Hyperbaric oxygen treatment for intrauterine limb ischaemia: A newborn in the chamber

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Abstract

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Intrauterine limb ischaemia is a rare condition that may have devastating results. Various treatments are reported in the literature; however, results are not always promising and amputations may be required for some patients. Post-natal hyperbaric oxygen treatment (HBOT) may be a useful treatment option for the salvage of affected limbs. A patient who was born with total brachial artery occlusion and severe limb ischaemia was referred for HBOT. The patient underwent the first HBOT session at her 48th hour of life. A total of 47 HBOT sessions were completed (243.1 kPa [2.4 atmospheres absolute], duration 115 minutes being: 15 minutes of compression; three 25-minute oxygen periods separated by five-minute air breaks; and 15 minutes of decompression), four in the first 24 hours. Full recovery was achieved with this intense HBOT schedule combined with anticoagulation, fasciotomy and supportive care. The new-born tolerated HBOT well and no complications or side effects occurred. To the best of our knowledge, our patient is one of the youngest patients reported to undergo HBOT.

Introduction

Intrauterine limb ischaemia, also called neonatal gangrene, is a rare condition that may have devastating results. A definitive management algorithm has not yet been defined. Several treatments including thrombolysis, systemic anticoagulation and surgical or radiological thrombectomy have been reported, however amputation may be inevitable.[1] Hyperbaric oxygen treatment (HBOT) may be a useful option for the salvage of affected limbs. The case is presented of a neonate born with severe intrauterine limb ischaemia and successfully treated with HBOT combined with anticoagulation, fasciotomy and supportive care.

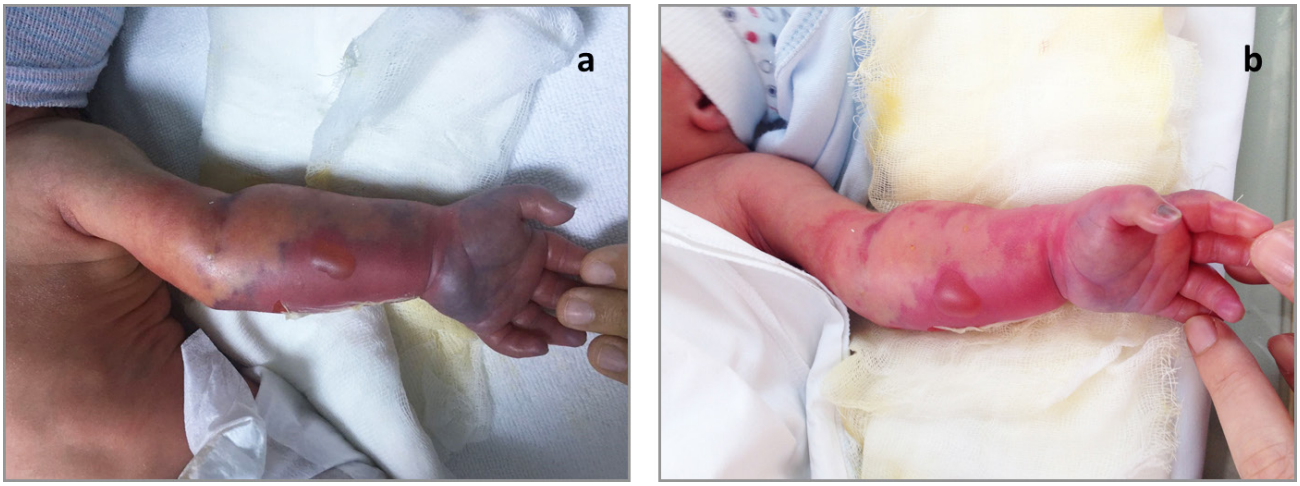
Case report

A 2,960 g female baby was born to a gravida two para one mother at 39 weeks of gestation via caesarean section due to breech presentation. The 23-year-old mother was an undocumented migrant unknown to medical services and had not received any antinatal care. She did not report any medical conditions and her physical examination was unremarkable. The baby's vitals were normal but a marked cyanosis of the left forearm was noted at delivery. Spontaneous movement and reflexes of this extremity were absent. Heparin infusion was started immediately but there were no improvements. Amputation was considered and the patient was transferred to our hospital at age 36 hours for the intervention. She was admitted to neonatal intensive care in order to monitor for possible heparin-related or further thromboembolic problems.

