

CASE REPORT

Anesthetic management of a case of alkaptonuria

Pratheeba. N, DNB*, Neha Singh, MD*, Ranjan R.V, DA, DNB**, T. R. Ramachandran, MD***, Sageev Koshy George, MD***, Ramya GS, MD****

Assistant Professor, **Associate Professor, *Professor, ****Postgraduate Resident
Department of anesthesiology, Pondicherry Institute Of Medical Sciences , Pondicherry*

Correspondence: Dr. Pratheeba Natarajan, Department of Anesthesiology, Pondicherry Institute of Medical Sciences, Kanagachettikulam, Pondicherry 605014 (India); Cell: 09894919554; e-mail: pratheeba.rk@gmail.com

ABSTRACT

Alkaptonuria is a rare inherited autosomal recessive disorder of metabolism due to deficiency of homogentisic acid oxidase. This results in deposition of homogentisic acid in almost all the collagenous structures of the body leading to progressive multisystem involvement (alkaptonuric ochronosis) and poses a big challenge in anesthetizing such patients. We present one such case posted for total hip replacement and its successful management under general anesthesia.

Key words: Alkaptonuria; Ochronosis; Homogentisic acid oxidase; Ochronosis

Citation: Pratheeba N, Singh N, Ranjan RV, Ramachandran TR, George SK, Ramya GS. Anesthetic management of a case of alkaptonuria. *Anaesth Pain & Intensive Care* 2013; 17(2):179-181

INTRODUCTION

Alkaptonuria is an autosomal recessive inherited disorder of tyrosine metabolism in which there is a deficiency of homogentisic acid oxidase.¹ This leads to the deposition of a polymer of homogentisic acid, an ochre colored pigment in the cartilages and connective tissue.² It is characterized by a triad of homogentisicaciduria, ochronosis and arthritis.²

Alkaptonuria occurs about 1 in 250000 to 1 in 1000000, the incidence being much higher in Slovakia upto 1 in 19000.³ The most common clinical manifestations of this disorder are severe arthritis and pain, restrictive lung disease, coronary artery disease, valvular heart disease, nephrolithiasis and other renal complications³.

Therefore the successful anesthetic management of these patients depends on the thorough evaluation and optimization of comorbidities, to prevent the associated perioperative complications.

CASE REPORT

A 50 yr old male patient came to our hospital with complaints of pain in the left hip, low backache and difficulty in walking since one year for which he was on tablet diclofenac sodium 50 mg thrice daily. He was a known hypertensive since 2 years, controlled with tablet atenolol 25 mg once a day. On examination, patient was conscious and oriented with a heart rate of 80/min and blood

pressure of 130/80mmHg. Examination of cardiovascular and respiratory systems was normal. Black pigmentation of the sclera was observed along with auricular cartilage thickening. Airway examination revealed Mallampati Class II with adequate mouth opening and normal thyromental distance and minimal restriction of neck movements. Spine examination revealed narrowed intervertebral disc spaces. Investigations revealed hemoglobin of 13mg/dL, biochemical reports were within normal limits. Chest x-ray and 12 lead electrocardiograph were normal. A lumbosacral X-ray revealed sclerosis and narrowing of all the disc spaces (Fig 1). These x-ray findings along with black pigmentation of sclera and auricular cartilage thickening made us suspect a metabolic abnormality in the patient. On further detailed questioning, the patient reported a blackish discoloration of urine and staining of the undergarments which prompted us to do a urinalysis which revealed urine discoloration when exposed to air. A diagnosis of ochronosis of the left hip with severe secondary osteoarthritis was made. The patient was accepted for cemented total hip arthroplasty on the left side under ASA functional class II. A general anesthesia with controlled ventilation was planned. A written informed consent was obtained and the antihypertensive was continued on the morning of surgery. Patient was kept nil oral for 8 hours.

In the OR, an 18G intravenous cannula was placed in

anesthetic management of a case of alkaptonuria

the left forearm. Standard monitors EKG, SpO₂ and NIBP were instituted. Difficult intubation cart was kept ready. After preoxygenation for three minutes, patient was premedicated with 100 mcg fentanyl. Anesthesia was induced with inj. propofol 100 mg and atracurium 25 mg was given to facilitate intubation. Laryngoscopy revealed a Cormack-Lehane grading of II which improved to grade I with external laryngeal manoeuvre. The trachea was intubated with 8.0 mm endotracheal tube.

Anesthesia was maintained with isoflurane in oxygen and nitrous oxide and atracurium. Analgesia was maintained by bolus doses of fentanyl. Surgery lasted for two and half hours. Patient was reversed with neostigmine and glycopyrrolate and extubated once he was fully conscious.

