Case study

Anesthetic Management of Rare Diseases: Insights from Four Compelling Case Reports

ABSTRACT

Background:

Rare diseases, with a prevalence of 4% globally, oftenmanifestwith diverse and challengingclinicalpresentations. Anesthetic management for these conditions demands a nuancedunderstanding of pathophysiology, potential complications, and interactions withanesthetic agents.This studyaims to shed light on the anesthetic challenges posed by rare diseasesthrough a detailedanalysis of four cases. By exploring the complexitiesencountered in Hurler'sdisease, Rubinstein-Taybi syndrome, Churg-Strauss Syndrome, and Xeroderma Pigmentosum, we seek to contribute valuable insights into the adaptabilityrequired in anestheticapproaches for these unique patient populations.

Discussion

Through the exploration of four distinct cases, we have unraveled the intricaciessurroundinganesthetic management in rare diseases. Each case highlighted the imperativeneed for adaptability, meticulous planning, and collaboration acrossmedical disciplines to ensure favorable perioperativeoutcomes.

The success in managingHurler'sdiseaseunderscored the significance of tailored plans integrating enzyme replacement therapy and detailedpreoperativeassessments. Similarly, addressingdifficultairway challenges in Rubinstein-Taybi syndrome showcased the adaptability essential in unique anatomical scenarios.Carefulconsideration of Churg-Strauss Syndrome'scomplexitiesemphasized the avoidance of specific agents and meticulous monitoring. The case of Xeroderma Pigmentosum highlighted the importance of adaptability, shiftingfrominsufficient spinal anesthesia to generalanesthesiapromptly.

Conclusion

These observations stress the criticalrole of a patient-centricapproach, multidisciplinary collaboration, and adaptability in navigating the diverse challenges presented by rare diseases.

In conclusion, thisstudyoffersvaluable insights intorefininganestheticstrategies, ensuringpersonalized and safe care for patients with rare diseases.

Keywords: Anesthetic Challenges-Rare Diseases-Perioperative Care - Case Reports

INTRODUCTION

About 4% of the global population suffers from a rare disease [1]. Beyond the medical aspect, economic, organizational, and political approaches are crucial for the evolution of the world of rare diseases. Rare diseases are characterized by their low prevalence, affecting a small number of individuals. Despitetheirrarity, theirsignificanceisconsiderable due to the substantial number of affected patients.

Beyond medical aspects, itis essential to consider economic, organizational, and political dimensions to advance the management of rare diseases. Comprehensiveapproachesrequire multidisciplinary collaboration involvingvarioushealthcareprofessionalssuch as pediatricians, endocrinologists, geneticists, orthopedists, general surgeons, anesthesiologists, and specialists in physical medicine and rehabilitation. This approach aims to develop an optimal therapeutic plan and improve the quality of life for patients with rare diseases.

The definition of the rarity of a disease may vary across regions and evolve over time. In Europe, a disease is considered rare when it affects a maximum of 5 people per 10,000. However, there are over 6000 rare diseasesworldwide, emphasizing the diversity and complexity of these conditions [2].

The European Society of Pediatric Anesthesiology (ESPA) and the European portal for rare diseases, Orphanet, have contributed to establishing an open-accessdatabaseedicated to anesthesia in patients with rare diseases. This project, calledOrphanAnesthesia, aims to provide recommendations for ensuringsafeanaesthetic management of these patients. Sinceitsimplementation in 2011, this web platform has facilitated the active participation of specialized physicians worldwide, working together to achieve the project's main goal: publishing recommendations for safe anesthetic management of patients with rare diseases.

In the North American context, statistics estimate that 8% of the population under 25 years old has a rare disease or genetic syndrome, compared to 5% for those over 25 [3]. Over the years, advances in understanding the pathophysiology, metabolic context, and genetic origin of rare diseases have led to significant progress in therapy, classification, and genetic counselling for patients and families. However, due to the low prevalence of these diseases, many healthcare professionals are stillunfamiliar with this patient population, creating a lack of knowledge and skills necessary for early diagnosis, comprehensive care, and appropriate rehabilitation to ensure an acceptable quality of life.

