CASE REPORT

Pulmonary Alveolar Microlithiasis with Klippel-Feil Syndrome: The Eye Does Not See What The Mind Does Not Know

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ABSTRACT:
Pulmonary alveolar microlithiasis is a rare idiopathic disorder characterized by multiple microliths in the alveoli. Chest X-ray examination show miliary mottling mimicking Tuberculosis. Klippel-Feilsyndromeinclude short neck, low hairline and decreased cervical spine movements. It is a congenital anomaly characterized by the fusion of cervical vertebrae and various congenital defects. The present case report is about a 12-years old girl whose Chest X- ray, CT scanand clinical examination revealed KlippelFeil syndrome and Pulmonary alveolar microlithiasis. Open lung biopsy confirmed the pulmonary alveolar microlithiasis. To the best of our knowledge combination ofPulmonary alveolar microlithiasisandKlippel-Feil syndrome has never been reported before.

Keywords: Pulmonary alveolar microlithiasis, misdiagnosis, Klippel-Feil syndrome

INTRODUCTION:

Pulmonary Alveolar Microlithiasis(PAM) was first described by Friedrich in 1856 and by HarbitzIn 1918.[1]

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Received: 15-07-2015
Revised: 29-07-2015
Accepted: 30-07-2015

It has been reported as an uncommon idiopathic disease characterized bymultiplemicroliths in the alveoli. Few familial cases have also been reported. It is regarded as an autosomal recessive lung disease.From clinical point of view it is important as pulmonary tuberculosis hasbeen reported to be the most common misdiagnosis in these cases. About 576 cases of PAM have been reported from Europe and Asia.[2,3]

Klippel-Feil syndrome was described in detail by Mauric Klippel and AndreFeil In 1912. The syndrome is characterized by three signs including short neck, low hairline and decreased cervical spine movements. The syndrome is associated with multiple congenital anomalies including fusion of 2 vertebrae or fusion of complete cervical spine, congenital scoliosis, Sprengel's deformity, renal aplasia, synkinesis, congenital heart defects , brain stem abnormalities, congenital cervical stenosis, syndactyly, and hearing loss. It has been mentioned that about 50% of the cases with congenital defects of cervical spine have all the three signs[4]. Pulmonary alveolar microlithiasis with Klippel-Feil syndrome has never been reported before. In this report of rare combination we aim to emphasize a high index of suspicion for uncommon disordersto avoid misdiagnosis and inappropriate management.

Case Report:

A twelve year old girl with the history of,off and on cough and repeated chest infections since birth was investigated at PNS-Shifa, Karachi- Pakistan. She was previously given a short trial of antituberculous therapy without any clinical improvement or changes in chest X-Ray findings. HRCT Chest showed randomly distributed micro-nodules with the evidence of calcification in both the lungs along bronchovascular fissures and alveoli.

Block vertebrae C2-3 and C5-6 with Omovertebral bone extending from left pedicle of C5 vertebrae to elevated inferior medial border of Scapula was seen. Spina bifida of TV12 was seen. Rudimentry right cervical rib was present.She was labeled as case of Springel deformity of scapula with omovertebral bone,block cervical vertebrae C2-3 and C5-6 as part of Klipper-Feil syndrome (Figure1a,1b,2a). On Further investigations Ultrasound KUB/Pelvis showed congenitally absent left kidney.The laboratory investigations including hematological profile,

biochemical profile including serum calcium and electrolytes were unremarkable.Mantoux Tuberculin skin test was negative. Echocardiography did not reveal any abnormality and spirometry was also within normal limits. The histopathological examination of open lung biopsy revealed chronic inflammatory changes with

Figure: 1a
Omovertebral bone on left with raised left scapula.Multiple fine pulmonary nodules in both lungs mainly in middle and lower zones.

