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Case report

Idiopathic pleuroparenchymal fibroelastosis – A rare idiopathic interstitial pneumonia

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ABSTRACT

Idiopathic pleuroparenchymal fibroelastosis is a rare idiopathic interstitial pneumonia. It was first described in 2004 and subsequently included in the ATS/ERS classification of idiopathic interstitial pneumonia in 2013. There have been few cases reported so far. The diagnostic criteria is still emerging and its etiology is being questioned. We report a case of pleuroparenchymal fibroelastosis probably idiopathic, the first of its kind to be reported from India, and a brief review of the literature.

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1. Introduction

Idiopathic pleuroparenchymal fibroelastosis is a chronic idiopathic interstitial pneumonia, characterised by upper lobe predominance, significant involvement of the pleura and a histopathology revealing subpleural fibroelastosis. It was first described in 2004 and subsequently included in the ATS/ERS classification of Idiopathic Interstitial Pneumonia (IIP) in 2013 under the category of rare IIP's. Sporadic cases and few series have been reported from all across the globe, but none of these have been from India. We report a case of pleuroparenchymal fibroelastosis probably idiopathic, the first of its kind from India.

2. Case description

A 41 year old lady presented with dry cough and progressive breathlessness for a year. She was evaluated in another centre with a CT thorax and VATS biopsy 3 months into illness. This showed fibrosing interstitial pneumonia (the slides reviewed in our centre was reported as organizing pneumonia). Post biopsy, she developed a left sided loculated pneumothorax, and this remained even after intercostal drainage. She was treated with oral corticosteroids. After a brief period of stability, her symptoms continued to progress. Azathioprine was added on for another 3 months with no response and hence stopped. She was then briefly initiated on Pirfenidone, which was stopped due to intolerance. When she presented to us, she was only on oral steroids. In the mean time, she developed a spontaneous pneumothorax on right side which completely resolved with intercostal tube drainage. There was no history suggestive of a connective tissue disorder. Her co-morbidities were type 2 diabetes mellitus, hypothyroidism and primary infertility. On examination, she was not clubbed. She had reduced air entry in the left infraclavicular region and bilateral diffuse crackles and squeaks. Her room air saturation was 95% but she quickly desaturated to 82% on exertion. Her ABG revealed chronic type 2 respiratory failure with hypoxia. Her CT scan (Fig. 1) revealed loculated pneumothorax in left upper zone, pleural and subpleural parenchymal fibrosis with upper lobe predominance. The fibrotic changes have significantly worsened compare to previous CT picture.

The differentials considered were idiopathic pulmonary fibrosis, idiopathic pleuroparenchymal fibroelastosis and chronic hypersensitivity pneumonitis. Absence of response to steroids and absence of triggering factors dissuaded a diganosis of chronic hypersensitivity pneumonitis. She was started on the maximum tolerable dose of Pirfenidone(400 mg thrice a day) and the oral

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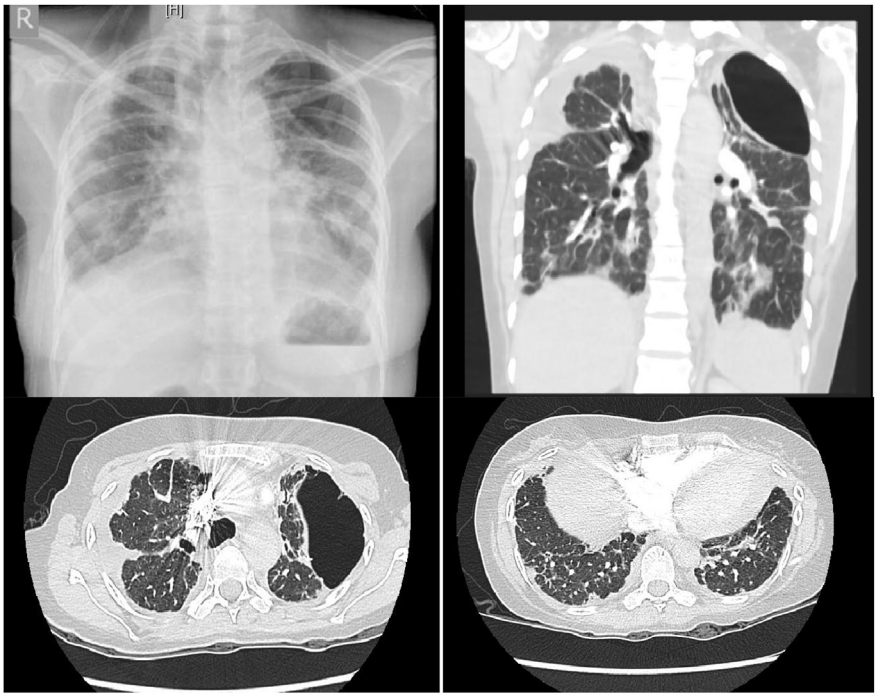

