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CASE REPORT

ADVANCED

CLINICAL CASE

Eisenmenger Syndrome in Case of Extended Goldenhar Complex Treated With Heart-Lung Transplantation

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ABSTRACT

A patient diagnosed with expanded Goldenhar complex with oculoauriculovertebral spectrum complicated with complex pulmonary and congenital heart disease, underwent successful heart-lung transplantation 21 years ago, with excellent functional outcome and good quality of life. Heart-lung transplantation can be an option of care for patients with expanded Goldenhar complex. (**Level of Difficulty: Advanced.**) (J Am Coll Cardiol Case Rep 2022;4:699-703)
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HISTORY OF PRESENTATION

A 29-year-old woman was evaluated for severe fatigue, recurrent chest pains, dyspnea on minimal effort, and hypoxemia refractory to oxygen therapy. Height was 59 inches and her weight was 40.9 kg. She showed right hemifacial microsomia, congenital right fascial palsy, loss of hearing, and anotia of the right ear. She had severe scoliosis. Cardiopulmonary abnormalities included mild cyanosis, increased jugular vein distention, and heart sounds present on the right hemithorax disclosing a soft holosystolic murmur. Her right hemithorax presented basal dullness to percussion, with lung sounds diminished at the apex and absent at the base. The left lung was hyperresonant, with diminished sounds throughout. The abdomen showed normal sized liver on the right side, and extremities were normal.

LEARNING OBJECTIVES

- To be able to recognize new manifestations of Goldenhar syndrome presenting as EGC including dextrocardia associated with patent ductus arteriosus, Eisenmenger syndrome, right pulmonary agenesis, and congenital tracheal abnormalities.
- To be able to consider de potential role of HLT in the management of these complex cases.

PAST MEDICAL HISTORY

Patient had diagnosis of Goldenhar syndrome from birth due to her consistent clinical features. She had received facial reconstructive surgeries, insertion of Harrington instrumentation to manage scoliosis, and surgical reimplantation of ureters to correct vesicoureteral reflux. She had been diagnosed with dextrocardia, patent ductus arteriosus (PDA), mitral regurgitation with preserved left ventricular function, and biventricular hypertrophy, considerably worse on the right ventricular cavity. Smoking history was negative.

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The authors attest they are in compliance with human studies committees and animal welfare regulations of the authors' institutions and Food and Drug Administration guidelines, including patient consent where appropriate. For more information, visit the Author Center.

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ABBREVIATIONS AND ACRONYMS

CHD = congenital heart disease

EGC = expanded Goldenhar complex

FVC = forced vital capacity

FEV_1 = forced expiratory volume in first second of expiration

HLT = heart-lung transplantation

PDA = patent ductus arteriosus

POD = postoperative day

DIFFERENTIAL DIAGNOSIS

After living with dextrocardia and PDA, development of dyspnea, fatigue, chest pains, and refractory hypoxemia was consistent with severe pulmonary hypertension and Eisenmenger's syndrome. In addition, she had primary pulmonary disease that could contribute to her symptoms.

Her diagnosis of Goldenhar syndrome was established due to ear malformations combined with mandibulofacial dysostosis,[1] but the presence of vertebral abnormalities qualified her as having oculoauriculovertebral spectrum.[2] In addition, her multiple extrafascial abnormalities more accurately defined her condition as expanded Goldenhar complex (EGC).[3]

INVESTIGATIONS

Chest radiographs, thoracic computed tomography, and a bronchoscopic procedure disclosed a deformed and contracted right hemithorax with crowding of the ribs, and tracheal-mediastinal shift to the right; her trachea and left main bronchus progressed as a single channel with absent carina and absent posterior membranous wall with complete tracheal rings. She had agenesis of the right lung with compensatory hyperinflation of the left lung with transmediastinal herniation into the right upper hemithorax. The lung parenchyma showed significant emphysematous changes. Chest radiograph disclosed in addition the presence of Harrington instrumentation for severe scoliosis. A bronchoscopic procedure disclosed abnormal trachea with absent posterior membranous wall and complete tracheal rings (see clinical features on **Figure 1**). Transesophageal echocardiography disclosed dextrocardia, PDA was present with severe pulmonary hypertension, and a contrast (bubble) injection showed the presence of a right-to-left shunt preferentially into the abdominal aorta, associated with an enlarged and hypokinetic right ventricle with severe tricuspid regurgitation. There was left atrial enlargement with significant mitral regurgitation. Pulmonary function tests showed that forced vital capacity (FVC) was 0.81 L (27% of normal predicted), forced expiratory volume in the first second of expiration (FEV_1) was 0.43 L (16% of normal predicted), and the FEV_1-to-FVC ratio was 53%, consistent with severe obstructive and restrictive lung disease. Resting arterial blood gases on room air disclosed a pH of 7.42, partial arterial pressure of carbon dioxide of 40 mm Hg, and partial arterial pressure of oxygen of 62 mm Hg, with hemoglobin 15.1 g/dL, and parameters of renal and hepatic function were within normal limits.