The complexity of rare diseases requires a holistic and multidisciplinary approach to optimize care and meet the specific needs of patients. Patient associations, reference centers, and collaborative networks are essential to support research, improve knowledge, promote access to care, and facilitate information exchange amonghealthcare professionals. Translational research, aiming to transformscientificdiscoveries into clinical applications, is a crucial field to accelerate progress in the field of rare diseases.

In the field of anesthesia, it is essential to adapt protocols and management strategies to consider the specificities of patients with rare diseases. This includes a thorough assessment of medical history, understanding the specificrisksassociated with each rare disease, detailed preoperative planning, appropriate selection of drugs and anesthetic techniques, close monitoring during and after surgery, and adequate management of postoperative pain. The anesthesia team must be well-informed and able to collaborate withother specialists to offer optimal care and avoid potential complications. Rare diseases represent a complex challenge for the healthcare system and require a comprehensive approach involving collaboration from different stakeholders. Research, continuous medical education, and public awareness are essential to improve the management of patients with rare diseases.

By working together, we can advance knowledge, develop new therapies, and provide optimal support to individuals affected by these rare conditions.

In the context of this study, we have attempted to provide an overview of the anesthetic management of patients with rare diseases through the analysis of four cases collected at Mohammed VTeaching Military Hospital of Rabat (MTMH). Ourhospital has had the opportunity to treat patients with rare diseases, providing a basis for analyzing these cases and exploring the specific challenges they pose. Through these observations, a better

understanding of the considerations specific to the anesthetic management of patients with rare diseases has been acquired

Case Presentation

Case 1 :

This case involves a 19-year-old patient scheduled for surgical repair of an umbilical hernia, presenting with Hurler's disease (mucopolysaccharidosis type I) managed with weekly enzyme replacement therapy. The preoperative assessment revealed a non-schooled patient with growth retardation, craniofacial dysmorphia, skeletal deformities, joint stiffness, and an umbilical hernia with a parietal defect. Airway evaluation indicated facial dysmorphia, limited mouth opening, Mallampati class IV, and a short, restricted-mobility neck. (Photo 1). Radiographicfindings included leftward tracheal deviation. Cardiovascular examination revealed a systolic para-sternal murmur, and echocardiography indicated moderately diagnosed aortic disease with aorticannular size of 19mm and moderate mitral insufficiency on a remodeled valve.

Pre-anesthetic medication included hydroxyzine, and in the operating room, the patient was positionedsupine with monitoring. Due to anticipated difficult intubation, fiberoptic bronchoscopy was employed for airway control. Naphazoline nebulization, nasal packing with lidocaine gel, bilateral laryngeal block, and intra-tracheal block were performed. Atropine was administered for anti-salivary effect. Anesthetic induction comprised fentanyl, propofol, and rocuronium, with maintenance using a mixture of oxygen-nitrous oxide (60%-40%) and 0.6 CAM sevoflurane. The 55-minute procedure involved prosthetic hernia repair with minimal bleeding, and the patient was extubated after complete awakening, resumption of spontaneous ventilation, and total reversal of neuromuscular blockade. Transfer to the surgicalwardoccurredtwohours postoperatively. Postoperative analgesia included intravenous paracetamol and nefopam for two days. Following the resumption of bowel function, oral intake recommenced, and the patient was discharged on the third day. This case illustrates anesthetic management of a Hurler’s disease patient undergoing repair, employing-meticulous airway preparation, fiberoptic bronchoscopy, and a carefully anesthetic plan to ensure perioperative safety and optimal postoperative outcomes

Case 2:

A 15-year-old adolescent with a familial form of Rubinstein-Taybi syndrome admitted for the excision with tympanoplasty of a left cholesteatomatouschronic otitis media.

Clinical examination revealed a cooperative patient weighing 34 kg with psychomotor retardation. Facial dysmorphia-included epicanthus, coarse facial features, low hairline, hypertrichosis, antimongoloideye orientation, thick eyebrows, stubby hands and feet, short and broad thumbs and big toes.

