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A Rare Case of Lung Hypoplasia, Cardiac Anomalies and Ovarian Tumour in a Patient with MRKH Syndrome

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Abstract

Hypoplasia of the lung is an uncommon congenital abnormality of the respiratory system in contrast to Pulmonary agenesis. Mayer-Rokitansky-Küster-Hauser (MRKH) syndrome is the congenital absence of the upper two-thirds of the vagina and uterus with normal secondary sexual characteristics, ovary, and normal karyotype. Here we describe a case of left lung hypoplasia and congenital cardiac malformations with MRKH syndrome and Leiomyoma of the ovary. A 31-year-old female presented with cough with expectoration, left side chest pain and breathlessness for four years to Jawaharlal Institute of Postgraduate Medical Education and Research (JIPMER). She was evaluated for amenorrhea and diagnosed as MRKH syndrome and the patient underwent right side oophorectomy for right ovarian torsion with a tumour. Computed Tomography Pulmonary Angiogram (CTPA) and fiberoptic endoscopy were suggestive of left lung hypoplasia, and the patient was advised symptomatic treatment for lung hypoplasia and planned for vaginoplasty.

***Keywords*:** Pulmonary hypoplasia, Infertility, Mullerian aplasia, congenital bronchiectasis, Left-sided superior vena cava, ovarian Leiomyoma.

Introduction

Pulmonary Hypoplasia is a developmental lung anomaly characterized by a decrease in the number of airway, alveoli and lung cells leading to a net reduction in the lung's size and

weight. It can be either unilateral or bilateral.[1] Estimated prevalence of pulmonary Hypoplasia is 1-2 per 12000 births although the exact prevalence is not well known.[2] Pulmonary Hypoplasia usually presents with other associated cardiovascular,gastrointestinal, and genitourinary tract anomalies. The onset of Clinical manifestations usually depends upon the degree of Hypoplasia.[3]

Mayer-Rokitansky-Küster-Hauser (MRKH) syndrome is a rare congenital problem in women and it is characterized by failure of the appropriate development of the uterus and the vagina with normal external genitalia and normal ovarian function. They develop secondary sexual characteristics during puberty (e.g., breast development and pubic hair) but present with primary amenorrhea. The estimated incidence of Mayer-Rokitansky-Küster-Hauser syndrome (MRKH syndrome) is 1 in 4500 female births.[3] Most cases are sporadic. Autosomal dominance with an incomplete degree of penetrance and variable expressivity is the mode of inheritance in this syndrome. Here, we are report a rare left lung hypoplasia case associated with cardiac anomalies, with MRKH.

Case Report

A 31-year-old unmarried female patient presented with four years of cough with whitish expectoration, left side dull aching chest pain, and difficulty in breathing. Breathlessness progressed from Modified Medical Research Council grade 1 to 3 over these four years and was not associated with palpitations, wheeze, or orthopnea. She had no history of loss of weight, loss of appetite, abdominal distension, bilateral leg swelling, or reduced urine output. History of pulmonary tuberculosis at the age of 2 years with an intake of antituberculosis drug therapy was there but no documentation available regarding treatment.

She also had a history of amenorrhea but with no family history suggestive of Mullerian tract/cardiac/renal/ lung/ skeletal anomalies. Initially patient underwent traditional medicine treatment for amenorrhea after that patient went to another hospital to evaluate amenorrhea in 2017.Then she was referred to our institute for further evaluation.

During the evaluation, blind vaginal pouch with an absent uterus with a normal ovary found in the ultrasound abdomen and pelvis. In view of suspecting MRKH syndrome following investigations was done. Karyotyping 46XX, FSH (Follicle stimulating Hormone) =5.7 IU/L (Normal Range-1.5-12.4 IU/L), LH (Luteinizing Hormone) =7.25 IU/L (1.09-9.2 IU/L),

Prolactin= 18ng/mL (Normal Range<25ng/mL), Testosterone= 0.7 nmol/L (Normal Range 0.5-2.4 nmol/L) and Estrogen 118 pg/ml(Normal Range 30-400pg/ml) and advised about vaginoplasty and surrogacy. But patient did not come for a follow-up after that,in 2021 patient presented to the Obstetrics department with abdominal pain with outside Magnetic Resonance Imaging (MRI) film, which showed right sided ovarian tumor with torsion and features of MRKH syndrome such as absence of the uterus, hypoplastic vaginal canal with normal bilateral kidney.

The patient underwent emergency laparotomy for ovarian torsion and the right ovary was removed with a tumor followed by peritoneal cytology, and infracolic-omentectomy. Ovarian tumour histopathology was a benign spindle cell tumor suggestive of leiomyoma with torsion-related changes.

