Alkaptonuria is a rare inherited genetic disorder of tyrosine metabolism characterized by the triad of homogentisic aciduria, ochronosis, and arthritis.[1] The condition is rare, affecting one in 250,000 to one million people worldwide.[2] The clinical manifestations include a history of urine turning dark on standing and on alkalization due to elimination of excessive amounts of homogentisic acid (HGA); ochronosis, a blue-black pigmentation of connective tissues and cartilages; and arthritis of weight bearing joints.[3-5] The most common clinical manifestations of ochronosis involve the musculoskeletal, respiratory, airway, cardiovascular, genitourinary, cutaneous, and ocular systems [Table 1]. We report the successful perioperative anesthetic management of an alkaptonuric patient with multiple comorbidities. Patient’s consent has been obtained for presenting this case report.

**Case Report**

A 56-year-old, 45 kg lady, with complaints of pain and discharge from the right hip, was scheduled for revision total hip replacement (THR). A review of her medical history revealed alkaptonuria, hypothyroidism, rheumatoid arthritis, hypertension, diabetes mellitus, and Pott’s spine with disc prolapse. We report the perioperative anesthetic management of a 56-year-old alkaptonuric patient, with multiple comorbidities scheduled, for revision total hip replacement. A review of her medical history revealed alkaptonuria, hypothyroidism, rheumatoid arthritis, hypertension, diabetes mellitus, and Pott’s spine with disc prolapse. We want to highlight the need of thorough preoperative evaluation in patients of alkaptonuria, as it is associated with multiple comorbidities. The systemic involvement should determine the anesthetic plan. Caution should be exercised during positioning to prevent injury to the joints and the spine.
pregabalin 150 mg twice a day and methylcobalamin were started preoperatively.

Investigations including hematological (hemoglobin, 12.6 g/dL), renal, liver functions, thyroid function, and coagulation profile were normal. Chest X-ray demonstrated cardiomegaly (cardio-thoracic ratio of 0.6) and the 12-lead electrocardiogram (ECG) was normal. An echocardiogram revealed a left ventricular ejection fraction of 50% without any regional wall motion abnormalities, left ventricular dysfunction, or aortic valve involvement. Pulmonary function tests showed a FVC of 62%, FEV1 of 57%, PEFR of 79%, and FEV1/FVC of 93% of the predicted values. Ultrasound abdomen showed mild hepatomegaly with fatty liver, cholelithiasis, and bilateral mild hydrenephrosis.

The patient was accepted for revision THR under ASA functional class 3, explaining the high perioperative risk due to multiple comorbid illnesses. She was advised to continue all medications till the morning of surgery except metformin. Steam inhalation and preoperative incentive spirometry were also advised. Morning serum electrolytes (including calcium), blood sugar, urine ketones, and sugar were advised. General anesthesia with endotracheal intubation and controlled ventilation was planned.

In the operating room, after application of ECG, pulse oximeter (SpO2), and noninvasive blood pressure (NIBP) monitors, the intravenous line was secured. Difficult airway cart, including a gum elastic bougie and intubating laryngeal mask airway, was kept ready. After preoxygenation, anesthesia was induced with intravenous fentanyl 100 mcg and propofol 70 mg. After ensuring optimal bag and mask ventilation, neuromuscular blockade was achieved with atracurium 25 mg to facilitate tracheal intubation. The laryngoscopic view was Cormack and Lehane grade III which improved slightly with optimal external laryngeal manipulation and trachea was intubated with the help of gum elastic bougie, after three attempts. Capnography and temperature monitoring were initiated. Anesthesia was maintained with isoflurane in oxygen and nitrous oxide with neuromuscular junction monitor-guided top up doses of atracurium. Fentanyl bolus of 20 mcg was administered when required (total dose 200 mcg). The surgery lasted for 3 h and vitals were stable all through. The blood loss was estimated to be 900 mL, and it was replaced with 1 L of lactated ringer solution, 500 mL hydroxyethyl starch 6%, and 350 mL of packed red blood cells. Intraoperative urine output was 250 mL, and blood sugar level was 107 mg/dL and 350 mL of packed red blood cells. Intraoperative urine output was 250 mL, and blood sugar level was 107 mg/dL and 350 mL of packed red blood cells. At the end of procedure, the neuromuscular block was reversed and trachea extubated after return of protective airway reflexes. The patient was shifted to a high dependency unit for observation. Postoperative hemoglobin was 10.2 g/dL. All preoperative drugs were continued and intravenous paracetamol 500 mg thrice a day was advised for pain control. For breakthrough pain intravenous tramadol (50 mg) was advised. Next day, the patient was shifted to the ward and advised regular physiotherapy with follow-up in the orthopedics clinics.