MANAGEMENT

The combination of Eisenmenger's syndrome with severe obstructive or restrictive lung disease indicated the option of heart-lung transplantation (HLT). Her listing occurred prior the lung allocation score system implemented in 2005; therefore, she gathered time on the waiting list, conforming to donor limitations pertinent to her small frame.

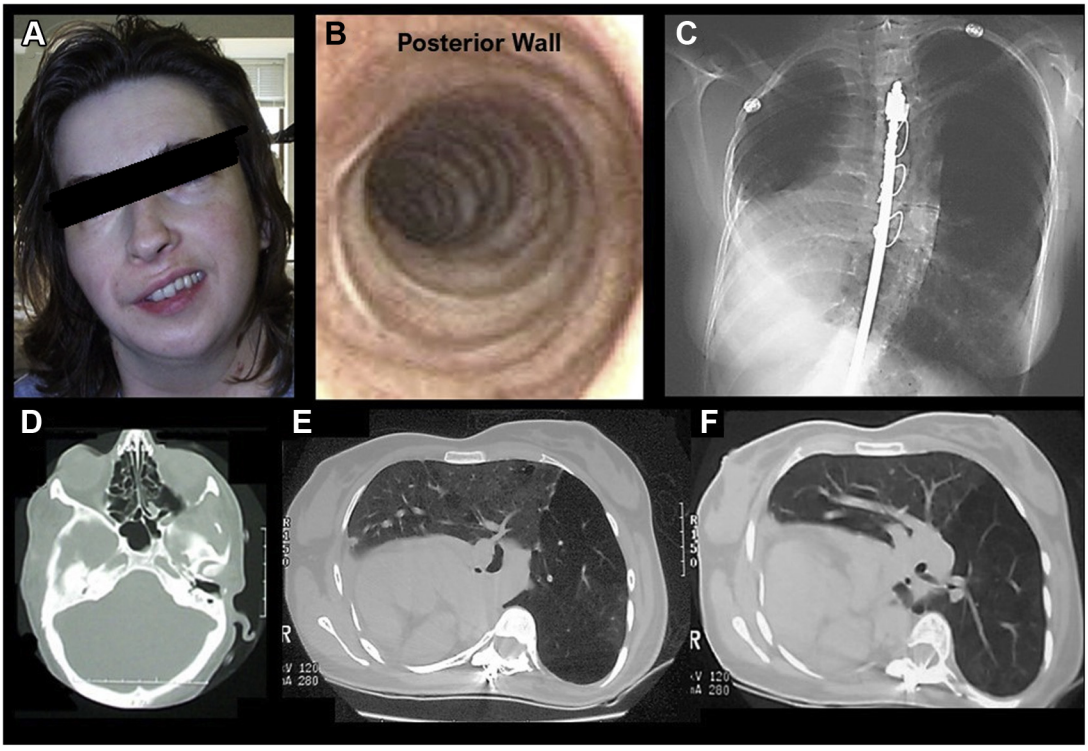
At 33 years of age, she underwent HLT via transverse sternal thoracotomy (clamshell incision) implanting organs from a young donor after brain death. Donor and recipient were blood type O positive, both negative for cytomegalovirus antibodies. Intraoperative findings and postoperative course are described on **Figure 2**. Her postoperative course was uncomplicated and she was extubated to continuous positive pressure ventilation via mask on postoperative day (POD) 5, started on oxygen therapy via nasal cannula on POD 6, and weaned off oxygen on POD 36. Her immunosuppression regimen did not include induction therapy; she initially received intravenous cyclosporine, azathioprine, and methylprednisolone and subsequently was switched to oral cyclosporine, azathioprine, and prednisone. On POD 20, cyclosporine was discontinued due to intolerance and substituted with oral tacrolimus. On POD 37, she received methylprednisolone followed by an oral prednisone tapper to treat mild acute rejection. On POD 112, she had symptomatic minimal acute rejection, receiving another course of methylprednisolone and initiation of mycophenolate mofetil in lieu of azathioprine. Weeks later, azathioprine was reinitiated because of gastrointestinal intolerance to mycophenolate. She had no subsequent episodes of acute rejection.