She had no pallor, clubbing, or clinically palpable generalized lymphadenopathy on examination. Her room air saturation was 96%, her blood pressure was 110/70 mm of Hg, and her Pulse rate was about 95/min. She had tanner grade 4 pubic hairs and breasts. Examination of external genitalia showed a blind vagina. On chest examination, she had left side tracheal deviation with the same side decreased vesicular breath sounds with biphasic coarse inspiratory crepitations. Chest X-ray revealed cystic changes on the left side with ipsilateral mediastinal and tracheal shift with compensatory hyperinflation on the right side (Figure 1 a). Severe restrictive abnormality (FEV1/FVC-0.85, FVC-43%, FEV1-50% of the predicted value) was found in spirometry. Given all these clinical and imaging features, a left lung developmental anomaly was suspected and a contrast-enhanced Pulmonary Angiogram (CTPA) done for the left main pulmonary artery size. CTPA showed left lung volume loss with multiple thin and thick-walled cystic areas connected to lobar bronchus with no evidence of lung parenchyma. Herniation of right upper lobe parenchyma into left hemi thorax and small caliber of left main pulmonary artery [0.67cm], lobar and segmental arteries than right side suggestive of left lung hypoplasia with cystic bronchiectasis with left superior vena cava (Figure 1 b) and right aortic arch (Figure 1c) was noted. Fiber optic bronchoscopy showed Right side and left lower lobe were normal bronchopulmonary segment with left side upper lobe bronchus does not sudivide further (Figure 2 a&b). This confirmed our suspicion of left lung developmental anomaly, and a diagnosis of left lung hypoplasia (Grade 3 monaldi classification of hypoplasia) was made. 2D Echocardiography was done, which showed moderate tricuspid regurgitation with dilated coronary sinus and left-sided superior vena

cava. Patient was advised for pulmonary rehabilitation (Breathing exercises, Active cycle breathing technique and postural drainage for left lung), pneumococcal and influenza vaccination and advised for pneumonectomy. However, the patient was not willing to undergo for surgical procedure. The Patient was explained about vaginoplasty and surrogacy in view of MRKH but patient was not willing to undergo surgical procedures.

Informed consent was obtained for publication of the patient's clinical images and history.

Discussion

Two types of Mayer-Rokitansky-Küster-Hauser (MRKH) syndrome are there which include type I (isolated) or Rokitansky sequence and type II or MURCS association (Mullerian duct aplasia, renal dysplasia, and Cervical Somite anomalies.[4]The association of MRKH with lung malformation mimicking bronchiectasis and heart malformations is very uncommon. Severe cardiac defects evocating Holt-Oram or velocardiofacial-like syndromes requiring surgery were reported in other case studies. The reported malformations were conotruncal defects such as pulmonary valvular stenosis,[5] aortopulmonary window.[6]But in our case presented with left superior vena cava.

In most studies, uterine leiomyoma was found in patients with MRKH syndrome but very rarely was ovarian leiomyoma. Ovarian tumour is difficult to examine in MRKH, mainly in patients without vaginal reconstruction. Hence appropriate imaging is also needed to look for pelvic mass during MRKH evaluation.[7]Pulmonary Hypoplasia is defined as reduced lung tissue with hypo-plastic bronchi and vessels of varying degrees. Lung development starts from the 26th day of intrauterine life and is completed in the early post-natal period.[8] Pulmonary Hypoplasia may be primary or secondary. Primary pulmonary Hypoplasia is an intrinsic defect in lung development with an incidence of 1-2 cases per 12,2000 live births. Several mechanisms, like decreased hemi thoracic volume, decreased pulmonary vascular perfusion, fetal movements, and lung fields are implicated in secondary pulmonary hypoplasia. They are frequently associated with other congenital anomalies involving urogenital, cardiovascular system, central nervous system, and musculoskeletal abnormalities of the thoracic cage.[9] Lung developmental disorders constitute three main categories according to Boyden, which include agenesis (complete absence of the lung tissue), aplasia (absent lung tissue with rudimentary bronchus), and Hypoplasia (reduced lung tissues).[10] Pulmonary Hypoplasia has a spectrum of clinical manifestations from asymptomatic to

respiratory failure.[11] Most patients will develop respiratory distress as a newborn. However, our patient presented with respiratory symptoms at the age of 2 years but was diagnosed with pulmonary tuberculosis and treated; since then, the patient has had recurrent respiratory infections, which led us to think of bronchiectasis as the primary lung pathology.

