



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

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Authors' contributions

This work was carried out in collaboration among all authors. Authors MC, MA, WEJ and KAE did the conception, patient enrolment and interpretation. All authors contributed to literature review, final draft writing, and critical revision. All the authors have participated sufficiently in this work, take public responsibility for the content, and have made substantial contributions to this research. All authors read and approved the final manuscript.

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Case Study

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ABSTRACT

Background: Rare diseases, with a prevalence of 4% globally, often manifest with diverse and challenging clinical presentations. Anesthetic management for these conditions demands a nuanced understanding of pathophysiology, potential complications, and interactions with anesthetic agents. This study aims to shed light on the anesthetic challenges posed by rare

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diseases through a detailed analysis of four cases. By exploring the complexities encountered in Hurler's disease, Rubinstein-Taybi syndrome, Churg-Strauss Syndrome, and Xeroderma Pigmentosum, we seek to contribute valuable insights into the adaptability required in anesthetic approaches for these unique patient populations.

Discussion: Through the exploration of four distinct cases, we have unraveled the intricacies surrounding anesthetic management in rare diseases. Each case highlighted the imperative need for adaptability, meticulous planning, and collaboration across medical disciplines to ensure favorable perioperative outcomes.

The success in managing Hurler's disease underscored the significance of tailored plans integrating enzyme replacement therapy and detailed preoperative assessments. Similarly, addressing difficult airway challenges in Rubinstein-Taybi syndrome showcased the adaptability essential in unique anatomical scenarios. Careful consideration of Churg-Strauss Syndrome's complexities emphasized the avoidance of specific agents and meticulous monitoring. The case of Xeroderma Pigmentosum highlighted the importance of adaptability, shifting from insufficient spinal anesthesia to general anesthesia promptly.

Conclusion: These observations stress the critical role of a patient-centric approach, multidisciplinary collaboration, and adaptability in navigating the diverse challenges presented by rare diseases. In conclusion, this study offers valuable insights into refining anesthetic strategies, ensuring personalized and safe care for patients with rare diseases.

Keywords: Anesthetic challenges; rare diseases; perioperative care; case reports.

1. 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. Despite their rarity, their significance is considerable due to the substantial number of affected patients.

Beyond medical aspects, it is essential to consider economic, organizational, and political dimensions to advance the management of rare diseases. Comprehensive approaches require multidisciplinary collaboration involving various healthcare professionals such 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 diseases worldwide, 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-access database dedicated to anesthesia in patients with rare diseases. This project, called Orphan Anesthesia, aims to provide recommendations for ensuring safe anaesthetic management of these patients. Since its implementation 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 still unfamiliar 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 among health care professionals. Translational research, aiming to transform scientific discoveries 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 specific risks associated 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 with other 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 V Teaching Military Hospital of Rabat (MTMH). Our hospital 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.

2. 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 dysmorphism, skeletal deformities, joint stiffness, and an umbilical hernia with a parietal defect. Airway evaluation indicated facial dysmorphism, limited mouth opening, Mallampati class IV, and a short, restricted-mobility neck. (Photo 1). Radiographic findings 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.



Photo 1. Illustrating difficult intubation criteria in the patient showed facial dysmorphism with limited mouth opening, Mallampati class IV, and a thyromental distance of 30 mm with a short, restricted-mobility neck

Pre-anesthetic medication included hydroxyzine, and in the operating room, the patient was positioned supine 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 surgical ward occurred two hours 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 cholesteatomatous chronic otitis media.

Clinical examination revealed a cooperative patient weighing 34 kg with psychomotor retardation. Facial dysmorphism included epicanthus, coarse facial features, low hairline, hypertrichosis, antimongoloid eye 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. She was diagnosed 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 underwent functional endoscopic sinus surgery, during which severe hemodynamic 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 was then 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 evaluations were 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 after verifying 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%. Post operative analgesia included paracetamol (1g), nefopam (20 mg), and parecoxib (40 mg).

In the postoperative recovery room, the patient remained intubated and ventilated. Unexplained failure to wake up after about an hour prompted monitoring for residual postoperative curarization 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.

3. 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.

Perioperative Considerations in Anesthetizing Patients with Rare Diseases:

The clinical presentation of rare diseases varies widely, often posing diagnostic challenges due to their rarity and diverse manifestations affecting different organ systems [9,10]. Anesthesiologists must grasp common clinical features across various rare diseases to anticipate potential perioperative challenges [11].

Unique challenges in anesthetizing patients with rare diseases necessitate specific considerations for safe and effective perioperative care [12]. Disease-specific implications require an in-depth understanding of pathophysiology, associated complications, and potential interactions with anesthetic agents to tailor

anesthesia plans and anticipate perioperative risks [13].

Preoperative assessment is crucial, involving a comprehensive evaluation of comorbidities, organ function, and overall patient suitability for anesthesia and surgery. Collaboration with specialists from relevant fields ensures a holistic understanding of the rare disease, optimizing perioperative risks [14,15,16].

Careful selection and administration of anesthetic agents consider disease-specific factors, pharmacokinetics, pharmacodynamics, potential drug interactions, and known contraindications [17]. Customized anesthesia protocols may involve dosage adjustments, specific induction-maintenance-emergence techniques, and the use of adjunct drugs or regional anesthesia [13].

Perioperative management and monitoring require meticulous attention to vital signs, including hemodynamic parameters, oxygenation, and end-tidal carbon dioxide levels [18]. Continuous vigilance is essential, with a focus on cardiovascular stability and maintenance of adequate blood pressure and cardiac output, particularly in patients prone to cardiovascular instability [19].

Temperature regulation is critical, considering potential thermoregulation deficiencies in patients with rare diseases. Maintaining normothermia throughout the procedure optimizes patient outcomes and reduces the risk of surgical site infections [20].

Preventing disease-specific perioperative complications is crucial, requiring avoidance of known triggers or exacerbating factors. Anesthesiologists must possess in-depth knowledge of the patient's rare disease to anticipate and mitigate potential complications [21]. Postoperative care involves addressing specific needs of patients with rare diseases, ensuring adequate pain management, facilitating a smooth recovery, and providing appropriate postoperative monitoring. Effective communication with patients, caregivers, and the healthcare team is essential for addressing concerns, ensuring proper follow-up, and managing potential complications. By considering the unique clinical presentations and anesthetic considerations associated with rare diseases, anesthesiologists can deliver personalized and safe care to patients undergoing surgical interventions [21].

4. CONCLUSION

Rare diseases often pose challenges and stress for patients and their families, particularly in finding suitable treatments. Anesthetic management for rare diseases can be intricate due to the diseases' rarity and diverse clinical manifestations, necessitating specific considerations tailored to each patient.

Collaboration between health care professionals, patients, and specialists is crucial to ensuring safe and effective anesthesia. The complexity of anesthetic care for rare diseases underscores the importance of a multidisciplinary approach.

Despite the challenges, advancements in science and medicine provide hope for individuals affected by rare diseases. Progress in research and treatment has been substantial in recent years, offering promising prospects for improved outcomes.

Supportive associations and organizations play a vital role in providing emotional support and valuable resources for individuals with rare diseases. As science continues to advance and collaborative efforts persist, the outlook for those affected by rare diseases is increasingly optimistic.

CONSENT

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

ETHICAL APPROVAL

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

COMPETING INTERESTS

Authors have declared that no competing interests exist.

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