Cardiovascular and pulmonary examinations were unremarkable. Additionally, fine veins, limited mouth opening to two fingerbreadths, Mallampati classification II, and a flexible neck were noted.

In the operating room, standard monitoring was applied, including electrocardiogram, oximeter, and non-invasive blood pressure cuff. A 22G peripheral intravenous line was established on the dorsum of the hand, and fluid resuscitation with 5 mL·kg–1 of 0.9% saline was initiated. Following a three-minute preoxygenation with 100% FiO2, anesthesia induction commenced with fentanyl (3 µg·kg–1) and propofol (2.5 mg·kg–1), followed by rocuronium (0.6 mg·kg–1). Direct laryngoscopy revealed Cormack-Lehane grade IV, rendering intubation impossible.

Mask ventilation remained feasible, maintaining oxygen saturation at 98%. Employing a video laryngoscope (STORZ, D-78532 Tuttlingen, Germany) improved Cormack-Lehane grade to II, enabling intubation using a 5.5-mm armed tube with a flexible guide. Maintenance involved a 50% oxygen/air equimolar mixture, sevoflurane, and fentanyl.

The procedure lasted 80 minutes without complications, and extubation occurred incident-free in the postoperative recovery unit after complete awakening. After a two-hour stay in the recovery unit, the patient was transferred back to the admitting service.

Case 3:

A 36-year-old married woman and mother of two children with an 8-year history of asthma, currently managed with inhaled salbutamol and Symbicort. Shewasdiagnosed with Churg-Strauss Syndrome (CSS) two years prior due to recurring sinus-related symptoms, including cheek pain, nasal purulent discharge, and nasal polyps. Radiographic findings included bilateral interstitial infiltrates, peripheral eosinophilia, and negative antineutrophil cytoplasmic antibodies. The patient was treated with azathioprine (150 mg/day) and prednisone (40 mg/day initially, gradually reduced to 7.5 mg/day). Four months ago, she underwentfunctional endoscopic sinus surgery, during which severehemodynamic

deterioration occurred, requiring blood transfusion and vasoactive drugs due to significant bleeding.

Postoperatively, she developed diplopia, exophthalmos, and left eye adduction deficit. Orthoptic assessment revealed a left medial rectus muscle deficit, attributed to entrapment. The patient was scheduled for revision endoscopic sinus surgery.

Preoperative evaluation showed a height of 163 cm, weight of 86 kg, and BMI of 32 kg/m². Physical examination indicated diffuse bilateral wheezing. Laboratory results showed hemoglobin of 10.2 g/dL, total leukocyte count of 8400/mm³ with 500/mm³ eosinophils, normal renal function, and electrolytes. ECG and chest X-ray revealed normal sinus rhythm and minimal infiltrates in the bilateral lower lobe, respectively. Inhaled salbutamol and oral prednisone were continued until the day of surgery. On the morning of the operation, the patient received medication with midazolam (2 mg) and hydrocortisone (100 mg).

In the operating room, routine non-invasive monitoring was instituted. Baseline blood pressure and heart rate were 120/75 mmHg and 80 BPM, respectively, with a baseline SpO2 of 99%. General anaesthesia was induced with propofol (200 mg) and fentanyl (250 µg), followed by endotracheal intubation. Anaesthesia was maintained with sevoflurane (MAC 1.5), air, and oxygen (FiO2 50%), along with intermittent fentanyl boluses. No neuromuscular blocking agents were administered.

The operation proceeded without incidents, and adequate ventilation and blood pressure were maintained throughout. The entire anesthesia duration was 1 hour and 10 minutes, with no administration of anticholinesterase agents. At the end of the operation, sevoflurane was discontinued, and the tracheal tube was removed while the patient remained asleep. The patient wasthen transitioned to a facemask in the post-anesthesia care unit until fully awake.

