

Ultrasound-guided neural blockade in Proteus syndrome

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Summary: Proteus syndrome is a rare genetic disorder first described in 1979 and named after Proteus, a Greek demigod who was capable of changing his form to avoid capture. The incidence is < 1:1 000 000, but can be expected to be slightly higher in the surgical population, as these patients often present for repeat procedures. The disorder is characterised by sporadic and progressive overgrowth of tissue of any origin. Normal anatomy usually becomes distorted and serious functional and cosmetic sequelae may ensue. Regular anaesthetic interventions are required for diagnostic and therapeutic procedures, often to correct deformities related to overgrowth, tumour excision and otolaryngological procedures. Literature relating to the anaesthetic management of patients with Proteus syndrome is limited to case reports describing instances of general anaesthesia. Complications of general anaesthesia secondary to respiratory tract abnormalities appear prevalent. Regional anaesthesia is often used when respiratory compromise is anticipated due to any cause. Despite this, current guidelines suggest that regional anaesthesia be avoided in patients with Proteus syndrome, due to the gross anatomical variance and the high incidence of vascular abnormalities in these patients. The use of ultrasound-guided neural block enables practitioners to distinguish nerves from vascular structures and other tissues. It helps avoid neural injury during needle placement and improves success rate. This case report is the first to demonstrate the successful use of an ultrasound-guided regional anaesthetic technique in a boy requiring surgery to his right forearm.

Keywords: anaesthesia, local, nerve block, Proteus syndrome, ultrasound

Case presentation

A four-year-old boy (15 kg) with Proteus syndrome required debulking surgery of soft tissue overgrowth of his right forearm. This overgrowth appeared adipose in nature and was so excessive that he was unable to use the fingers on his right hand to grasp. To correct this, a staged debulking procedure was planned at an academic orthopaedic centre.

He had been diagnosed with Proteus syndrome as an infant, following disproportionate overgrowth of especially his right arm. It was noticed in the first three months of his life and appeared to accelerate over the next few years. The soft tissue overgrowth of the right arm involved the entire arm and included part of the thoracic wall. He also had overgrowth of the left forearm. He had marked lipodystrophy over the thoracic cage and a cerebriform nevus over the palmar surface of the left hand. Despite being microcephalic, he had normal neurodevelopmental milestones. There was no family history of genetic disease. He had had one previous uneventful general anaesthetic for debulking of the same arm.

Plain film X-ray of the arms showed distortion of phalanges as well as the carpal and metacarpal bones bilaterally, slight bowing of the right radius and ulna with normal humeri bilaterally. An MRI scan revealed a structurally normal brachial plexus on the right, surrounded by excess tissue which appeared to be adipose in nature. Vascular structures were normal, as was his chest X-ray.

Oral paracetamol 225 mg was administered one hour preoperatively. Inhalational induction was performed with sevoflurane/oxygen/nitrous oxide and IV access secured. After ensuring adequate bag-mask ventilation, fentanyl 30 µg, propofol 30 mg and cis-atracurium 2.25 mg were administered to facilitate intubation. No airway abnormalities were observed during laryngoscopy and intubation was easily performed using a size 5.0 cuffed endotracheal tube.

Maintenance was with isoflurane, oxygen 40% and air. Standard American Association of Anesthesiologists monitoring was used.

A supra-clavicular brachial plexus block was performed using a 50 mm Arrow Stimu-quick needle with ultrasound guidance (Ezono, 13-6 MHz linear probe). Adequate imaging of landmark structures was obtained. Bupivacaine 0.25% was used and 8 ml injected with adequate local anaesthetic spread visualised around the brachial plexus. A further 2 ml was injected over the medial upper arm for tourniquet pain. At the end of the procedure, diclofenac 12.5 mg was given rectally.

The procedure lasted three hours with no additional analgesia required. A tourniquet was used for part of the procedure. The total tourniquet time was 46 minutes. On emergence the child was calm with no pain. Routine postoperative analgesia was prescribed (oral paracetamol 225 mg 6-hourly, ibuprofen 75 mg 8-hourly). No postoperative opioids were required.

Ethical approval to publish this case was obtained from the Ethics Committee of the Faculty of Health Sciences, University of the Free State in Bloemfontein, South Africa. Informed consent was obtained from the child's mother.

Discussion

Proteus syndrome typically presents with sporadic and progressive overgrowth of tissue of any origin, with lesions occurring in a mosaic distribution.¹⁻³ It is agreed that the syndrome is likely due to a post-zygotic somatic mutation which survives by mosaicism, and is fatal to the conceptus when constitutive.^{1,4} Recent work has shown an association with a mutation in the AKT1 oncogene which encodes for AKT kinase, an enzyme responsible for mediating processes such as cellular proliferation and apoptosis.¹

Owing to the phenotypic heterogeneity as well as the rarity of this syndrome, controversy surrounding the clinical diagnosis remains.^{2,3} Clinical overlap with other overgrowth entities exists and many suggest that Proteus syndrome should be seen as part of a spectrum of similar disorders.¹⁻³ Recent guidelines recommend the use of stringent diagnostic criteria. Advocates cite different aetiologies and clinical courses as reasons for precise diagnosis.^{2,3,5} Indeed, when these criteria were matched to reported cases of Proteus syndrome, it was found that fewer than 50% of these patients actually had Proteus syndrome.⁵

This syndrome poses unique challenges to the anaesthetist and very few case reports are available in the literature to guide our practice.⁶⁻¹¹ Most commonly bone, connective tissue, adipose tissue and vasculature are affected, but any tissue can be involved.⁶ The systemic manifestations relevant to anaesthesia are summarised in Table 1.

