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CASE REPORT

A Rare Case of Lung Hypoplasia, Cardiac Anomalies and Ovarian Tumour in a Patient with Mayer-Rokitansky-Küster-Hauser 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. We report a 31-year-old female patient who presented in 2022 with cough with expectoration, left-side chest pain and breathlessness for 4 years to tertiary hospital, Puducherry, India. She was evaluated for amenorrhoea and diagnosed as MRKH syndrome and the patient underwent right-side oophorectomy for right ovarian torsion with a tumour. Computed tomography pulmonary angiogram and fiberoptic endoscopy were suggestive of left lung hypoplasia and the patient was advised symptomatic treatment for lung hypoplasia and planned for vaginoplasty for which she refused.

Keywords: Pulmonary Hypoplasia; Infertility; Mullerian Aplasia; Left-Sided Superior Vena Cava; Case Report; India.

Pulmonary hypoplasia is a developmental lung anomaly characterised 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 12,000 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 is characterised by failure of the appropriate development of the uterus and the vagina with normal external genitalia and normal ovarian function. Individuals develop secondary sexual characteristics during puberty (e.g. breast development and pubic hair) but present with primary amenorrhoea. The estimated incidence of MRKH syndrome is 1 in 4,500 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. We report a rare left lung hypoplasia case associated with cardiac anomalies, with MRKH.

Case Report

A 31-year-old unmarried female patient presented to tertiary care hospital, Puducherry, India, in 2022 with 4 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 4 years and was not associated with palpitations, wheezing or orthopnoea. She had no history of loss of weight, loss of appetite, abdominal distension, bilateral leg swelling or reduced urine output. She had a history of pulmonary tuberculosis at the age of 2 years with an intake of antituberculosis drug therapy but no documentation was available regarding the treatment regime.

She also had a history of amenorrhoea but with no family history suggestive of Mullerian tract/cardiac/renal/lung/skeletal anomalies. Initially, the patient underwent traditional medicine treatment for amenorrhoea and then went to a hospital to evaluate amenorrhoea in 2017. Then she was referred to the current institute for further evaluation.

During the evaluation, blind vaginal pouch with an absent uterus with a normal ovary was found on the ultrasound of her abdomen and pelvis. In view of suspecting MRKH syndrome, further investigations were done. Karyotyping 46XX, follicle stimulating hormone = 5.7 IU/L (normal range: 1.5–12.4 IU/L), luteinizing hormone = 7.25 IU/L (normal range: 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 Oestrogen = 118 pg/mL (normal range: 30–400 pg/mL) and she was advised about vaginoplasty and surrogacy. However, the patient did

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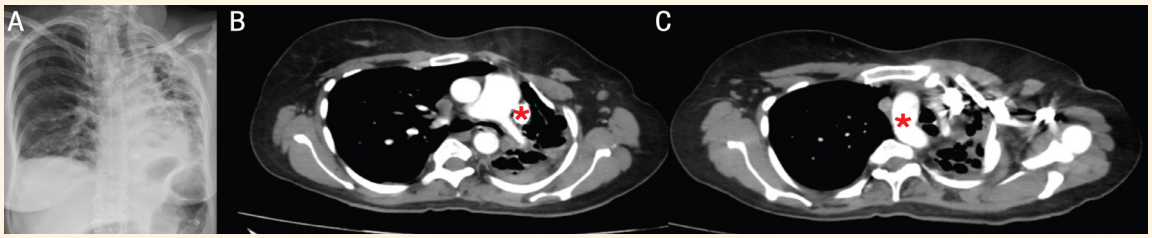

Figure 1: A: Chest x-ray of a 31-year-old female patient demonstrating a mediastinal shift to the left with crowding of ribs on the left with hypolucent opacity with ectatic changes on the left side. **B:** Computed tomography pulmonary angiogram (CTPA) showing left lung volume loss with multiple thin and thick-walled intercommunicating cystic areas and decreased caliber of the left main pulmonary artery (0.67 mm) and left superior vena cava (asterisk). **C:** CTPA showing right aortic arch (asterisk).