DISCUSSION

The term alkaptonuria was first described by Boedeker in 1891.³ Virchow in 1866 coined the term 'ochronosis' meaning yellow disease in Greek, because the accumulated pigment in the connective tissue was ochre coloured.⁴

Ochronosis is of historical importance, as it was one of the first conditions in which Mendelian recessive inheritance was proposed and also became the corner stone of the fundamental concept of inborn errors of metabolism.⁵

Alkaptonuria is an autosomal recessive inherited genetic disorder of tyrosine metabolism. The deficiency of the enzyme homogentisic acid oxidase results in the accumulation of homogentisic acid (HGA). Initially, it is excreted by the kidneys and that which is not excreted through urine is polymerized into ochre coloured pigment which is deposited within the cartilage and collagenous structures. This is known as endogenous ochronosis.⁶ There is no specific therapy for these patients, however dietary protein reduction and ascorbic acid intake reduces urinary excretion of homogentisic acid and possibly reverse bone abnormalities.⁵

The clinical manifestations per se determine the guidelines for the perioperative management of the patient with ochronosis as there are no preset guidelines. The anesthetic technique is dependent on the evaluation and optimization of the systemic dysfunction.^{7,8}

The pigment deposition in the cartilages of the skeletal system results in severe pain as a result of brittleness, fragmentation and destruction. These changes stress the importance of proper padding and careful positioning of the patient.⁹ Degenerative changes in the spine comprise of disc calcification, narrowing of intervertebral disc spaces and in extreme cases may lead to cord compression, which makes preoperative neurological examination mandatory. Difficulty in performing regional blocks is expected in these patients (as evident from the x-ray of the spine of our patient), hence regional anesthesia was deferred and

general anesthesia was contemplated.

The cartilaginous tissue of the respiratory system may also be affected by ochronosis with heavy deposition of the pigment in the laryngeal, tracheal and bronchial cartilages resulting in hoarseness, dyspnea and difficult airway access.⁴ Hoarseness may indicate narrowing of glottis and may necessitate a smaller sized tube. Deposition of pigment and the degenerative changes in the cervical spine may result in the restriction of motion cervical spine further adding to the difficulty in airway management. ⁴Our patient had minimal restriction of the cervical spine, laryngoscopic grading was Cormack Lehane grade II. Intubation was done in the second attempt successfully with external laryngeal manoeuvre and gum elastic bougie. Involvement of the cartilaginous structures of the respiratory system may cause restrictive pathology signaling the need for a thorough preoperative pulmonary function analysis.⁸



Figure 1: X-ray LS spine (PA and lateral views) showing sclerosis of all disc spaces

A spectrum of cardiovascular abnormalities such as calcified and stenotic valves, atherosclerosis and conduction blocks mandate an extensive evaluation of the cardiovascular system, thereby helping us in the tailoring of the anesthetic technique and also in deciding about invasive monitoring usage.¹⁰ Our patient did not have any of the above mentioned cardiovascular abnormalities except for hypertension which was under control, hence the need for invasive monitoring did not arise. Excessive pigment

deposition in the nails may interfere with pulse oximetry.²

Renal dysfunction as a result of inadequate excretion of HGA often results in renal calculi, UTI, obstructive uropathy and eventually renal failure, which was not seen in our patient.¹¹ Our patient was on non-steroidal anti-inflammatory agents for nearly a year for chronic pain, so renal function tests, electrolytes and coagulation profile were done, as long term usage may result in platelet dysfunction, prolongation of bleeding time and gastrointestinal bleed.¹² The coagulation profile may indicate if central neuraxial blockade can be safely given, but regional anesthesia in this patient has its own demerits.

CONCLUSION

Although rare, the anesthetic management of a patient with alkaptonuric ochronosis can be complex and challenging. Numerous literature is available which describe the clinical manifestations of this disease but very minimal information is available regarding the anesthetic management. Since there are no set guidelines for the anesthetic management, the systemic involvement should determine the anesthetic plan. A thorough preoperative evaluation, optimization with due anesthetic considerations for musculo-skeletal and collagen vascular disorders may be beneficial in the management of these patients.

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Resources for Researchers

Two very helpful manuals have been developed by the WHO Regional Office for the Eastern Mediterranean.

- Manual for editors of health science journals, available at; <http://www.emro.who.int/emame/index.htm>
- A practical guide for health researchers” (WHO Regional Publications Eastern Mediterranean Series 30) by MF Fathalla and MMF Fathalla, available at; <http://whqlibdoc.who.int/emro/2004/9290213639.pdf> .

This resource contains guidance on writing manuscripts for publication as well as guidance on other research-related activities.

The two manuals together provide a lot of solid practical advice that researchers can use to write better articles, and that editors can use to produce stronger journals.