Diagnosis of pulmonary Hypoplasia with MRKH syndrome is rare in adulthood. Left lung hypoplasia is more common than right, and in our patient, a chest x-ray was suggestive of decreased volume loss with increased opacity on the affected side. A severe Restrictive pattern was seen in spirometry, and computed tomography pulmonary angiography (CTPA) was used to diagnose pulmonary Hypoplasia. Before diagnosing pulmonary Hypoplasia, we must evaluate for other conditions similar to Hypoplasia, including non-cystic bronchiectasis, and congenital airway malformations, and sequestration.[12] In all these scenarios, the usually standard caliber/size of same side pulmonary artery size will be expected.

Treatment for lung hypoplasia in adults were mainly supportive measures which include recurrent infection control measures, expectorants for symptomatic management, and management of other complications. Prophylaxis treatment for pneumococcus, Respiratory syncytial virus (RSV), and influenza is recommended. Prognosis in such cases is based on the remaining lung parenchyma and the presence of associated anomalies. [13]

Cases with polycystic ovaries and ovarian tumors have been described in women presenting otherwise with the usual 46, XX karyotype. In Yalavarthi S et al. study, the case of sertoliform endometrioid carcinoma associated with MRKH syndrome is reported.[14]
In MRKH syndrome 40% of upper urinary tract malformations are found which includes ectopia of one or both kidneys (17%), unilateral renal agenesis (23–28%), horseshoe kidney, renal Hypoplasia (4%), and hydronephrosis. In MURCS patients 10–25% of them had Auditory defects or deafness and 30–40% of the skeletal abnormalities of the spine were also found in these cases.[15]

Case reports by Bach et al[16] described the association of MRKH syndrome with pulmonary agenesis. However, our case report is left lung hypoplasia with cardiac anomalies and MRKH syndrome with ovarian Leiomyoma.

Conclusion

Pulmonary Hypoplasia affects the lung and airways and can be easily missed, especially in those with previous pulmonary tuberculosis treatment history, unless the treating physician has a high index of suspicion. We must evaluate anyone with recurrent respiratory symptoms since childhood and primary amenorrhea for the congenital lung anomaly and other system congenital malformations. Urinary anomalies are the most common anomaly associated with MRKH syndrome, but lung hypoplasia association is infrequent. Once suspected, it would be easy to diagnose with available investigations and further follow-ups in those with lung hypoplasia with MRKH syndrome.

Authors' Contribution

PU made the diagnosis in pulmonary medicine part and helped in writing the case report. AA diagnosed MRKH and helped in revising case report. SC wrote the paper and followed the case and collected details. DP helped in drafting article and images. VK helped in writing report. All authors approved the final version of the manuscript.

References

1. Laudy JA, Wladimiroff JW. The fetal lung. 2: Pulmonary hypoplasia. Ultrasound Obstet Gynecol. 2000;16:482–94. DOI: 10.1046/j.1469-0705.2000.00252.x
2. Kant S. UNILATERAL PULMONARY HYPOPLASIA – A CASE REPORT. Lung India . 2007;24:69–71. DOI: 10.4103/0970-2113.44215
3. Griffin JE, Edwards C, Madden JD, Harrod MJ, Wilson JD. Congenital absence of the vagina. The Mayer-Rokitansky-Kuster-Hauser syndrome. Annals of Internal Medicine. 1976;85:224–36. DOI: 10.7326/0003-4819-85-2-224
4. Opitz JM. Vaginal atresia (von Mayer-Rokitansky-Küster or MRK anomaly) in hereditary renal adysplasia (HRA). American Journal of Medical Genetics. 1987;26:873–6. DOI: 10.1002/ajmg.1320260414
5. Kula S, Saygili A, Tunaoğlu FS, Olguntürk R. Mayer-Rokitansky-Küster-Hauser syndrome associated with pulmonary stenosis. Acta Paediatr. 2004;93:570–2. DOI: 10.1080/08035250310023773
6. Ulrich U, Schrickel J, Dorn C, Richter O, Lewalter T, Lüderitz B, et al. Mayer-von Rokitansky-Küster-Hauser syndrome in association with a hitherto undescribed variant

of the Holt-Oram syndrome with an aorto-pulmonary window. Human Reproduction. 2004;19:1201–3. DOI: 10.1093/humrep/deh198