Her level of lung function peaked 1 year after transplantation (FVC = 1.37 L [44% of normal predicted]; FEV_1 = 1.28 L [52% of normal predicted]; FEV_1/FVC ratio = 93%).

FOLLOW-UP

Her lung function has remained stable for more than 2 decades, and she only recently had a mild decline consistent with chronic lung allograft dysfunction stage 1 (FVC = 1.29 L; FEV_1 = 1.00 L; FEV_1/FVC ratio = 77%). She maintains normal arterial oxygen saturation (97%) on room air. Current echocardiography shows normal left and right ventricular function with estimated pulmonary arterial systolic

FIGURE 1 Clinical and Imaging Findings Before Heart-Lung Transplantation



(A) Facial features showing mild right microsomia and right facial palsy. **(B)** Proximal trachea showing complete tracheal rings with absent membranous posterior wall. **(C)** Chest radiograph showing dextrocardia, absent right lung with enlarged left lung herniating into right hemithorax, scoliosis, and surgically inserted Harrington instrumentation. **(D)** Computed tomography of the head showing absence of right inner ear structures and anotia; left side shows inner ear structures and normal external ear. **(E, F)** Two chest computed tomography views showing dextrocardia, absent right lung, single left pulmonary artery, and enlarged left lung with transmediastinal herniation of the left lung into the right hemithorax. Lung parenchyma shows emphysematous changes.

pressure of 20 mm Hg; exercise echocardiography shows increased systolic function without segmental wall motion abnormalities.

She has been married for 21 years and is currently caring for 3 grandchildren. She is gainfully employed and maintains a Karnofsky Performance Status Scale score of 90. Quality-of-life assessment using the Medical Outcomes Study 36-Item Short Form Health Survey indicated normal functional results, superior to those reported for lung transplant recipients who do not have development of chronic lung allograft dysfunction.[4]

DISCUSSION

Chromosomal abnormalities, single-gene sequence variations, and nongenetic causes (gestational diabetes, teratogenic agents, or viral infections during gestation) are considered potential causes of oculoauriculovertebral spectrum, for which the prevalence is 3.8 cases per 100,000 births.[5] Clinical phenotypes range from subtle facial anomalies and small skin tags to what is described as full EGC with congenital anomalies present in multiple organs. Congenital heart disease (CHD) associated with PDA is rarely present in EGC, and the presence of pulmonary abnormalities such as hypoplasia or aplasia has been only rarely described.[5,6]

Our patient presented a constellation of cardiopulmonary findings not previously reported with EGC, including dextrocardia combined with PDA with right-to-left shunt, secondary pulmonary arterial hypertension, and secondary right ventricular enlargement and dysfunction. These cardiovascular abnormalities were combined with agenesis of the right lung, emphysema, and hyperinflation of the left lung, combined with congenital tracheal abnormalities.

