level of the bone tissue, the dorsolumbar spine rotoescoliosis stands out, with levoconvex deviation at the dorsal level that causes deformation of the costal arches and dextroconvex deviation in the lumbar region, associated with a decrease in the height of some vertebral bodies and spaces, as well as sclerosis of the terminal plates (**Figure 1**). Analyzing the risks and benefits in the context of this patient, it was decided to try management with ultrasound-guided neuroaxial blockade.



**Figure 1. Abdominal AP radiograph: rotoescoliosis and dorsolumbar deviation.**

Chest X-ray: tracheal deviation to the right, thoracic deformation, Cardiomegaly. Previous preparation of difficult airway equipment and premedication with Paracetamol 1 g IV, Dexamethasone 8 mg IV. The patient was admitted to the ward with baseline vital signs of blood pressure 122/64mmHg, MAP 95mmHg, heart rate 72 bpm, respiratory rate 14 rpm, SpO2 98% with supplemental oxygen through nasal prongs at 2 liters per minute. The patient is placed in a seated position (Vallejo position), asepsis and antisepsis of the thoracolumbar region is performed with Chlorhexidine 4%, sterile fields are placed and ultrasound tracing is performed at the lumbar level, in gray scale, with a low frequency convex transducer in a transverse and longitudinal manner, visualizing the decrease of the intervertebral spaces mostly accentuated at L3-L4, L4-L5 level secondary to osteodegenerative changes characterized by shortening of the pedicles and decrease of the interspinous spaces, in relation with dextroconvex rotoescoliosis previously described; in topography of intervertebral space L1-L2, L2-L3, spinal canal is identified with a decrease in its amplitude, which does not allow adequate visualization of CSF. It was decided to infiltrate skin and subcutaneous cellular tissue at L2-L3 level for its approach. A Whitacre 25G spinal needle

was introduced through a 20Gx38mm hypodermic needle guided by ultrasound in three occasions without observing cerebrospinal fluid outflow, so it was decided to try epidural anesthesia. The Touhy 17G needle was introduced with ultrasound-guided technique in plane and direct visualization of the needle trajectory to the epidural space, which was reached at 6 cm at the first attempt, verified with positive Pitkin's test, epidural catheter was introduced without difficulty, permeability was checked and it was fixed at 10 cm to the skin. Subsequently, 2% Lidocaine was administered through peridural catheter with fractional boluses of 2 ml during 20 minutes, the total dose was 10 ml to reach T4 dermatome, which was measured with temperature test. During transanesthesia the patient remains hemodynamically stable with vital signs in normal physiological parameters. Surgery begins without incident, the only live product is born, 2350 grams, crying and breathing at birth, with Apgar score 8/9. The epidural catheter is removed without complications after completion of the surgery. It was decided to complete with Dexketoprofen 50 mg IV as part of the postoperative analgesia management. The binomial is discharged without complications 48 hours later.



**Figure 2. Chest X-ray: tracheal deviation to the right, thoracic deformation, Cardiomegaly**

### DISCUSSION

Achondroplasia is the most common skeletal dysplasia associated with disproportionate short stature. It is crucial to know the multiple anatomical and physiological alterations generated due to endochondral ossification, which is why airway and neuroaxis management in these patients is considered a challenge for the anesthesiologist. 18, 19, 20,29,30