Case 4 :

A 24-year-old woman of Sub-Saharan African origin, diagnosed with Xeroderma Pigmentosum (XP) since childhood, was admitted for a femoral neck fracture following a stairway fall, necessitating surgical fixation. Preoperative evaluation could not determine the genetic type of her XP. She exhibited minor cutaneous manifestations on her face and hands, with no history of tumor surgery.

Neurological examination revealed a slight decrease in IQ, terminal tremors in the extremities, and an ataxic gait. The patient was calm, cooperative, oriented in time and space, with preserved muscle strength and normal deep tendon reflexes. Preoperative MRI showed

no signs of cerebral anomalies. Cardiovascular, pulmonary, and laboratory evaluationswere normal. The patient received oral hydroxyzine premedication (50 mg the day before and 50 mg on the morning of the intervention).

In the operating room, standard monitoring was initiated, including SpO2 and NIBP. A 16G peripheral venous catheter was secured, and 1g of cefazoline was administered. The patient was positioned sitting for spinal anesthesia, and hyperbaric bupivacaine (12.5 mg) and fentanyl (25 µg) were injected using a 25G Tuohy needle afterverifying cerebrospinal fluid flow. However, motor and sensory blocks were insufficient.

With a Bromage score of 4 and a significant response to the needle, the approach was shifted to a general anesthesia induced by propofol 150mg, fentanyl 250µg, and cisatracurium 8mg, maintained by 2% sevoflurane with a 50% oxygen-air mixture. The procedure lasted 80 minutes without incidents. The patient's blood pressure ranged from 136 to 92 mm Hg (maximum), 81 to 56 mm Hg (minimum), heart rate was 85 to 105 beats/minute, and SpO2 ranged from 98 to 100%. Postoperativeanalgesiaincluded paracetamol (1g), nefopam (20mg), and parecoxib (40mg).

In the postoperative recovery room, the patient remained intubated and ventilated. Unexplained failure to wake up after about an hour prompted monitoring for residualpostoperativecurarization and administration of neostigmine. While motor response was satisfactory, the patient did not wake up or resume spontaneous ventilation after two hours, leading to a blood test (sodium, urea, glucose) showing no abnormalities. Three hours later, signs of awakening and spontaneous breathing were observed. Despite extubation, the patient became agitated, with persistent abnormal movements. Examination revealed signs of pyramidal irritation, including heightened reflexes and a present Babinski reflex, necessitating transfer to the MRI room for a scan, which showed no lesion explaining the symptoms. While agitation decreased, other neurological disturbances persisted for over three post operative days, including memory issues such as false recognition and confusion in time and space. These were attributed to neurological deterioration in XP. Neurological follow-up was recommended.

DISCUSSION:

The management of rare diseases poses distinctive challenges in the field of anesthesiology, requiring a nuanced and adaptable approach to ensure optimal patient outcomes [4]. This discussion delves into five illustrative cases that underscore the intricacies of anesthetic management for patients with rare conditions. Each case provides a unique perspective,

offering insights into the strategies employed to navigate the complexities associated with rare diseases.

The Case 1 highlights the successful anesthetic management of a patient with Hurler's disease undergoing umbilical hernia repair. Meticulous attention to airway preparation, fiberoptic bronchoscopy, and a carefully tailored anesthetic plan contributed to perioperative safety and favorable postoperative results. The integration of enzyme replacement therapy and detailed preoperative assessments played a pivotal role in the overall success of the procedure[5].

In Case 2, the challenges of difficult airway management in an adolescent with Rubinstein-Taybi syndrome undergoing tympanoplasty were effectively addressed. The utilization of a video laryngoscope showcased adaptability to unique anatomical features, ensuring successful intubation and a complication-free surgical procedure.[6].

Case 3 delves into the management of a patient with Churg-Strauss Syndrome undergoing revision endoscopic sinus surgery. The careful consideration of the underlying condition, coupled with the avoidance of neuromuscular blocking agents and meticulous intraoperative monitoring, contributed to a smooth and uneventful procedure. [7].

The case involving a woman with Xeroderma Pigmentosum (Case 4) presented challenges during anesthesia induction due to insufficient spinal anesthesia. The ability to shift to general anesthesia, adapt to the patient's response, and closely monitor for postoperative complications showcased adaptability in the face of unexpected challenges[8]..

