Anaesthetic management of patients with Xeroderma Pigmentosum. A series of three cases

GS Shrestha,[1] RP Sah,[2] AG Amatya[1] and N Shrestha[1]

Department of Anaesthesiology, 1Institute of Medicine, Tribhuvan University Teaching Hospital, Kathmandu, Nepal; [2]Chitwan Medical College, Chitwan, Nepal

Corresponding author: Dr. Gentle Sunder Shrestha, MD Anaesthesiology, Lecturer, Department of Anaesthesiology, Institute of Medicine, Tribhuvan University Teaching Hospital, Maharajgunj, Kathmandu, Nepal; e-mail: gentlesunder@hotmail.com

ABSTRACT

Xeroderma pigmentosum is a rare autosomal recessive disorder with clinical and cellular hypersensitivity to ultraviolet radiation and defective DNA repair. Skin cancer, mainly on the face, head or neck is very common. Inhalational anaesthetic agents and muscle relaxants are best avoided due to the possibility of inducing DNA damage and prolonged effects of muscle relaxants. These patients may have a difficult airway. These patients may have immature brain development which may render them sensitive to synergistic effect of benzodiazepines and opioids as seen in the first case. Total intravenous anaesthesia is preferred. Nonsteroidal anti inflammatory agents and opioids for multimodal analgesia may be beneficial.

Keywords: Xeroderma Pigmentosum, anaesthetic management, apnoea.

Xeroderma pigmentosum is a rare autosomal recessive disorder with clinical and cellular hypersensitivity to ultraviolet radiation and defective DNA repair. In these patients, repair of ultraviolet induced DNA damage is impaired owing to mutation in genes that form part of a DNA-repair pathway. Skin cancer develops in affected children in an alarming rate. Majority of the skin cancer occurred on the face, head or neck in the form of basal cell or squamous cell carcinoma. Ocular abnormalities in the parts exposed to ultraviolet radiation included ectropion, corneal opacity and neoplasms. Associated neurological abnormalities are not uncommon.[1-2] There is possibility of difficult airway and neuromuscular problems.[3] Little information exists about the optimal anaesthetic management of these patients.

CASE 1

An 18 year old male (42 kg) with infected pyogenic granuloma of the face presented with a chief complaint of mass in the face since two months. The mass was blackish, soft, fungating, bled to touch and progressively increasing in size. It was obscuring the vision of right eye. There were multiple small lesions on both sides of ala of nose. Difficult face mask ventilation was anticipated. Other parameters of airway assessment were normal. Physical examination findings and laboratory investigation reports were within normal limits. Excision of the mass with cheek rotational advance flap was planned under total intravenous anaesthesia.

Patient was transferred to operation theatre. After establishing intravenous access, ECG, pulse oxymeter and blood pressure cuff were attached. After preoxygenating the patient with 100% oxygen, Midazolam 2mg IV was administered, followed by Pethidine 30 mg IV. Patient suddenly became unresponsive and apnoeic. Oxygen saturation dropped upto 60%. The huge mass on the face prevented effective mask ventilation with the adult sized face mask. A paediatric sized face mask was placed over mouth and patient was ventilated by pinching the nostrils. Endotracheal intubation was done. Anaesthesia was maintained with Propofol 100μg/kg/min and intermittent doses of Vecuronium 1 mg was given for muscle relaxation. Volatile anaesthetic agents were avoided. At the end of surgery, muscle relaxation was reversed with Neostigmine and Atropine and patient was extubated uneventfully. Throughout the perioperative period, exposure to light was minimized. Postoperative period was uneventful and patient was discharged home on second postoperative day.

CASE 2

A 13 year old male patient (26 kg), with well differentiated Basal Cell Carcinoma had the history of pigmentous lesions over face and other parts of body since the age of one and half year. The lesions were progressively increasing in number and size. Skin biopsy done two years back revealed well differentiated basal cell carcinoma. Since 15 days, he was having pain over both eyes, progressively increasing in intensity and associated with swelling, discharge and extreme photophobia. Patient was planned for excision and skin grafting over the face and dorsum of hands. There was no significant past history and there was no history of similar illness in family members. His mother was explained about the nature of the disease and adviced to prevent exposure to sunlight. Physical examination findings and laboratory investigation reports were within normal limits. The clustered large skin lesions around the nose was indicating the possibility of difficult mask ventilation. Airway assessment was normal.

Patient was fasted overnight before surgery. Patient was not premedicated with benzodiazepines. In the morning of surgery, he was brought to preanaesthesia preparation room, where he was put in a dark place. Injection Diclofenac Sodium 100 mg was given intramuscularly

30 minutes before induction of anaesthesia. In the operating room, after establishing an intravenous access and after attaching ECG, pulse oxymeter and blood pressure cuff, Pethidine 15 mg IV was given as an analgesic. It was followed by slow induction with Inj. Propofol 70 mg. Spontaneous ventilation was maintained throughout the induction. Classic LMA (Laryngeal Mask Airway) No. 2.5 was inserted and anaesthesia was maintained with infusion of Propofol at 100 to 150μg/kg/min. Spontaneous ventilation was maintained throughout the surgery. At the end of surgery, LMA was removed and patient recovered from anaesthesia uneventfully. His postoperative period was uneventful, grafts were taken up well, wounds were healthy, there were no new neurological problems and patient was discharged home on seventh postoperative day.

