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CASE REPORT

General anesthesia for old Werner syndrome patient: a case report

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Abstract Werner syndrome (WS) is a rare autosomal recessive, premature aging disorder whose clinical manifestations include short stature, bilateral cataracts, diabetes mellitus, hypertension, and atherosclerosis. WS first manifests during adolescence and patients usually die at 40–50 years of age. Only symptomatic treatment options available according to clinical manifestations. In anesthetic management, they need to be considered to elderly patients. Difficult intubation is expected and the patients are regarded as a high-risk group for anesthesia, owing to the concomitant cardiovascular and cerebrovascular disorders. The anesthetic management of WS requires a meticulous preoperative history taking, physical examination, and preparation for cardiovascular events.

Introduction

Werner syndrome (WS) is a rare autosomal recessive, premature aging disorder affecting 1 in 1 to 10 million individuals of the population. The incidence of WS is significantly higher in Japan and North Sardinia. It occurs due to the mutation of the *WRN* gene that inactivates the function of helicase involved in DNA replication, repair, and telomere maintenance.[1]

The clinical features of WS include senile appearance, short status, muscle hypoplasia, progeroid changes in hair, bird-like facies, skin ulcers, and voice abnormalities. Progressive manifestations such as bilateral cataracts, osteoporosis, hypogonadism, diabetes mellitus, hypertension, atherosclerosis, and neoplasms lead to death.[2] The disease first manifests during adolescence and patients usually die at the age of 40–50 years. There are no disease-targeting treatments for WS, and only symptomatic treatments are available.

Atherosclerosis is one of the key features of WS. Peripheral arterial occlusive disease is common among patients, and intractable skin ulcers or gangrene of the lower limb may also occur.[2] We described a rare case of an old patient with WS who was administered general anesthesia for femoral popliteal bypass surgery.

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Case presentation

The patient provided written consent for the publication of this case report. The study was conducted in accordance with the Declaration of Helsinki, and the protocol was approved by the ethics committee of Kyung Hee University Hospital (ethics code:2020-07-007, approval date: 2020.07.03).

A 65-year-old man diagnosed with WS was scheduled for femoral popliteal bypass surgery. The patient had an intractable skin ulcer with claudication due to peripheral arterial occlusive disease, and the vascular surgeon decided on surgical intervention.

The patient met all the cardinal signs and symptoms of WS.[2] He was 152 cm tall and weighed 38 kg. He had been prescribed aspirin, candesartan, trimetazidine, alogliptin, glimepiride, rosuvastatin, ezetimibe, sarpogrelate, limaprost, thioctic acid, and oxycodone for hypertension, stable angina, diabetes mellitus, cerebral infarction, and pain from calcific tendinitis of both Achilles tendon and right elbow. He underwent cataract surgery for both eyes under local anesthesia in his thirties, and completely lost his hair in his forties.

Physical examination revealed that the patient had a pinched face with small chin and sparse pubic hair. The patient's voice was high pitched and he stated that he had a ''feminine'' voice since childhood. The patient's American Society of Anesthesiologists (ASA) physical status was III.

We decided to administer general anesthesia after a cautious review of the patient. Regional anesthesia was excluded because his prothrombin time was prolonged (15.2 s) and activated partial thromboplastin time was 53.5 s. Intraoperative heparin use and possibility of a prolonged operation duration led us to select general anesthesia for the procedure.

We identified that the patient had severe limitations in flexion and extension of neck during the airway assessment. In addition to the poor dentation and relatively small chin, the thyromental distance was 5 cm, and his mouth opening was restricted to 2 fingers' distance (Fig. 1). The Mallampati grade was III. Right vocal cord paralysis was observed by an otolaryngologist (Fig. 2). We predicted difficulty in intubation and prepared a McGrath Mac videolaryngoscope (Covidien France SAS, Paris, France) with endotracheal tubes of various sizes. Moreover, an airway emergency cart was prepared, including a fiberoptic bronchoscope, before the patient was brought to the operating room.

Noninvasive blood pressure, heart rate, electrocardiography, oxygen saturation, bispectral index, and train-of-four (TOF) monitoring was performed during the entire duration of anesthesia. His blood pressure, heart rate, and peripheral oxygen saturation were 173/83 mmHg, 118 beats per min, and 100%, respectively, on arrival at the operating room. He was premedicated with glycopyrrolate 0.2 mg and preoxygenated with 100% oxygen for 5 minutes. We used propofol 60 mg and remifentanil 1 $\mu g.kg^{-1}.min^{-1}$ for anesthesia induction. TOF monitoring was performed at 15-seconds intervals by using the right ulnar nerve. After checking that the patient had attained a state of unconsciousness, manual ventilation was initiated with sevoflurane 2.5%, and rocuronium 40 mg was injected. The difficulty in mask ventilation was relieved by intraoral airway placement and the two-handed technique. Intubation was performed successfully with an endotracheal tube with an internal diameter of 7.0 mm using a videolaryngoscope, taking great care to avoid further damage to the already paralyzed vocal cord. Subsequently, continuous arterial pressure monitoring was performed through the left radial artery, and a central line was inserted into the right internal jugular vein under ultrasound guidance.