The physiological airway changes of pregnancy are further affected by the presence of limited cervical flexion and extension, atlantoaxial instability, foramen magnum stenosis, mandibular prognathism, pharyngeal hypoplasia and upper airway hypotonia 21,22. Neck extension in achondroplastic patients with atlantoaxial instability must be limited or avoided to prevent cervicomedullary compression and secondarily compression of the brainstem that could lead to sudden death due to central respiratory failure, The expansion of the thoracic circumference during pregnancy is limited due to costovertebral deformities, this combined with a large uterus that occupies space in the thoracic cage, which will seriously affect pulmonary functional residual capacity and alveolar closure volume in a way that will favor the formation of atelectasis and hypoxemia of rapid onset. 3,23,32 To this is added the presence of obstructive sleep apnea, as in the case of this patient, making manual ventilation, such as intubation, difficult.<sup>30</sup> There are multiple case reports in the literature demonstrating the difficult airway management of this population. Sagastume, et al Presents the case of a pregnant woman with achondroplasia with predictors of difficult airway such as wide, short neck, bilateral mammary hypertrophy, limited cervical mobility, Mallampati III, managed under general anesthesia with rapid sequence induction where she evidenced a Cormack-Lehane 4 not modifiable with BURP after conventional laryngoscopy with secondary desaturation and inability to ventilate that was resolved with position and placement of ramp, then videolaryngoscopy was performed and glottic opening was observed with decreased light, edema and abundant secretions. Finally, intubation was achieved with a smaller diameter endotracheal tube with a metallic guide.<sup>23</sup> Rojas et al. Reports a case of a 21-year-old pregnant woman with Hallermann-Streiff syndrome or Francois dyscephaly, a rare disease associated with mid-facial hypoplasia (bird-like facies), cataracts, severe scoliosis and achondroplasia. On examination of the airway with micrognathia, thyromental distance of 5 cm, mouth opening of 2 cm, Mallampati II, conventional laryngoscopy and Sellik maneuver were performed, revealing Cormack-Lehane III, which was intubated at the first attempt with the help of Bougie. 35 Huang et al. They report a case of failed awake intubation with videolaryngoscope and successful intubation following the use of fibrobronchoscope.<sup>11</sup>

General anesthesia has traditionally been considered the technique of choice in this type of patient despite the risks and difficulties involved; however, there are no specific guidelines established for anesthetic management in achondroplastic patients, and it is avoided whenever possible.<sup>34,39</sup>

On the other hand, the spinal deformities presented by our patient, such as lumbar lordosis, scoliosis, narrow spinal canal and decreased interpedicular distance, make neuroaxial anesthesia techniques difficult, and the behavior and intrathecal distribution of the local anesthetics administered are also uncertain. Determining the dose and volume of the appropriate local anesthetic in patients with short stature is further complicated by the changes in vertebral anatomy, which can suddenly propagate an iatrogenic dural puncture, difficulty in catheter placement or air embolism, which is why some anesthesiologists prefer to use modulating techniques, such as epidural or the combination of epidural and spinal, instead of administering a single intrathecal dose and decreasing the dose of local anesthetics. 27,28 In fact, a high incidence of total spinal anesthesia has been seen even after the use of low and titrated doses of local anesthetics.<sup>14</sup> Ravenscroft et al. 1998 mentions a case of successful cesarean section in an achondroplastic patient managed under subarachnoid block with a 30% decrease in the dose of local anesthetic.<sup>36</sup> DeRenzo et al 2005 recommend the use of epidural, combined, or continuous intrathecal methods with fractional and incremental low doses of local anesthetics.<sup>37</sup> Given the aforementioned antecedents and the failure of single-dose blockade on several occasions, it was decided to use ultrasound-guided peridural neuroaxial blockade. The use of this tool in neuroaxial blockade has been shown to significantly improve the success rate in the first attempt compared to traditional techniques based on palpation of anatomical landmarks. A 2023 meta-analysis by Zhang et al. report that real-time ultrasound achieves a success rate of 82.8%, while ultrasound-assisted ultrasound achieves 67.1%. In contrast, the traditional technique presents a success rate of only 0.1%. These results confirm the superiority of ultrasound-guided techniques over conventional palpation, although no significant differences are observed between real-time and assisted ultrasound.<sup>25</sup> In obstetric and obese patients, the use of ultrasound before the procedure increases the probability of success in the first puncture attempt, with a relative risk of 1.46 compared to the technique based on palpation.<sup>26</sup> Santillan et al. in 2022 recommend the use of low frequency convex transducer for lumbar scanning as it provides better visualization and definition of deep structures. The Vallejo position, which was used in this case, has been shown to improve the opening of interspinous and intervertebral spaces in patients with difficult access to the neuroaxis.<sup>38</sup>