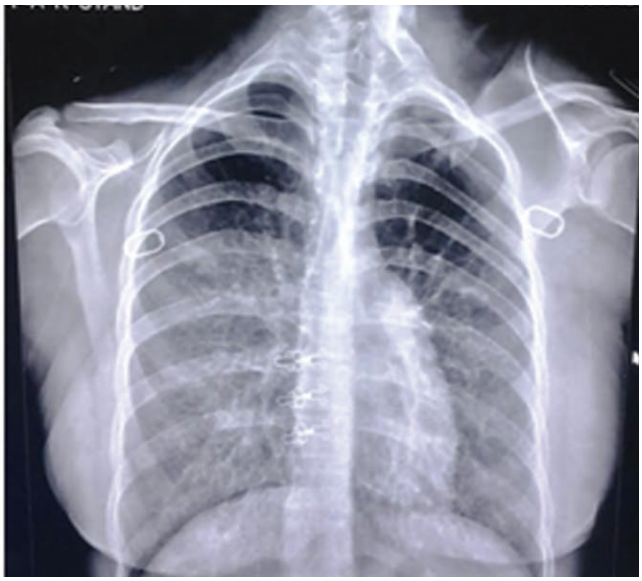
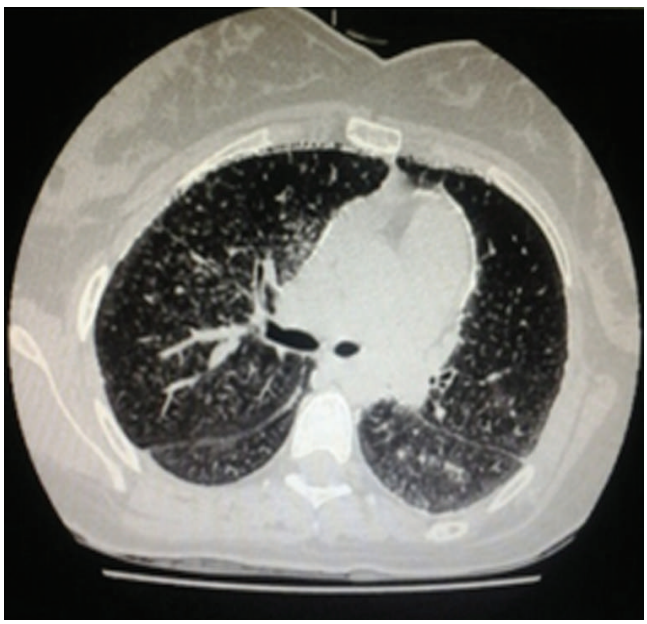


Figure: 1b
Micronodules and calcifications along bronchovascular bundles.



of any calcium metabolism disorder. The cases have multiple calcipheritesof variable sizes within the alveoli and along bronchovascular fissures. The final diagnosis of Pulmonary Alveolar Microlithiasis was made (Figure 2b). The detailed examination of her siblings did not reveal any abnormality.

Figure: 2a
Subpleural calcification giving "Black pleura sign"

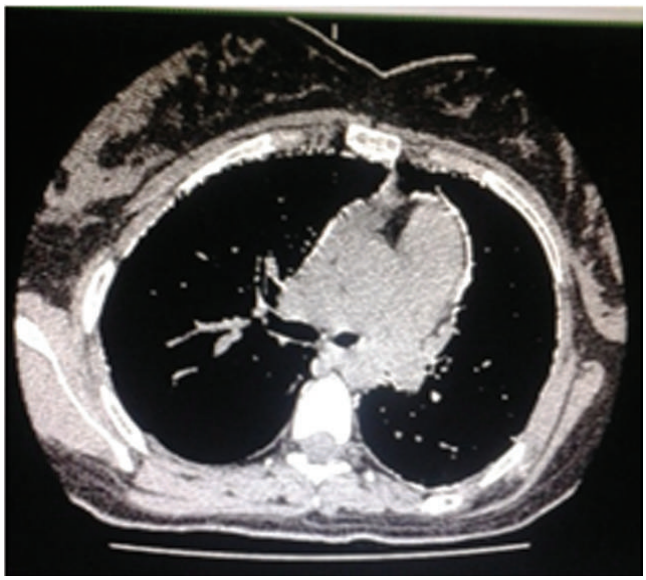
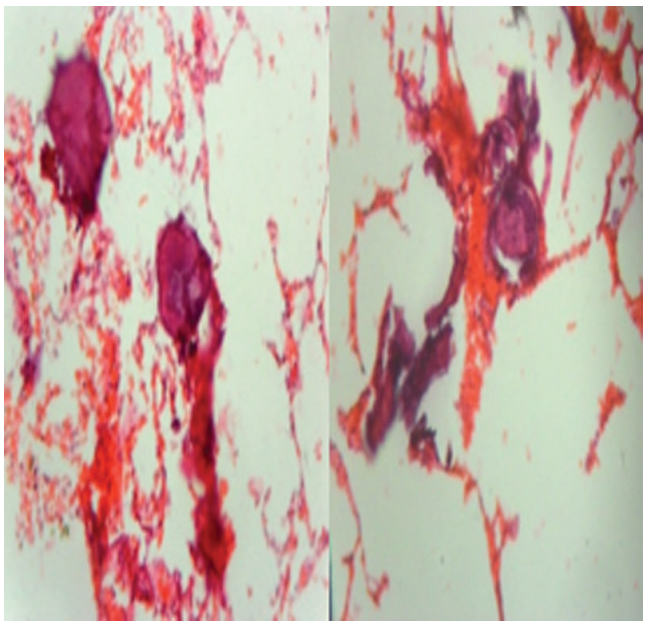


