Case Report

# Dyskeratosis congenita induced cirrhosis for liver transplantation-perioperative management

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## ABSTRACT

Dyskeratosis congenita (DC) is an inherited disorder with progressive multisystem involvement. End stage liver disease (ESLD) in patients with DC is rare. We describe the perioperative management of a patient with DC induced ESLD and severe hepatopulmonary syndrome for living donor liver transplantation.

**Key words:** Cirrhosis, dyskeratosis congenita, liver transplant, transplant

## INTRODUCTION

Dyskeratosis congenita (DC) is an inherited disorder with progressive multi-system involvement leading to bone marrow failure (BMF), squamous cell carcinoma, pulmonary fibrosis (PF), etc.[1] End stage liver disease (ESLD) in DC has been rarely reported. Liver transplantation (LT) for cirrhosis secondary to DC has not been reported previously and we describe here the perioperative management of the same.

## CASE REPORT

A patient with diagnosed DC at 25 years of age presented with ESLD to our institute in his 34$^{th}$ year. Past history included haematopoietic stem cell transplant (HSCT) for BMF secondary to DC. Patient was diagnosed with cirrhosis post-HSCT and was kept on medical management for 9 years. At the time of presentation he was not on any immunosuppressant.

Clinical examination revealed multiple dental caries, reticulate skin pigmentation, nail dystrophy, severe clubbing, epiphora, enlarged liver with irregular margins, splenomegaly and ascites. Pre-operative liver function tests showed hypoalbuminemia (2.6 g/dl) with slightly elevated transaminases. There was no anaemia and transjugular liver biopsy was confirmatory of cirrhosis.

His primary complaint was of gradually increasing dyspnoea, more in the sitting position. Systemic examination, chest X-ray and pulmonary function tests were normal. Oxygen saturation ($SpO_2$) on room air in sitting position was 88%. On arterial blood gas (ABG) analysis, partial pressure of oxygen ($PaO_2$) was 51.3 mm Hg with widened alveolar arterial oxygen gradient ($PAO_2$–$PaO_2$ = 59.7 mm Hg) [Table 1]. ABG with 100% $O_2$ supplementation demonstrated an increased $PaO_2$ (158 mm Hg) and $SpO_2$ of 100% [Table 1].

High resolution computerized tomography (CT) demonstrated mild bilateral interstitial lung disease (ILD) [Figure 1]. Saline contrast echocardiography (SCE) suggested severe right to left intrapulmonary shunting and macroaggregated albumin scan (MAA) demonstrated a 21% shunt fraction. CT pulmonary angiography was normal and excluded any major A-V communication. Pre-operative echocardiography was normal. Child-Turcotte-Pugh score was 10 (Child C) and model for end stage liver disease score was 14. Patient was diagnosed with cirrhosis secondary to

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**Table 1: Arterial blood gas values at various time points**

| Arterial blood gas parameters | Pre-operative sitting position (room air) | Pre-operative supine position (room air) | Pre-operative sitting ($FiO_2$ 100%) | At extubation ($FiO_2$ 50%) | At discharge (room air) |
|---|---|---|---|---|---|
| pH | 7.445 | 7.5 | 7.410 | 7.317 | 7.383 |
| $PaCO_2$ (mm Hg) | 26.1 | 27 | 30.1 | 33 | 24.7 |
| $PaO_2$ (mm Hg) | 51.5 | 60.6 | 158 | 118 | 70.6 |
| $HCO_3$- (mEq/L) | 17.6 | 17.5 | 18.7 | 17.6 | 17.3 |
| P (A-a) $O_2$ (mm Hg) | 59.7 | 55 | 148 | 175 | 48.2 |
| $SpO_2$ (%) | 88 | 91 | 98 | 99 | 100 |

$PaO_2$: Partial pressure of oxygen, $SpO_2$: Oxygen saturation: P (A-a) $O_2$: Alveolar arterial Pressure Gradient

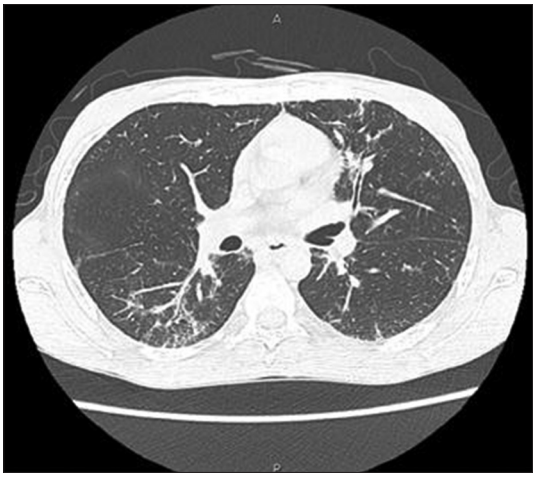

**Figure 1:** High resolution computerized tomography thorax showing mild bilateral interstitial lung disease

DC and posted for urgent living donor liver transplantation (LDLT).

Apart from standard anaesthesia monitoring, invasive haemodynamic monitoring (central venous pressure, invasive arterial blood pressures and continuous cardiac output monitoring using Flowtrac EV1000™ Edwards™ life sciences) were used.