7. Miao Y, Wen J, Huang L, Wu J, Zhao Z. Diagnosis and Management of Ovarian Tumor in Mayer-Rokitansky-Küster-Hauser (MRKH) Syndrome. Biomed Research International . 2018 ;2018:2369430. https://doi.org/10.1155/2018/2369430
8. Papadopoulos D, Misthos P, Chorti M, Skopas V, Nakou A, Karagianidis N, et al. Unilateral pulmonary hypoplasia in an adult patient. Monaldi Archives for Chest Disease. 2018;88. DOI: 10.4081/monaldi.2018.829
9. Liners J, Médart DL, Collignon L. Primary Pulmonary Hypoplasia. Journal of the Belgian Society of Radiology . 2019 ;103. DOI: http://doi.org/10.5334/jbsr.1717
10. Boyden EA. Developmental anomalies of the lungs. The American Journal of Surgery. 1955;89:79–89. DOI: 10.1016/0002-9610(55)90510-9
11. Gülen F, Kar S, Midyat L, Demir E, Özyurt S, Özyürek AR, et al. A rare clinical presentation of pulmonary hypoplasia. Open Journal of Pediatrics. 2011;01:75–8. DOI:10.4236/ojped.2011.14018
12. 3D Imaging in Unilateral Primary Pulmonary Hypoplasia in an Adult: A Case Report. https://www.hindawi.com/journals/crira/2011/659586/
13. Thomas RJ, Lathif HC, Sen S, Zachariah N, Chacko J. Varied presentations of unilateral lung hypoplasia and agenesis: a report of four cases. Pediatric Surgery International. 1998;14:94–5. DOI: 10.1007/s003830050447
14. Yalavarthi S, Jadhav VA, Kumar SS, Pavani M. Mayer–Rokitansky–Kuster–Hauser syndrome: Syndrome of Mullerian agenesis – A report of two cases. Medical Journal of Dr DY Patil University . 2017;10:207. **DOI:** 10.4103/0975-2870.202095
15. Morcel K, Watrin T, Pasquier L, Rochard L, Le Caignec C, Dubourg C, et al. Utero-vaginal aplasia (Mayer-Rokitansky-Küster-Hauser syndrome) associated with deletions in known DiGeorge or DiGeorge-like loci. Orphanet Journal of Rare Disease. 2011 ;6:9.
16. Bachh AA, Pulluri S, Beigh A, Raju C, Deshpande R. Pulmonary Aplasia with Unusual Associations in a Woman. Iranian Journalof Medical Sciences. 2014;39:148–51. PMID: 24644386

