Klippel–Feil syndrome with associated agenesis of lung and gall bladder presenting with asthma and allergic rhinitis

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ABSTRACT

Klippel-Feil syndrome (KFS), a triad of short neck, limitation of neck movement and low posterior hairline, is characterized by presence of congenitally fused cervical vertebrae and is often associated with multiple congenital anomalies. A 35-year-old male was referred for evaluation of an 'opaque hemithorax'. This led to a diagnosis of KFS, agenesis of left lung and gall bladder. The patient had history of wheezing dyspnea with nasal symptoms, which were diagnosed as asthma and allergic rhinitis. A high index of suspicion is required to recognize such a patient, and efforts should be made to seek other congenital anomalies.

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Klippel-Feil syndrome (KFS), a triad of short neck, limitation of neck movement and low posterior hairline, is characterized by presence of congenitally fused cervical vertebrae and is often associated with other congenital anomalies, notably of musculoskeletal, cardiovascular, genitourinary and neurological systems.[1] Agenesis of lung or gall bladder has rarely been reported with this syndrome. A MEDLINE search from 1966 to date revealed only 2 reports,[2,3] in the English language literature, of KFS with agenesis of lung. One other patient had agenesis of right upper and middle lobes with hypoplasia of right lower lobe.[4] Congenital absence of gall bladder with KFS has been described only once.[5] However, to our knowledge, the association of KFS with agenesis of lung and gall bladder in the same patient is yet to be documented. We describe a 35-year-old man with KFS, cervical kyphoscoliosis associated with agenesis of lung and gall bladder, who presented with bronchial asthma and allergic rhinitis.

Case Report. A 35-year-old, HIV-negative, non-diabetic married male, a non-smoker, was referred for evaluation of a left 'opaque hemithorax'. His clinical course during the past 3 years was characterized by episodic productive cough and wheezing dyspnea for which he had received frequent courses of antibiotics. A fortnight prior to referral, on a presumptive diagnosis of a massive left-sided pleural effusion, he received anti tuberculous therapy (ATT), without relief. On presentation, a history suggestive of bronchial asthma and allergic rhinitis was elicited. An atopic background was present; his mother and sister had asthma and rhinitis. There was no history of congenital anomalies in the family. He had fathered a premature daughter who died at 3 months after an illness.

Physical examination revealed a short-statured individual in no acute distress. There was no clubbing or cyanosis. He had a low-lying posterior

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hairline, short neck and webbing, with painless restriction of the neck movements that were more pronounced on the left. The left shoulder was higher than the right and left side of the chest appeared more prominent than the right side. A rib hump was noticed posteriorly, on the left side, when the patient was asked to bend forward. He walked with a limp on the right side, and the right leg appeared shorter than the left. These skeletal deformities were present ever since he could recall. The chest was markedly asymmetrical with pectus excavatum. The left side was flattened with decreased movements with ipsilateral shift of mediastinum. Auscultation revealed bilateral polyphonic rhonchi with basal, coarse crepitations that were more pronounced on the right side.

Hemogram and serum biochemistry were normal. Sputum examination was negative for pathogenic organisms. Chest radiograph **(Figure 1)** showed an opaque left hemithorax, herniation of the right lung, left displacement of the mediastinum and heart with multiple costovertebral anomalies. Antero-posterior and lateral views of the cervical spine revealed occipitalization of the atlas and fused third, fourth and fifth cervical vertebrae **(Figures 2a and 2b)**. Scoliosis of the cervical spine with concavity to the left side along with hemi-vertebrae and spina bifida of the lower cervical vertebrae was also observed.

On pulmonary function testing, the forced vital capacity (FVC) was 1.2 L (34% predicted); forced expiratory volume in 1 sec (FEV1) was 0.89 L (29% predicted), while FEV1/FVC ratio was 0.74. The patient demonstrated an improvement of 230 ml (12%) in FEV1, 2 minutes after administration of 200 µg inhaled salbutamol. Total lung capacity (TLC) was 1.9 L (39% predicted). Diffusion capacity was low (27% predicted) but diffusion per unit lung volume was normal (88%). A bronchoprovocation test was not carried out in view of low baseline FEV1. The patient had positive skin reactivity against locally prevalent common aeroallergens. An ultrasonographic examination of the chest and abdomen did not show any fluid collection. However, the gall bladder was not visualized. A normal cardiac function, with an ejection fraction of 57%, was seen on echocardiography. Pulmonary artery was mildly dilated, and only the right pulmonary branch was seen. Computed tomogram (CT) of the thorax confirmed the lack of division of bronchus and absence of left lung with right lung herniation. The CT angiography confirmed the absence of left pulmonary artery **(Figure 3).** The CT of the abdomen showed an absent gall bladder with an empty fossa **(Figure 4)**. Patient did not consent to fiberbronchoscopy.