Throughout these cases, a patient-centric approach, adaptability to unique challenges, and close collaboration between medical disciplines emerge as common threads. These instances underscore the critical importance of tailoring anesthetic strategies to the specific needs of patients with rare diseases, emphasizing comprehensive preoperative assessments and the collaborative efforts of a multidisciplinary team in ensuring successful perioperative care.

PerioperativeConsiderations in Anesthetizing Patients with Rare Diseases :

The clinicalpresentation of rare diseases varies widely, oftenposing diagnostic challenges due to theirrarity and diverse manifestations affectingdifferentorgansystems [9,10]. Anesthesiologists must graspcommonclinicalfeaturesacrossvarious rare diseases to anticipatepotentialperioperative challenges [11].

Unique challenges in anesthetizing patients with rare diseasesnecessitatespecificconsiderations for safe and effective perioperative care [12]. Disease-specific implications require an in-depthunderstanding of pathophysiology, associated complications, and potential interactions withanesthetic agents to tailoranesthesia plans and anticipateperioperativerisks [13].

Preoperativeassessmentis crucial, involving a comprehensiveevaluation of comorbidities, organfunction, and overall patient suitability for anesthesia and surgery. Collaboration withspecialistsfrom relevant fieldsensures a holisticunderstanding of the rare disease, optimizingperioperativerisks [14,15,16].

Carefulselection and administration of anesthetic agents considerdisease-specificfactors, pharmacokinetics, pharmacodynamics, potentialdrug interactions, and knowncontraindications [17]. Customizedanesthesiaprotocolsmay

involve dosage adjustments, specific induction-maintenance-emergence techniques, and the use of adjunctdrugs or regionalanesthesia [13].

Perioperative management and monitoring requiremeticulous attention to vital signs, includinghemodynamicparameters, oxygenation, and end-tidal carbondioxidelevels [18]. Continuous vigilance is essential, with a focus on cardiovascularstability and maintenance of adequateblood pressure and cardiac output, particularly in patients prone to cardiovascularinstability [19].

Temperatureregulationiscritical, consideringpotentialthermoregulationdeficiencies in patients with rare diseases. Maintainingnormothermiathroughout the procedureoptimizes patient outcomes and reduces the risk of surgical site infections [20].

Preventingdisease-specificperioperative complications is crucial, requiringavoidance of known triggers or exacerbatingfactors. Anesthesiologists must possess in-depthknowledge of the patient's rare disease to anticipate and mitigatepotential complications [21].Postoperative care involvesaddressingspecificneeds of patients with rare diseases, ensuringadequate pain management, facilitating a smoothrecovery, and providingappropriatepostoperative monitoring. Effective communication with patients, caregivers, and the healthcare team is essential for addressingconcerns, ensuringproper follow-up, and managingpotential complications.By considering the unique clinical presentations and anestheticconsiderationsassociated with rare diseases, anesthesiologists can deliver personalized and safe care to patients undergoing surgical interventions [21].

CONCLUSION

Rare diseasesoften pose challenges and stress for patients and their families, particularly in findingsuitabletreatments. Anesthetic management for rare diseases can beintricate due to the diseases' rarity and diverse clinical manifestations, necessitatingspecificconsiderations tailored to each patient.

Collaboration betweenhealthcareprofessionals, patients, and specialistsis crucial to ensuringsafe and effective anesthesia. The complexity of anesthetic care for rare diseasesunderscores the importance of a multidisciplinary approach.

Despite the challenges, advancements in science and medicineprovidehope for individualsaffected by rare diseases. Progress in research and treatment has been substantial in recentyears, offeringpromising prospects for improvedoutcomes.

Supportive associations and organizationsplay a vital role in providingemotional support and valuableresources for individualswith rare diseases. As science continues to advance and collaborative efforts persist, the outlook for those affected by rare diseasesis increasinglyoptimistic.

- **Ethical Approval**

  As per international standards or university standardswrittenethicalapproval has been collected and preserved by the author(s).