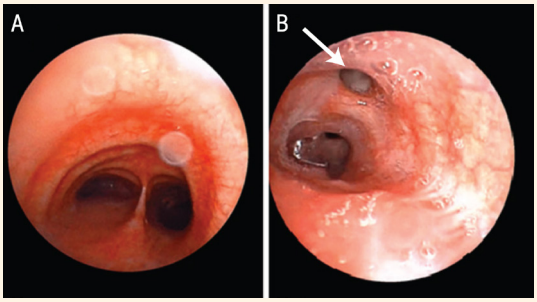

Figure 2: A: Fibreoptic bronchoscopy showing the main carina with bilateral patent bronchi. **B:** Left side secondary carina with lobar bronchi (arrow indicating left upper lobe single bronchial opening without subdivision).

not attend any follow-up appointment. In 2021, the patient presented to the Obstetrics Department with abdominal pain with a magnetic resonance imaging scan done elsewhere, showing right-sided ovarian tumour with torsion and features of MRKH syndrome such as absence of the uterus, hypoplastic vaginal canal with normal bilateral kidneys.

The patient underwent emergency laparotomy for ovarian torsion and the right ovary was removed with a tumour 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 generalised lymphadenopathy on examination. Her room air saturation was 96%, her blood pressure was 110/70 mmHg, and her pulse rate was approximately 95 beats/min. She had Tanner stage 4 pubic hairs and breasts. Examination of external genitalia showed a blind vagina. On chest examination, she had a left-side tracheal deviation and decreased vesicular breath sounds on the same side 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 1A]. 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 (0.67 cm), lobar and segmental arteries compared to right side pulmonary artery suggestive of left lung hypoplasia with cystic bronchiectasis with left superior vena cava and right aortic arch were noted [Figures 1B and 1C]. Fiber optic bronchoscopy showed the right-side and left lower lobe were normal; the bronchopulmonary segment with left-side upper lobe bronchus did not subdivide further [Figures 2A and 2B]. This confirmed the suspicion of left lung developmental anomaly and a diagnosis of left lung hypoplasia (Grade 3 Monaldi classification of hypoplasia) was made. Two-dimensional echocardiography showed moderate tricuspid regurgitation with dilated coronary sinus and left-sided superior vena cava. The patient was advised for pulmonary rehabilitation (breathing exercises, active cycle breathing technique and postural drainage for the left lung), pneumococcal and influenza vaccination and pneumonectomy. However, the patient was not willing to undergo a surgical procedure. In view of MRKH, the patient was explained the procedures of a vaginoplasty and surrogacy but she was not willing to undergo surgical procedures.

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

Discussion

There are 2 types of MRKH syndrome which include type I (isolated) or Rokitansky sequence and type II

or MURCS association (Müllerian duct aplasia–renal agenesis–cervicothoracic somite dysplasia).[4] The association of MRKH with lung malformation mimicking bronchiectasis and heart malformations is very uncommon. Severe cardiac defects that evocate 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 and aortopulmonary window.[5,6] The current case presented with left superior vena cava.

In most studies, uterine leiomyoma was found in patients with MRKH syndrome but ovarian leiomyoma is very rarely reported. Ovarian tumour is difficult to examine in MRKH, mainly in patients without vaginal reconstruction. Hence appropriate imaging is needed to identify a 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 12,000 live births. Several mechanisms, such as 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 3 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, the current 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 the treating physicians 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 the current 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 CTPA was used to diagnose pulmonary hypoplasia. Before diagnosing pulmonary hypoplasia, other conditions similar to hypoplasia must be evaluated, including non-cystic bronchiectasis, 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 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 tumours have been described in women presenting otherwise with the usual 46XX karyotype. In Yalavarthi *et al*.'s 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% had auditory defects or deafness and 30–40% of skeletal abnormalities of the spine were found in these cases.[15]

A case report by Bach *et al*. described the association of MRKH syndrome with pulmonary agenesis.[16] However, the current patient had 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. Physicians should evaluate anyone with recurrent respiratory symptoms since childhood and primary amenorrhea for congenital lung anomaly and other 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 and AA made the diagnosis. SC collected patient details. PU, SC, DP and VK drafted the manuscript. DP

provided the images. AA revised the manuscript. All authors approved the final version of the manuscript.

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