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Several documented cases prove the optimization of neuroaxial techniques with the use of ultrasound. As Erdogan et al. in 2016 presents the successful case of cesarean section in 107 cm tall achondroplastic pregnant patient with hyperlordosis and non-severe kyphoscoliosis. She was managed with combined neuroaxial anesthesia (Intrathecal and Peridural) guided by ultrasound with a convex probe, L3-L4 intervertebral space block was performed at the first attempt without complications. Peridural space was found 7 cm from the skin, permeable peridural catheter was placed and 4 cm were left inside. The local anesthetic used was 0.5% hyperbaric bupivacaine with 10 ug of fentanyl with a total volume of 1.2 ml intrathecal reaching diffusion up to metamere T5 with adequate motor and sensory blockade that allowed cesarean section. On elevation of the uterus, the patient felt pain and discomfort and was managed with lidocaine 2% 3 ml twice every 5 minutes through a peridural catheter. 33 Very similar to our case is the one reported by Cao et al. in 2021. reports the use of epidural anesthesia guided by real time ultrasound in an achondroplastic pregnant woman 120 cm tall after two unsuccessful attempts at subarachnoid approach, it was decided to place and manage through the epidural catheter with lidocaine 2% and subfentanyl 7.5 ug in total 17 ml which were fractionated during 15 minutes until reaching diffusion to T4, without complications in the transoperative period.<sup>3</sup> The dose of local anesthetic was lower in our patient. Another case of favorable ultrasound-guided combined anesthesia is reported by Majeed, et al 2017 a primigesta without achondroplasia, but with severe scoliosis, tracheal deformity, cardiopulmonary compromise and history of spinal instrumentation, scheduled for secondary correction, was managed with ultrasound-guided peridural block with convex probe at the first attempt.<sup>40</sup>

It is of great importance to mention that in the case of our patient, in addition to finding predictors of ventilation and difficult intubation, she has a diagnosis of type I hypersensitivity to opioids corroborated after provocation test, which is relatively rare, an additional situation that concerned us after the possibility of requiring general anesthesia and/or postoperative pain management. In a study by Li PH et al. in 2017 reported a 15% diagnosis rate of opioid hypersensitivity after provocation testing, only 15 of 98 patients with suspected opioid hypersensitivity were diagnosed with allergy as such. This suggests that many of the suspected reactions are not true IgE allergies, as most of these are due to direct mast cell degranulation. 17,24.

### CONCLUSION

We consider that neuroaxial anesthesia is an effective alternative for the management of achondroplastic patients operated for cesarean section. We confirm that the use of ultrasound exponentially improves the rate of successful blocks at the first attempt in patients with difficult access to

the neuroaxis, and also reduces the rate of complications in its approach. The neuroaxial titration of local anesthetics must be careful, so the use of a peridural catheter is recommended, since it provides the opportunity to control the level of block more safely and thus not have an abrupt impact on the hemodynamic status of the patient, and also allows us to administer additional doses to the epidural space if necessary.

Although there are reported cases of the use of general anesthesia with good outcome, it increases the likelihood of complex airway management in a population that already presents a high risk, so it is suggested to avoid it whenever possible and to have difficult airway equipment available. The use of opioids is frequently used because of their excellent analgesic effects, and they also allow the reduction of local anesthetic doses in the neuraxis; however, our patient presented a type I hypersensitivity reaction to opioids documented after provocation tests, which is very rare. This case highlights the importance of a thorough multidisciplinary preoperative evaluation in order to individualize the anesthetic management according to the characteristics of each patient to ensure the safety and well-being of the patient during and after the surgical procedure.

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