The heart rate decreased as the surgery progressed and was maintained within the range of 70 to 90 beats per min. The blood pressure was stabilized during the surgery using phenylephrine 0.5–1.51 $\mu g.kg^{-1}.min^{-1}$ and remifentanil 0.25–0.5 $\mu g.kg^{-1}.min^{-1}$. An infusion of 500 mL of volulyte and 1000 mL of plasma solution and transfusion of 2 units of red blood cells were performed. We maintained sevoflurane at a minimum alveolar concentration of 1.0, considering that the body is older than the chronological age. The depth of anesthesia was maintained properly between 35 and 50 bispectral index values during surgery, without significant changes on electroencephalography. The total anesthesia time was 5 hours and 15 minutes.

Concerned about respiratory depression, we did not use any other analgesics except fentanyl in intravenous patient-controlled analgesia (IV-PCA) for postoperative pain control. The IV-PCA regimen consisted of fentanyl 500 μg and ramosetron 0.6 mg and was programmed to deliver 2 $mL.h^{-1}$ as a background infusion, a demand volume of 0.5 mL, and a lock-out interval of 15 minutes with a total volume of 100 mL.

After surgery, post-tetanic count of 2 was checked, and muscle relaxation was reversed by sugammadex 150 mg (4 $mg.kg^{-1}$). Extubation was performed after confirming a TOF ratio of 0.9 and spontaneous ventilation. However, his drowsiness persisted. He did not respond to light stimuli but only to painful stimuli. The bispectral index remained between 70 and 80. He was transferred to the intensive care unit (ICU) for monitoring of consciousness and vital signs. He became alert within 12 hours and was transferred to the general ward in 2 days. As staying in ICU, only a single dose of meperidine 25 mg was administered intravenously except IV-PCA for postoperative pain, and the pain was managed under 3 points in numerical rating scale. The patient was referred to a physiatrist for rehabilitation due to the risk of aspiration due to vocal cord paralysis. He was discharged from the center 14 days after surgery without any complications.

Discussion

WS is a rare autosomal recessive disease caused by loss-of functions mutations in the *WRN* gene that impair DNA replication, repair, and telomere maintenance.[1] It is also known as adult progeria because the symptoms start in early adolescence, which is considerably late compared to Hutchinson-Gliford progeria syndrome. The average lifespan ranges from 30 to 54.3 years. The main causes of death include myocardial infarction and malignancy, and there are no specific treatments that target the syndrome itself.

Our patient was fairly old considering the average lifespan of patients with WS. Recently, treatment with HMG-CoA reductase inhibitors (statins) and peroxisome

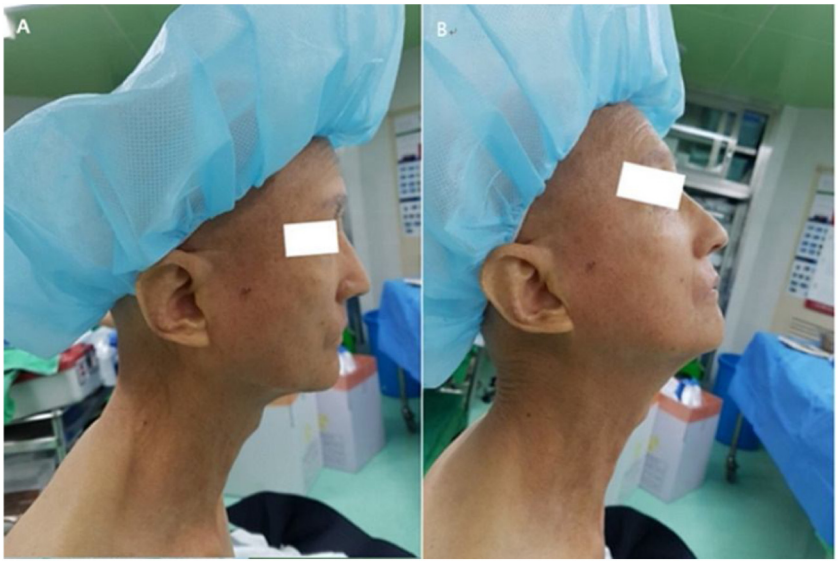

Fig. 1 Patient airway assessment before anesthesia in neutral position (A) and neck extension (B).