Figure: 2b
Histopathology section showing multiple calcispherites within the alveoli of lung parenchyma. H and E 100×



DISCUSSION:

Pulmonary Alveolar Microlithiasis (PAM) is an uncommon disease presenting as multiple calcipherites within the lung parenchyma and alveoli in the absence

been reported worldwide with significant number from Europe, Turkey and Asia. Cases can be seen in any age but usually present at younger age. There is no specific gender predisposition. Friedrich in 1856, Sosman in 1957 and Harbitz described this condition in 1918.

Recently it has been studied that gene SLC 34A2 coding for type IIb sodium-dependent phosphate transporter and its function is associated with the condition and it has provided some insight to the pathogenesis of this disorder. The Confirmation of diagnosis of PAM can be done by demonstrating the mutation in the SLC34A2 gene[5]. The disorder is slowly progressive. Most of the cases remain asymptomatic[6,7].Progressive dyspenea and respiratory failurehas been observed after 4th decade. Plain X Ray chest interpreted in the light of cough is misdiagnosed as Tuberculosis and treated without any improvement. At present there is no definitive treatment to reduce or halt the progression of the disease process. Systemic corticosteroids, calcium-chelating agents and serial bronchopulmonary lavage have been tried with some improvement [8].Symptomatic treatment and appropriate antibiotic therapy with regular follow up is the only choice presently available. In our case the history of chronic cough and repeated chest infection was present. The patient was empirically given a trial of anti tuberculous therapy also. Her CT chest and X-Ray findings did not show any improvement. Her biochemical profile and test for tuberculosis were also negative.

Maurice Klippel and Andre Feil first described Klippel-Feilsyndrome in 1912. The patients classically had short neck, low hairline and decreased movements of cervical spine. There is congenital failure of segmentation of cervical vertebrae resulting due to failure of normal segmentation of cervical somites at 3-8 weeks gestation. This leads to fused cervical vertebrae at multiple levels[9]. There is a whole spectrum of deformity from fusion of 2 vertebrae to fusion of complete cervical spine. Fusion of C-2 & C-3 is most common. The syndrome can be associated with other deformities such as and Sprengel's deformity.Sprengel's deformity is a complex congenital deformity of shoulder. It is characterized by the congenital elevation of scapula and is the most common congenital shoulder abnormality. Definitive diagnosis can be made on radiography, but CT or MRI is required for the confirmation. This deformity was present in our case along with other deformities including block vertebrae C2-3 and C5-6, Omovertebral bone extending from left pedicle of C5 vertebrae to elevated inferior medial border of Scapula. Our case also showed spina bifida of TV12, rudimentary right cervical rib was present. The ultrasound KUB/Pelvis of this case showed congenitally absent left kidney. Klippel- Feilsyndrome with renal aplasia has been reported as a common finding. Other congenital defects including, synkinesis, congenital heart defects, brain stem abnormalities, congenital cervical stenosis, syndact and hypoplastic thumb and some degree of hearing loss has been reported with different frequency[10,11,12]. The CT scan or MRI is important to evaluate such cases. Recent studies have confirmed that syndrome develops as a result ofmutations in the GDF6 and GDF3 genes. Familial Klippel-Feil-syndrome gene locus has been studied on the long arm of chromosome [8]. These genes provide instructions for protein synthesis that belong to the bone morphogenetic protein family, which in turn are involved in regulating the growth and maturation of bone and cartilage.The condition is inherited in an autosomal dominant pattern.The deformities are usually painless and many patients are not diagnosed until adolescence. The non-surgical management in cases with significant movement restrictions is usually un-successful. Surgical managementis indicated for children between 3-8 yrs of age with significant deformities only[14].

CONCLUSION:

PAM can easily be misdiagnosed as Miliary Tuberculosis. Klippel-Feil syndrome can be seen associated with multiple congenital defects. PAM with Klippel-Feil syndrome has never been reported before. By reporting this rare combination we aim to emphasize a high index of suspicion for uncommon disorders to avoid misdiagnosis and inappropriate management.

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