**Discussion**

Alkaptonuria is a rare inherited genetic disorder of phenylalanine and tyrosine metabolism. A toxic tyrosine byproduct HGA accumulates in blood and is excreted in urine in large amounts due to a lack of enzyme homogentisic acid oxidase. Excessive HGA accumulates in the body and binds irreversibly to collagen. Endogenous ochronosis results from the deposition of this brown-colored pigment in the cartilaginous and musculoskeletal system in the body. There is no cure for this disorder and medical treatment is based on its symptomatology, comprehensive preoperative evaluation, and discussions of risk are essential while caring for these patients.

The presence of alkaptonuria along with multiple comorbidities made the perioperative management of our patient challenging.
Care of the patient with alkaptonuric ochronosis is complex and challenging. There are no formal guidelines for the perioperative management of the patient with ochronosis. Organ and tissue involvement will influence the anesthetic technique. A thorough evaluation of the type and severity of systemic dysfunction is essential before administration of anesthesia.

The deposition of pigments makes the cartilage of the joints prone to destruction and makes the joints painful. The cartilage of the airway and respiratory system too may be affected in ochronosis. Heavy deposition of the pigment in the laryngeal, tracheal, and bronchial cartilages may result in hoarseness, dysphagia, and difficult airway management. In our patient, the laryngeal view did not improve much with optimal external laryngeal manipulation, probably due to associated rheumatoid arthritis and pigment deposits in the laryngeal cartilages. Restrictive pulmonary disease was present in the case described which may have resulted from ochronotic fibrosis of the costal cartilages. We optimized the patient with incentive spirometry prior to the surgery.

Degenerative changes occur in spine, vertebral discs, and some neurological deficit may be present. Our patient had some joint deformity due to cartilage destruction and thus difficulty was faced during positioning. The patient was positioned carefully, and pressure points were adequately padded to prevent any undue pressure on the diseased joints. Our patient had a history of Pott’s spine and history of prior spine surgery. In the patient of alkaptonuric ochronosis, the dura and arachnoid membrane are made vulnerable by HGA and could be damaged. The central neuraxial block was thus not preferred as the technique of choice. Such patients may be on long-term aspirin or NSAID therapy which may result in platelet dysfunctions, prolonged bleeding time, and gastrointestinal bleeding.

Cardiovascular abnormalities such as calcified and stenotic valves, generalized atherosclerosis, and conduction blocks may also be associated with ochronosis. A thorough preoperative evaluation of the cardiovascular status is essential. The accumulation of HGA predisposes the patient to the formation of renal calculi which in turn can be responsible for frequent urinary tract infections, obstruction, and potentially failure. Our patient did not have any clinical symptoms related to kidney, but ultrasound revealed hydronephrosis. Renal evaluation should be done and dosages should be modified according to the renal dysfunction. Abnormalities in renal tubular function may result in inadequate excretion of HGA leading to a higher plasma level and thus increased depositions in tissues. This may lead to increased severity of various system dysfunctions. Associated comorbidities such as diabetes and hypertension, as seen in our patient, too increase the chance of renal compromise in the perioperative period. Inability to monitor regional oxygen saturation, due to pigment deposition, has been reported in a patient with alkaptonuria. Caution should be exercised in pulse oximeter monitoring of patients with excessive pigment deposition.

To conclude, alkaptonuric patients may have multiple associated comorbidities mandating a thorough preoperative evaluation. The impact of involvement of various systems should be considered before deciding the anesthetic technique to be used.

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