CASE 3

A six year old (weight 20 kg) male patient presented with complaints of spots over sun exposed parts of the body since nine months of age and swelling over dorsum of nose since one month. Those spots were of varying size and progressively increasing in number. There was no significant past medical and surgical history. There was no history of similar illness in his family members. Physical examination findings and laboratory investigation reports were within normal limits. Three pea sized warty black nodule were noted over dorsum of nose which was firm and tender. Multiple black maculopapular lesions were present over the sun exposed areas. Excision of nodule and skin grafting was planned.

After overnight fasting, Ketamine 75mg and Atropine 0.4mg was given intramuscularly in preparation room. Patient was shifted to operation theater after he was adequately sedated. Venous access was established with 22 G cannula. Ketorolac 10 mg was administered intramuscularly. After preoxygenation with 100% oxygen, patient was induced with Propofol 50 mg. Fentanyl 10μg was given intravenously. Classic LMA No. 2 was inserted and anaesthesia was maintained with infusion of Propofol at 100 to 200 μg/kg/min. Analgesia was supplemented with local infiltration of 0.25% Bupivacaine. Throughout the surgery, spontaneous respiration was preserved and the vital parameters were within normal limits. At the end of surgery, LMA was removed and recovery was timely and uneventful. Following surgery, wounds were healthy and there were no new neurological problems. On the second postoperative day, he was discharged home.

DISCUSSION

Halothane has possible genotoxic side effects in patients with deficient DNA repair.[4] Other inhalational agents like Sevoflurane and Isoflurane were also demonstrated to induced DNA damage in human lymphocytes.[5] Moreover, use of volatile agents may cause transient worsening of neurological symptoms and can derange Nucleotide Excision Repair (NER). Minimum usage of muscle relaxants with monitoring of neuromuscular blockade is recommended since these patients are sensitive to muscle relaxants due to the neuronal dysfunction and muscle atrophy. There is a possibility of difficult endotracheal intubation and prolonged effect of muscle relaxants. So, total intravenous anaesthesia is considered to be more appropriate.[6-8] In the above cases, surgery was planned under total intravenous anaesthesia with the aim to avoid volatile agents and muscle relaxants, but in the first case, patient became apnoeic after administering Midazolam and Pethidine, mask ventilation was very difficult and patient desaturated. So the patient was immediately intubated and muscle relaxants had to be used. Immature brain development and regression from normal brain development has been shown in these patients which increased with advancing age, suggesting a chronic progressive neurologic degenerative disease.[9] Apnoea in the first case may be due to increased sensitivity of these patients to the synergistic effect of opioids and benzodiazepines. To avoid these complications, in the second and third cases, we avoided concomitant administration of a benzodiazepine and pethidine. To reduce the dose requirement of opioids, we supplemented analgesia with Diclofenac in second case and Ketorolac together with infiltration of wound with Bupivacaine in third case. Patients maintained spontaneous ventilation throughout the procedure with uneventful recovery. We could also avoid laryngoscopy and intubation in second and third cases.

To conclude, patients with xeroderma pigmentosum may be very sensitive to the synergistic effect of benzodiazepines and opioids and multimodal analgesia with the use of nonsteroidal anti inflammatory agents and local anaesthetic agents may be beneficial. Total intravenous anaesthesia and avoiding muscle relaxants when feasible may be beneficial. Studies involving larger number of patients would be helpful to discover more about the optimal anaesthetic management of patients with xeroderma pigmentosum.

REFERENCES

1. Kraemer KH, Lee MM, Scotto J. Xeroderma pigmentosum: cutaneous, ocular, and neurologic abnormalities in 830 published cases. *Arch Dermatol* 1987; 123: 241-50.
2. Van Steeg H, Kraemer KH. Xeroderma Pigmentosum and the role of UV-induced DNA damage in skin cancer. *Mol Med Today* 1999; 5: 86-94.
3. Butler MG, Hayes BG, Hathaway MM, Begleiter ML. Specific genetic diseases at risk for sedation/anesthesia complications. *Anesth Analg* 2000; 91: 837-55.
4. Reitz M, Lanz E. DNA strand breaks in cells with DNA repair deficiency after halothane exposure in vitro. *Arzneimittelforschung* 1993; 43: 418-20.
5. Karabyk L, Sardas S, Polat U, Kocabas NA, Karakaya AE. Comparison of genotoxicity of sevoflurane and isoflurane in human lymphocytes studied in vivo using the comet assay. *Mutation Res/ Genetic Toxicol Environ Mutagen* 2001; 492: 99-107.
6. Ryohei M, Taro N, Tetsuya K, Shosuke T. Anesthesia for a patient with xeroderma pigmentosum. *Masui* 2007; 56: 439-41.
7. Yoshiki M, Hitoshi I, Mioko O, Eichi N, Yasufumi A, Akiyoshi N. Anesthesia for a patient with xeroderma pigmentosum. *Japanese J Anesthesiol* 2002; 51: 169-71.
8. Masako S, Tetsuro K, Reiko U, Takeshi S. Anesthetic management of a patient with xeroderma pigmentosum. *Masui* 2006; 55: 215-7.
9. Mimaki T, Tagawa T, Tanaka J, Sato K, Yabuuchi H. EEG and CT abnormalities in xeroderma pigmentosum. *Acta Neurol Scand* 1989; 80:136-41.