Consent

As per international standards or university standards, patient(s) and Parental written consent has been collected and preserved by the author(s).

REFERENCES

1. Cortial L, Nguyen C, Julkowska D, Cocqueel-Tiran F, Moliner AM, Blin O, Trentesaux V. Managing rare diseases:examples of national approaches in Europe, North America and East Asia. *Rare Dis OrphanDrugs J* 2022;1:10. http://dx.doi.org/10.20517/rdodj.2022.02

2. Moliner, A.M., Waligora, J. (2017). The European Union Policy in the Field of Rare Diseases. In: Posada de la Paz, M., Taruscio, D., Groft, S. (eds) Rare

DiseasesEpidemiology: Update and Overview. Advances in ExperimentalMedicineand Biology, vol 1031. Springer, Cham. https://doi.org/10.1007/978-3-319-67144-4_30

3. Dawkins HJS, Draghia-Akli R, Lasko P, Lau LPL, Jonker AH, Cutillo CM, Rath A, Boycott KM, Baynam G, Lochmüller H, Kaufmann P, Le Cam Y, Hivert V, Austin CP; International Rare DiseasesResearch Consortium (IRDiRC). Progress in Rare DiseasesResearch 2010-2016: An IRDiRC Perspective. Clin TranslSci. 2018 Jan;11(1):11-20. doi: 10.1111/cts.12501. Epub 2017 Oct 23. PMID: 28796411; PMCID: PMC5759730.

4. Schimpf J, Münster T. Seltene Erkrankungen in der Anästhesie : Wissensbeschaffung und Kernpunkte der perioperativen anästhesiologischen Versorgung [Rare diseases in anesthesia : Knowledge mining and core points of perioperative anesthesiological care]. Anaesthesiologie. 2023 Dec;72(12):907-918. German. doi: 10.1007/s00101-023-01353-6. Epub 2023 Nov 10. PMID: 37947803.
5. W, Kumar G, Belani, Elizabeth A, Braunlin A, Bruce H,Paul R. Harmatz J. Anaesthesia and airway management in mucopolysaccharidosis. J InheritMetab Dis (2013) 36:211–219
6. Imai T, Sakai D, Schol J, Nagai T, Hiyama A, Katoh H, Sato M, Watanabe M. Rubinstein-Taybi syndrome withscoliosistreatedwith single-stage posterior spinal fusion: illustrative case. J Neurosurg Case Lessons. 2021 Mar 15;1(11):CASE20110. doi: 10.3171/CASE20110. PMID: 35855076; PMCID: PMC9241218.
7. Barbosa H, Brás A, Martins M, Coroa M, Marcos A. Anesthesia management in a patient withChurg-Strauss syndrome in the ambulatorysetting: A case report. Rev Esp AnestesiolReanim (Engl Ed). 2023 Dec;70(10):593-595. doi: 10.1016/j.redare.2022.03.005. Epub 2023 Sep 4. PMID: 37666453.
8. Shrestha GS, Sah RP, Amatya AG, Shrestha N. Anaesthetic management of patients withXeroderma pigmentosum. A series of three cases. Nepal Med Coll J. 2011 Sep;13(3):231-2. PMID: 22808824
9. Gorini, F., Coi, A., Mezzasalma, L., et al. (2021). Survival of patients with rare diseases:a population-basedstudy in Tuscany (Italy). Orphanet Journal of Rare Diseases, 16(1), 275
10. Mitani AA, Haneuse S. Small Data Challenges of Studying Rare Diseases. JAMA Netw Open. 2020 Mar 2;3(3):e201965. doi: 10.1001/jamanetworkopen.2020.1965. PMID: 32202640.