Upon arrival, cyanosis was evident from the midline between elbow and shoulder to the tip of the fingers (Figure 1a). The arm was cold up to the shoulder and flaccid. There were blisters some of which were sloughing on the arm and hand. Peripheral pulses were non-palpable. Colour Doppler revealed the absence of flow in brachial, radial and ulnar arteries, indicating a thrombus in the axillary artery. Computed tomography angiography confirmed the occlusion. Venous flow was normal. The patient was evaluated by the vascular surgeons and neither thrombectomy nor recombinant tissue plasminogen activator (rtPA) were found appropriate due to the risks involved and the delay. A shoulder disarticulation was proposed.

Meanwhile the patient was referred to the hyperbaric medicine department for HBOT. After careful evaluation she underwent her first treatment at her 48th postnatal hour. Significant improvement was not observed after the first session but since the baby was not ready for amputation yet, a second HBOT session was given six hours later. Warming

Figure 1
Patient's arm at presentation (a) and after the second HBOT session (b). Restoration of reperfusion can be observed clearly



and a pinkish colour change was observed in the ischaemic extremity during this session and persisted afterwards (Figure 1b). As evidence of tissue perfusion was noted, surgery was postponed and further HBOT was planned.

During the first day, she underwent two more HBOT sessions with six-hour intervals between. For the following eight days HBOT was given every eight hours. Ischaemia regressed gradually. Afterwards, the patient underwent HBOT twice a day for a week and then once daily for five more days. HBOT was administered at 243.1 kPa (2.4 atmospheres absolute) for a total of 115 minutes. Treatment involved 15 minutes of compression; three 25-minute oxygen periods separated by five-minute air breaks; and 15 minutes of decompression. On the ninth day, plastic surgeons performed fasciotomy on the forearm and hand on suspicion of compartment syndrome although there were no suggestive signs (Figure 2). Intravenous heparin infusion (20 $mg \cdot kg^{-1} \cdot hour^{-1}$) was changed to subcutaneous enoxaparin (1.8 $mg \cdot kg^{-1} \cdot day^{-1}$) at the end of one week. Petrolatum based gauze dressings were applied daily to all wounds. At the end of 47 sessions HBOT was stopped as tissue perfusion was restored and significant healing was observed in the fasciotomy wound. No side effects or complications related to HBOT were recorded. Physiotherapy was started in the second week. Antibiotic therapy and fluid replacement were provided during the course of treatment.

Etiological studies were performed after admission. Plasma protein C, protein S, antitrombin III, and homocysteine levels were within the normal ranges for neonates. Screening for Factor V Leiden, methylenetetrahydrofolate reductase and prothrombin 20210 gene mutations were negative. Antiphospholipid and anticardiolipin antibodies were also normal. Echocardiography did not show any pathological findings. All metabolic studies were within normal limits.

Eventually, the size of the volar fasciotomy wound and the wound on the dorsal forearm reduced more than 75%. The hand wounds closed totally (Figure 3). Skin grafting was not necessary. On her repeat Doppler studies, collateral circulation was visualised. The arm and hand gained motor function. Arm development was normal and shoulder to elbow and elbow to wrist length did not differ from the opposite extremity. Physical therapy was planned for slight ulnar deviation of the hand. The patient was discharged on the 48th day of life with daily enoxaparin to be given weekly. All wounds closed in the first month after discharge. No wound or ischaemia related problems occurred during six months follow up.

Discussion

HBOT is a non-invasive treatment modality where patients breathe 100% oxygen under pressure higher than 101.3 kPa (one atmosphere absolute). It increases the dissolved oxygen content in the blood plasma and so provides hyperoxygenation to tissues that have increased oxygen demand or reduced supply. This increase in blood oxygen content and partial pressure also compensates for arterial vasoconstriction caused by hyperoxia. HBOT has been shown to promote vascular proliferation by increasing vascular endothelial growth factor elaboration and stem cell mobilisation as well as enhancing host defense against infections and regulating the anti-inflammatory response.[2,3] It has also been shown to have a role in ameliorating ischaemia-reperfusion injury which can be a major concern in the acute setting.[4]

HBOT has been used successfully for acute peripheral ischaemia like crush injuries, frostbites or other insults to circulation like thrombembolism.[5,6] By providing oxygenation until flow is restored or adequate collateral circulation is established, it increases viability and survival