Anaesthesia was induced with propofol (1.5 mg/kg), fentanyl (1.5 μgm/kg), and rocuronium (0.9 mg/kg) with modified rapid sequence induction. Maintenance of anaesthesia was with isoflurane in air (minimum alveolar concentration 1–1.2), with infusions of atracurium and fentanyl. Baseline ABG after induction of anaesthesia showed $PaO_2$ of 140 mm Hg with $FiO_2$ of 0.5.

Restrictive fluid strategy was adopted guided by stroke volume variation (SVV). Persistent SVV >13% in absence of sustained major vascular occlusion or arrhythmias was treated with 250 ml boluses of 5% albumin. Noradrenaline and vasopressin infusion were titrated for a targeted mean blood pressure >65 mm Hg. After reperfusion, $FiO_2$ requirements increased from 0.5 to 0.7 to maintain the $PaO_2$ above 100 mm Hg. Estimated blood loss during the surgical procedure was 2100 ml.

Patient was gradually weaned from mechanical ventilation and vasopressors and extubated on post-operative day 2 in the Intensive Care Unit. Post-extubation intermittent non-invasive bilevel positive airway pressure (BiPAP) support was provided. Oxygen was supplemented using venturi mask with FiO2 of 0.5 targeting $SpO_2$>88%. Immunosuppression was provided with steroids, tacrolimus and mycophenolate.

On post-operative day 7, patient developed tachypnoea, increased $O_2$ requirement, fever and productive cough. Chest auscultation revealed bilateral basal crepitations and basal lobe consolidation on chest X-ray. Oxygen requirements were increased and were provided via high concentration $O_2$ mask with reservoir bag to maintain acceptable levels of saturation. Non-invasive BiPAP support was provided intermittently. On availability of sputum culture reports (culture demonstrated *Escherichia coli* sensitive to carbapenems), patient was shifted from broad spectrum empirical antibiotics to culture specific antibiotics and patient gradually improved with decrease in oxygen requirements. Patient was discharged from the hospital on post-operative day 29 with a $PaO_2$ of 70 mm of Hg on room air, which at 2 months was 78 mm of Hg.

## DISCUSSION

Dyskeratosis congenita is a rare multisystem disorder characterized by the triad of abnormal skin pigmentation, nail dystrophy and mucosal leucoplakia.[2] Patients exhibit considerable clinical and genetic heterogeneity with X-linked recessive, Autosomal dominant and recessive forms. Defective telomerase function leads to premature stem cell exhaustion and tissue failure.

Bone marrow failure and PF are the most common causes of mortality(60–70% for BMF/15% for PF) in these patients.[3] HSCT is the only curative option for BMF but increases the risk of pulmonary complications.[4] Hepatic involvements including hepatomegaly, hemosiderosis, fibrosis, and cirrhosis have been reported in 10% of cases.[5-8] The aetiology of cirrhosis remains poorly understood with hemosiderosis as a probable cause.

Our patient presented with ESLD and progressive dyspnoea accentuated in the sitting position. Presence of severe hypoxemia and orthodeoxia and absence of ILD led to a probable diagnosis of Hepatopulmonary syndrome (HPS). Imbalance between vasoconstrictors and vasodilators leading to pulmonary vascular dilatation at the pre-capillary and capillary level in patients with liver disease results in HPS. Subsequent intrapulmonary shunting and V-Q mismatch causes progressive hypoxia, dyspnoea, and cyanosis. The patient reported here was fulfilling the criteria for HPS:[9] (1) Chronic liver disease (CLD), (2) alveolar-arterial oxygen gradient >15 mm of Hg and intrapulmonary shunt (demonstrated by SCE and MAA). Severe intrapulmonary shunting ~21% and $PaO_2$ of 51.5 mm of Hg on room air placed him in almost the very severe category of type I HPS. LT being a definitive treatment for HPS and severity of hypoxaemia limiting time for medical therapy trial, LT was offered to the patient on an urgent basis.

The prevalence of HPS in patients with advanced liver disease is approximately 16–33%.[10,11] Without LT the 5 years survival rate for cirrhotic patients with HPS reduces to 23%.[12] Mortality rate of patients with severe HPS undergoing LT is 30–67%.[12-14] However, more recently Gupta *et al*. in their study have reported a mortality rate of 9% in patients with severe HPS in peri-transplant period.[15] It has also been demonstrated that severity of pre-operative hypoxaemia correlates with the peri-transplant mortality.[11,12] Rapid progression of pre-operative hypoxaemia in these patients mandates minimal transplant waiting time.[12,15] LDLT reduces transplant waiting time and prevent functional status deterioration and thus provide good results in patients with severe HPS.[15]

The low acceptable thresholds of $PaO_2$ values were kept keeping in mind pre-operative severe HPS and hypoxaemia. Restrictive fluid therapy using SVV along with lung protective ventilation strategies (low tidal volume) were used to minimize pulmonary complications. Other supportive therapies like $O_2$ supplementation, incentive spirometry, intermittent non-invasive ventilatory support, adequate attention to asepsis and antibiotics were provided as per Institute's protocol.

## CONCLUSION

Chronic liver disease in patients with DC is rare. HPS can be an important cause of hypoxemia in patients of DC presenting with CLD. Directed pre-operative evaluation to determine the primary cause of hypoxaemia can help in identifying patients who may benefit from LT.

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