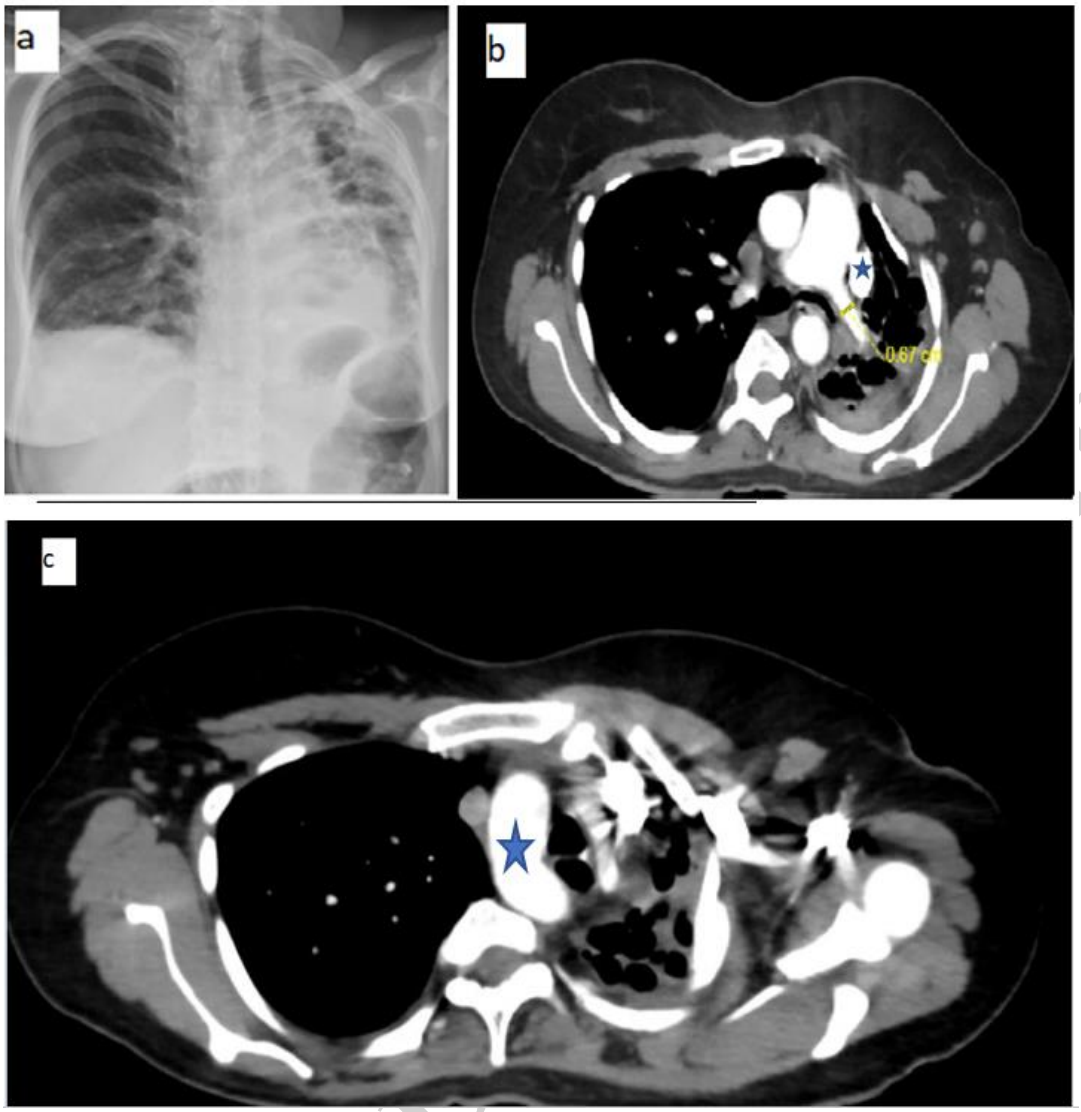

Figure 1: **A**: Chest x-ray demonstrating a mediastinal shift to the left with crowding of ribs on the left with hypolucent opacity with ectatic changes on the left side. **B**: CTPA showing a) left lung volume loss with multiple thin and thick-walled intercommunicating cystic areas and b) decreased caliber of the left main pulmonary artery (0.67mm) and left superior vena cava (asterisk), (**C**) CTPA showing right aortic arch(asterisk)

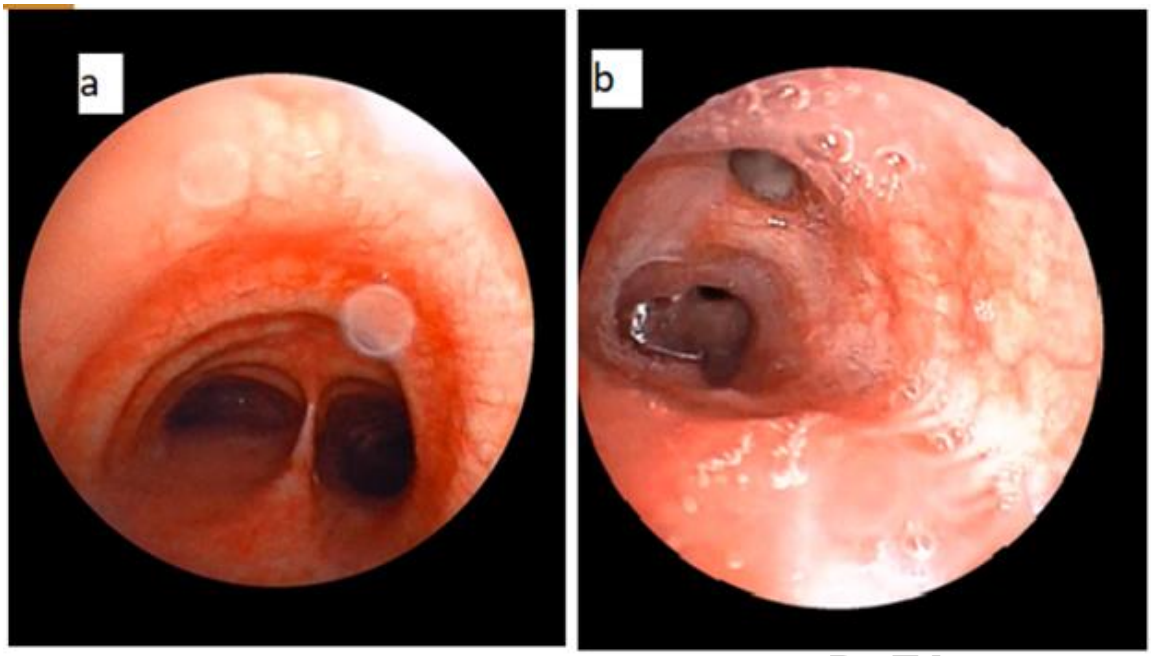

Figure 2: **A**: Fibreoptic bronchoscopy shows the main carina with bilateral patent bronchi. **B**: Left side secondary carina with lobar bronchi (White arrow showed left upper lobe single bronchial opening without subdivision)