Airway problems have been described in many case reports^{6,8,9,12} and a thorough airway assessment is necessary. Airway abnormalities, such as abnormal facial architecture, may be obvious. This would complicate bag-mask ventilation. However, unanticipated airway complications, which can be life-threatening, have been described.^{7,9} Equipment for a difficult airway should be available immediately whenever a patient with Proteus syndrome is to receive anaesthesia.^{9,10} For patients with preoperative symptoms or signs of upper airway obstruction, sedative premedication and perioperative opioids should be avoided and the patient should be nursed in a high care unit postoperatively.

Pulmonary manifestations are of particular interest and perioperative respiratory failure has been described.¹³ Careful pulmonary interrogation and investigation are vital. Pulmonary manifestations can be classified as primary or secondary.^{2,3,14}

Primary (parenchymal) manifestations include cystic lung changes and expanding multi-lobular bullae.¹⁴ Mucous retention and atelectasis can be expected. This is known to complicate as progressive emphysematous pulmonary disease.^{13,14} Pulmonary venous varicosities can occur, and may lead to airway obstruction or rupture with life-threatening haemoptysis.¹⁴ Secondary manifestations can result from thoracic cage abnormalities. The incidence of kyphoscoliosis in patients with Proteus syndrome is as high as 50%,¹⁵ and can result in severely restrictive lung function, which could mask an obstructive picture caused by emphysematous disease.

Cases with radiological evidence of primary pulmonary disease in asymptomatic individuals have been reported and poor mobility could also mask respiratory symptoms.^{13,14} Severe thoracic cage abnormalities could hide underlying primary disease on X-ray.¹³ An argument could be made that all patients should have a preoperative chest X-ray, and if any doubt arises a high-resolution CT of the chest should be performed. Nitrous oxide should be avoided in confirmed cases of cystic lung disease.¹³

If pulmonary manifestations are suspected, vigorous postoperative bronchial toilet and early extubation and ambulation are required to avoid mucous retention, atelectasis and respiratory compromise.¹³

Primary cardiac manifestations are not regarded as a hallmark of this syndrome.^{2,3} There has been a case report of cardiomyopathy and a myocardial mass in a patient with Proteus syndrome, but concerns as to whether this patient met the diagnostic criteria have been raised.⁵ A small patent ductus arteriosus has been reported.¹¹ Cardiovascular illness secondary to pulmonary disease occurs and pulmonary hypertension should be excluded.

The vascular system itself is often affected and deep venous thromboses and pulmonary emboli are common.^{2,3,5,16,17} This is likely due to vascular malformations, distorted anatomy and decreased mobility. Hypercoagulability per se has not been described.¹⁶ Consensus has not been reached regarding perioperative anticoagulant prophylaxis and should be considered on a patient-to-patient basis.^{2,3,17} Careful postoperative monitoring for thromboses and early ambulation should be encouraged.¹⁷

Nervous system manifestations are quite common but usually asymptomatic and often related to skeletal abnormalities. Seizure disorders and mental retardation are often related to underlying structural abnormalities. Intracranial neoplasms have been described.⁵ Dural sinus thrombosis has been reported¹⁸ and obstruction to dural venous drainage must be avoided and patients kept well hydrated. Spinal abnormalities (including skeletal abnormalities and vascular malformations) are highly prevalent^{2,3,5} and neuraxial techniques can be technically difficult and potentially hazardous. Ultrasound-guided placement of an epidural catheter without complication has been described.⁹

Abdominal problems are varied. Gut wall hamartomas can cause gastric outlet obstruction.³ Splenomegaly can occur.⁹ Renal abnormalities, in both structure and function, have been reported. This may be related to local anatomical obstruction

Table 1: Systematic considerations in Proteus syndrome of importance for the anaesthesiologist

System	Consideration	Suggestion
Airway	Difficult bag-mask ventilation; obstruction; failed intubation	Formal preoperative evaluation; difficult-airway aids in theatre
Respiratory	Severe obstructive and/or restrictive disease; pulmonary haemorrhage	Functional assessment; arterial blood gas analysis; high-resolution CT; avoid intubation and ventilation
Cardiovascular	Venous thromboembolism; fatal pulmonary embolism	Early ambulation; careful postoperative monitoring; anticoagulation on individual basis
Central nervous	Venous stroke; neoplasms	Support venous drainage; adequate hydration
Gastrointestinal	Gastric outlet obstruction	Rapid-sequence intubation
Genitourinary	Functional impairment; diabetes insipidus	Formal preoperative evaluation
Miscellaneous	Any organ system can be involved	Evaluate on a case-to-case basis; not at risk for malignant hyperthermia

causing hydronephrosis, urinary reflux with recurrent infections or possibly intra-parenchymal processes. The latter may also be responsible for nephrogenic diabetes insipidus.^{5,19}

Owing to the variable presentation of patients with Proteus syndrome, patients requiring anaesthesia need to be evaluated on an individual basis. Despite anticipated problems with general anaesthesia, it has generally been preferred over regional techniques. Although muscular overgrowth occurs, Proteus syndrome is not regarded as a muscular disease or a malignant hyperthermia risk factor.^{6,10} The high incidence of vascular, skeletal and soft tissue abnormalities has made the placing of neural blocks difficult. However, the growing experience with ultrasound-guided regional anaesthesia could change this obstacle as structures can now be visualised and neural blocks safely performed.

This case study has demonstrated how, despite distorted anatomy, a young patient with Proteus syndrome requiring forearm surgery successfully received a supraclavicular block, using an ultrasound-guided technique for needle placement. We recommend that practitioners experienced in ultrasound-guided neural blockade perform regional anaesthesia in selected patients with Proteus syndrome.

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