A diagnosis of KFS with kyphoscoliosis along with agenesis of lung and gall bladder, associated with bronchial asthma and allergic rhinitis was

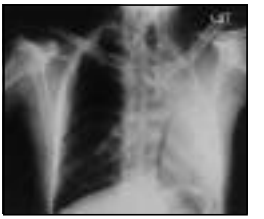

Figure 1 - X-ray chest, posteroanterior view, showing an opaque left hemithorax, herniation of the right lung, left displacement of the mediastinum and heart with multiple costovertebral anomalies.

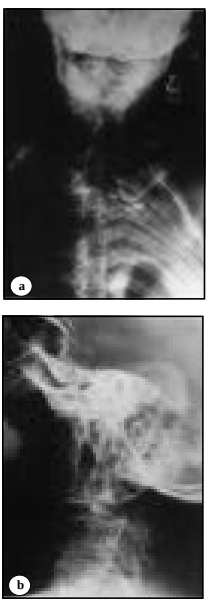

Figure 2 - X-ray of cervical spine. **(a)** Anteroposterior view showing scoliosis of the cervical spine, with concavity towards the left, hemivertebrae and fusion of cervical vertebrae. **(b)** Lateral view showing occipitalization of atlas with anterior subluxation of C2 over C3.

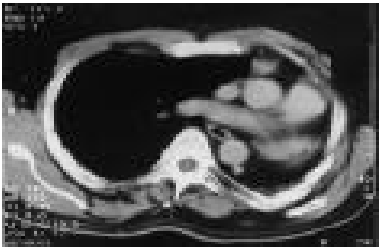

Figure 3 - Computed tomogram of thorax showing lack of division of bronchus, right lung herniation, absence of left lung and left pulmonary artery.

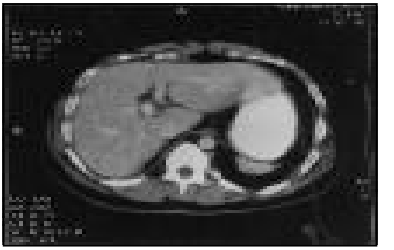

Figure 4 - Computed tomogram of abdomen showing empty gall bladder fossa.

made. The patient responded favorably to a combination of inhaled long acting bronchodilators and steroids along with supportive therapy.

Discussion. Klippel-Feil syndrome is often associated with multiple congenital anomalies.[6] Although KFS predominantly involves the musculoskeletal system, rarely pulmonary complications have been reported.[6] A relationship of occult respiratory dysfunction and craniovertebral anomalies have been previously postulated. In addition to bone impingement or traction on the brain stem, intrinsic malformations of the nervous system or disturbances of cerebrospinal fluid may also adversely affect respiratory function.[6]

However, agenesis of lung/lobes in association with KFS is yet to be highlighted. This association has been reported only 3 times before,[2-4] and it has been postulated that reduction in blood flow due to absent pulmonary vasculature or congenital kyphoscoliosis leading to reduction in intrathoracic space may result in lack of pulmonary growth.[7] Patients with agenesis of lung[7] and kyphoscoliosis[8] have been mistaken for non-resolving pneumonia and have received prolonged treatment without relief. Our patient had recurrent respiratory tract infections and received frequent courses of antibiotics for his ailment, though asthma and rhinitis were not diagnosed. However, an opaque hemithorax, thought to be due to massive tuberculous effusion, resulted in our patient receiving ATT. Such an occurrence is not uncommon in a region with high prevalence of tuberculosis. In the earlier 2 reports,[2,4] a chest radiograph carried out for repeated respiratory tract infection revealed an opaque hemithorax, which led to a diagnosis of agenesis of lung/lobes. Non-invasive techniques such as CT scan can prove a diagnosis of agenesis of the lung.[9] In our patient; CT angiogram was used conclusively to determine the lack of division of main bronchus and absence of left pulmonary artery. In a recent report,[10] allergic rhinitis and asthma have been described in a patient with unilateral lung agenesis diagnosed at 6 months of age, based on clinical features and spirometric evaluation. In our patient, however, the diagnosis of asthma and allergic rhinitis was established in later life while he was being evaluated for an opaque hemithorax.

In the only report[5] of an absent gall bladder with KFS, the agenesis was detected on autopsy in an otherwise asymptomatic patient. Among the musculoskeletal abnormalities, congenital scoliosis of the cervical spine is the most common abnormality.[6] However, this is usually not documented, as these patients are mostly asymptomatic. In our patient too, both agenesis of gall bladder and scoliosis of the cervical spine were detected while scouting for other systemic abnormalities.

Klippel-Feil syndrome often presents with multiple congenital anomalies. Though rare, agenesis of lung and gall bladder may occur with this syndrome. Investigations in a patient with KFS should be directed towards detecting associated anomalies for appropriate management.

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