11. Baynam G, Bowman F, Lister K, Improved Diagnosis and Care for Rare DiseasesthroughImplementation of Precision Public Health Framework. Adv Exp Med Biol. 2017;1031:55-94. doi: 10.1007/978-3-319-67144-4_4. PMID: 29214566.
12. Adachi T, El-Hattab AW, Jain R, Nogales Crespo KA, QuirlandLazo CI, Scarpa M, Summar M, Wattanasirichaigoon D. Enhancing Equitable Access to Rare Disease Diagnosis and Treatmentaround the World: A Review of Evidence, Policies, and Challenges. Int J Environ Res Public Health. 2023 Mar 8;20(6):4732. doi: 10.3390/ijerph20064732. PMID: 36981643; PMCID: PMC10049067.
13. Prottengeier, J., Weith, T. (2015). Maladies orphelines : impact sur la pratique de l'anesthésie. Current Opinion in Anaesthesiology, 28(6), 691-696.
14. Clark BM, Sprung J, Weingarten TN, Warner ME. Anesthesia for patients with mucopolysaccharidoses: Comprehensive review of the literature with emphasis on airway management. Bosn J Basic Med Sci. 2018 Feb 20;18(1):1-7. doi: 10.17305/bjbms.2017.2201. PMID: 28590232; PMCID:
15. Ahmed Z, Rufo PA. Pediatric Preoperative Management. 2022 May 29. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2023 Jan–. PMID: 32644624.
16. Zambouri, A. (2007). Preoperative evaluation and preparation for anesthesia and surgery. Hippokratia, 11(1), 13-21.
17. Adam MP, Mirzaa GM, Pagon RA, Wallace SE, Bean LJH, Gripp KW, Amemiya A, editors. GeneReviews® [Internet]. Seattle (WA): University of Washington, Seattle; 1993–2023. PMID: 20301295.
18. Avidan MS, Mashour GA. Prevention of intraoperative awareness with explicit recall: making sense of the evidence. Anesthesiology. 2013 Feb;118(2):449-56. doi: 10.1097/ALN.0b013e31827ddd2c. PMID: 23263014.
19. Dexter F, Bayman EO, Epstein RH. Statistical modeling of average and variability of time to extubation for meta-analysis comparing desflurane to sevoflurane. AnesthAnalg. 2010 Feb 1;110(2):570-80. doi: 10.1213/ANE.0b013e3181b5dcb7. Epub 2009 Oct 9. PMID: 19820242..
20. Sessler DI. Perioperative thermoregulation and heat balance. Lancet. 2016 Jun 25;387(10038):2655-2664. doi: 10.1016/S0140-6736(15)00981-2. Epub 2016 Jan 8. PMID: 26775126.
21. Gan TJ, Meyer TA, Apfel CC, Chung F, Davis PJ, Habib AS, Hooper VD, Kovac AL, Kranke P, Myles P, Philip BK, Samsa G, Sessler DI, Temo J, Tramèr MR, Vander Anesthesia guidelines for the management of postoperative nausea and vomiting.

AnesthAnalg. 2007 Dec;105(6):1615-28, table of contents. doi: 10.1213/01.ane.0000295230.55439.f4. PMID: 18042859.

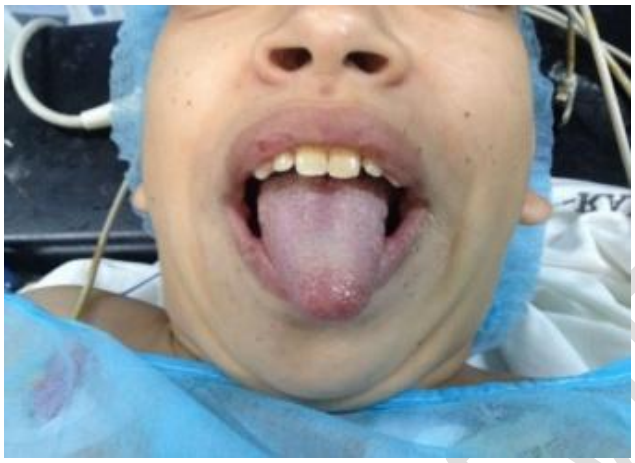

Photo 1. Illustratingdifficult intubation criteria in the patient showed facial dysmorphiawithlimitedmouthopening, Mallampati class IV, and a thyromental distance of 30 mm with a short, restricted-mobility neck.