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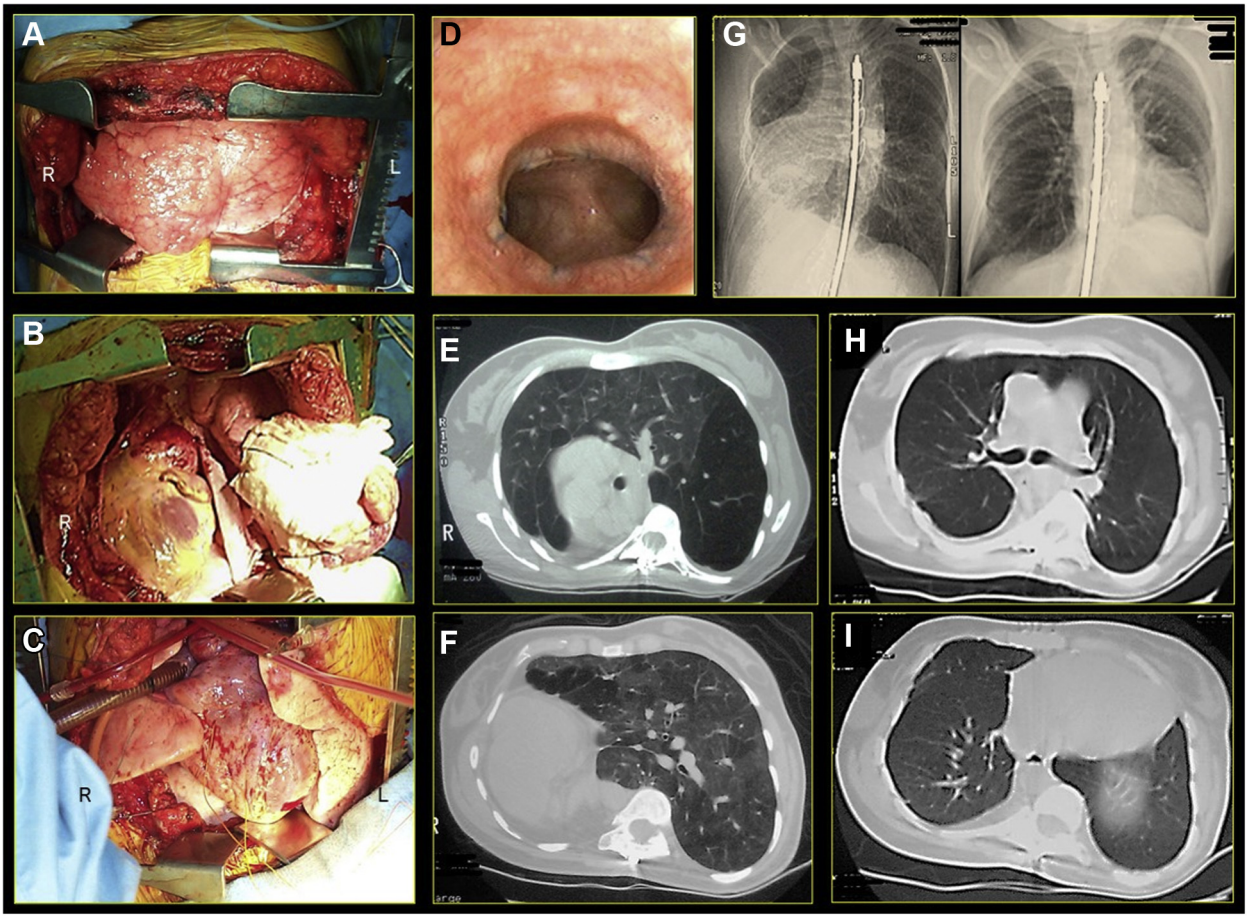
FIGURE 2 Intraoperative Findings and Post-Heart-Lung Transplant Changes



(A) Patient's chest open via clamshell incision and transverse sternal thoracotomy showing the compensatory hyperinflated left lung fully occupying the left hemithorax and herniating across the mediastinum, partially occupying the upper right hemithorax. **(B)** The left lung has been displaced to the left side, revealing the enlarged native heart in the right hemithorax. **(C)** Implanted heart-lung block is shown with both lungs and heart in normal anatomic position. **(D)** Distal tracheal anastomosis showing native trachea with absent posterior membranous wall. **(E, F)** Chest computed tomography views before heart-lung transplantation. **(G)** Chest radiographs **(left)** before and **(right)** after heart-lung transplantation. **(H, I)** Chest computed tomography showing changes after heart-lung block transplantation.

Although HLT has been an established alternative of care for patients with CHD and Eisenmenger syndrome,[7] this is the first case reported in which HLT has been successfully used to treat a patient with EGC with combined cardiopulmonary pathology, resulting in a good long-term functional outcome with excellent quality-of-life indicators.

CONCLUSIONS

Well-selected patients with EGC complicated by CHD or end-stage pulmonary diseases can derive long-term benefit from HLT utilizing specialized multidisciplinary medical and surgical care, despite the presence of multiple congenital anomalies.

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The authors have reported that they have no relationships relevant to the contents of this paper to disclose.

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KEY WORDS **congenital heart defect, genetic disorders, pulmonary atresia, pulmonary hypertension**