Figure 2
Arm during fasciotomy operation. Tissues are well perfused

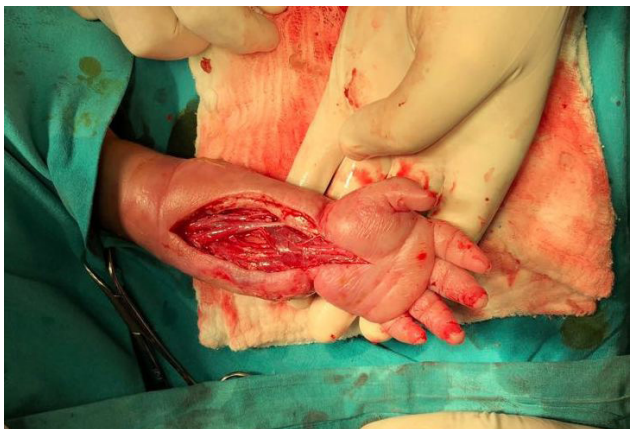
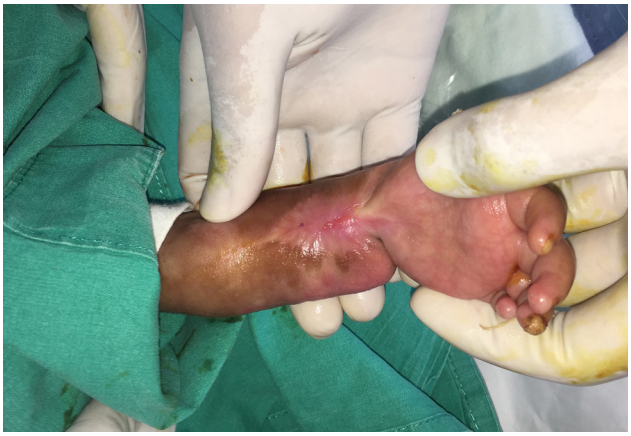


Figure 3
Arm just before discharge. Ischaemia regressed totally and fasciotomy wound almost closed



of poorly perfused tissues besides supporting collateral development. Infants are known to have a higher potential for early collateralisation compared to adults.[7] In this regard, it can be speculated that these effects of HBOT will be augmented and the chance of limb survival will be greater in infants even when total arterial occlusion is present. Indeed, there are a number of reports showing favourable results with HBOT in childhood acute ischaemic conditions, especially thromboembolic incidents.[8-10]

Current data on neonatal extremity ischaemia mostly comes from postnatal incidents which are typically iatrogenic.[1,11] Intrauterine ischaemia which comprises only a small proportion of all neonatal incidents is generally associated with foetal thromboembolism. Promising results have been reported with current treatment options; however, some patients remain unresponsive and require amputations.[12,13] Despite potential benefit, use of HBOT for intrauterine incidents is limited. In the only report available, an infant avoided a below-the-hip amputation but required below the knee amputation. In that case, daily HBOT was started on the seventh day, when leg ischaemia was unresponsive to thrombolysis.[14] The present case, on the other hand, underwent HBOT much earlier and with a considerably more aggressive schedule. Amputation was avoided without thrombolytic treatment.

Prompt initiation and frequent application of HBOT in the early period are of critical importance for the management of acute ischaemia. Skeletal muscle and nerves can tolerate interruption of blood flow for about 4–6 hours before necrosis and irreversible injury occur.[15] Therefore, it is crucial to oxygenate the compromised tissues within these intervals. A full recovery as achieved in our case may be achieved with an intense treatment schedule. Also, patients should be closely monitored for signs of reperfusion such as color change, warming and regaining movement. However, absence of these signs in the first sessions should not lead to early quitting of HBOT as clinically apparent change may be delayed.

Safety of HBOT in the paediatric patient population is considered a concern by some authors.[11] Its use for carbon monoxide intoxication, haemorrhagic cystitis, crush injuries or other peripheral ischaemic conditions like purpura fulminans in paediatric patients has been increasing lately and no serious side effects have been reported. Our patient, despite her young age and intense schedule, also tolerated the treatment well.

In this case, limb loss was avoided by applying HBOT early and with an intense schedule. We suggest that adjunctive HBOT may be useful for management of intrauterine arterial occlusions and should be considered for limb salvage.

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