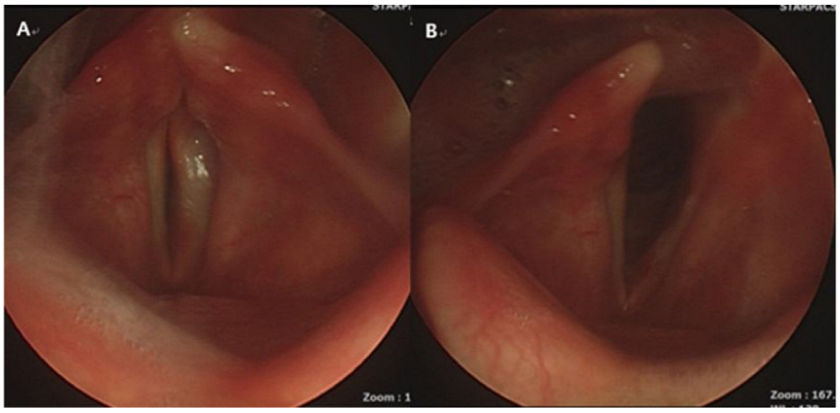

Fig. 2 Fiberoptic view of vocal cord before surgery. Closed (A) and open (B).

proliferator-activated receptor gamma agonists (pioglitazone) has prolonged the lifespan of these patients, by stabilizing the telomeres and preventing apoptosis.[3] These treatments prevent cellular dysfunction and delay fatal outcomes. Early diagnosis and administration of these drugs could aid in improving the quality of life and prolong the lifespan in patients with WS, despite the availability of only symptomatic treatment options according to the clinical manifestations.

The anesthetic management of patients with WS is challenging because of the possibility of a difficult airway and comorbidities that may cause complications during anesthesia and surgery. There are few studies and case reports on anesthesia in WS due to the rarity of the syndrome itself. Regional anesthesia or local anesthesia should be primarily considered if the patient does not have any coagulation disorders owing to the risk of managing a difficult airway.

However, the anesthesiologists chose general anesthesia for this patient after considering the preoperative medication, prolonged operation, intraoperative heparin use, and patient compliance. It is vital for the operators to be prepared for dealing with a difficult airway and cardiovascular compromise during anesthesia. The small mouth, poor dentition, mandibular hypoplasia, maxillary hypoplasia, and craniofacial abnormalities make intubation challenging, and it is essential to evaluate the patient's airway prior to surgery. Awake bronchoscopic intubation should be considered, and a difficult airway cart should be ready with the patient's arrival into the operating room. Small face masks and laryngeal mask airway might be required, because the patient's body is relatively small, and it is natural that a small endotracheal tube be used for intubation.

The accompanying comorbidities should be assessed meticulously before surgery. In addition to obtaining the medical history, a multidisciplinary approach, including a molecular biological assessment, is necessary. Patients with WS are considered to be at a high risk for myocardial infarction, cerebral infarction, and hemorrhage caused by atherosclerosis. Continuous arterial pressure monitoring is recommended along with preparation for extensive cardiovascular events.

Anesthesiologists are requested to consider residual effects of drugs because respiratory depression in WS patients can cause drastic outcome due to the patients' appearance. Extubation has to be performed after neuromuscular transmission confirmed complete recovery of muscle relaxation.

Also, pharmacodynamic and pharmacokinetic characteristics including drug interactions have to be reviewed in choosing anesthetics especially for opioids. Remifentanil was the only opioid used during anesthetic time in this case due to its very short life-time and not context-sensitive characteristic. Short-lived anesthetics are preferred for rapid emergence in general anesthesia of WS patients.

The volume of distribution of lipophilic drugs is increased, and most intravenous and inhalation agents used by anesthesiologists have a longer elimination phase, considering that the body age is far greater than the chronological age, and that the total body water decreases with aging.[4] The dose of anesthetics and other drugs should be adjusted in a manner similar to that for elderly patients.

Conclusion

Few studies have reported on general anesthesia in patients with WS. Preoperative evaluation including airway assessment is crucial, and preparation for a difficult airway and possible cardiovascular events are essential. All medications and anesthetic management should be provided according to the guidelines for the anesthetic management of elderly patients, considering that the body has aged more than the chronological age.

Conflicts of interest

The authors declare no conflicts of interest.

References

1. Goto M. Hierarchical deterioration of body systems in Werner's syndrome: implications for normal ageing. Mech Ageing Dev. 1997;98:239–54.
2. Takemoto M, Mori S, Kuzuya M, et al. Diagnostic criteria for Werner syndrome based on Japanese nationwide epidemiological survey. Geriatr Gerontol Int. 2013;13:475–81.
3. Yokote K, Saito Y. Extension of the life span in patients with Werner syndrome. J Am Geriatr Soc. 2008;56:1770–1.
4. Aurini L, White PF. Anesthesia for the elderly outpatient. Curr Opin Anaesthesiol. 2014;27:563–75.