Fig. 1. The chest x-ray and CT thorax revealed a left loculated pneumothorax, pleural and subpleural parenchymal fibrosis with upper lobe predominance and apical pleural thickening.

steroids were gradually tapered. She underwent pulmonary rehabilitation. She was also initiated on nocturnal Non-invasive Ventilation (NIV) at IPAP (Inspiratory Positive Airway Pressure) of 15 cm of H2O and EPAP (Expiratory Positive Airway Pressure) of 6 cm of H2O and long term oxygen therapy was initiated at 1 L/min. She represented with increasing shortness of breath, cough with purulent expectoration and pleuritic right sided chest pain. A CTPA was done to rule out a pulmonary embolism and revealed new areas of bilateral ground glass opacities. She was initiated on intravenous antibiotics. After an improvement for few days, she deteriorated with reduced sensorium secondary to worsening type 2 respiratory failure. Her supports on the NIV were increased. She succumbed to her illness in the next couple of days.

An autopsy was performed. The pleura appeared fibrotic and adherent to the underlying lungs. The right and left lungs were contracted and weighed 250 g and 335 g, respectively. Serial sectioning revealed areas of consolidation and fibrosis. On histopathological examination (Fig. 2), there was marked pleural fibrosis and elastosis with involvement of the underlying lung parenchyma. There was interstitial fibrosis and elastosis with some of the alveoli displaying type 2 pneumocyte hyperplasia. Overall, the features were in keeping with pleuroparenchymal fibroelastosis. As there were no precipitating factors, we concluded her to have had Idiopathic Pleuroparenchymal Fibroelastosis (IPPFE).

The various differentials considered were discussed with the patient and her husband. A few uncoventional treatments were given with good intentions (Pirfenidone for possible idiopathic pulmonary fibrosis and NIV for type 2 respiratory failure in the presence of a loculated pneumothorax), and these were discussed with the family prior to initiation.

3. Discussion

IPPFE is a rare and relatively new entity, first coined in 2004 by Frankel et al. [1], based on 5 patients identified between 1996 and 2001. Cases with similar description have been mentioned in the literature since 1992, especially from Japan. IPPFE was included in the new ATS/ERS classification of Idiopathic Interstitial Pneumonia (IIP) published in 2013 [2] under the rare IIP's. Including the first report in 2004, there have been 36 cases reported so far. Thirty cases have been elaborated in the case series and literature review published by Rosenbaum et al., in 2015 [3]. But among these, a case series of 4 patients from von der Thusen et al. [4] clearly describe PPFE secondary to bone marrow transplantation and hence cannot be counted as IPPFE. We identified 10 additional cases of IPPFE, half of these published in four different reports [5–8] in 2014 and 2015 and the other half in a single series in 2012 by Kusagaya et al. [9]. Nevertheless, none have been reported from India.

Chronic cough and shortness of breath are the usual symptoms of these patients, as in other IIP's. It appears that there is an increased propensity to pneumothorax in IPPFE compared to other IIP's. Among the cases reported, one patient had a presentation with recurrent pneumothorax [6]. There was another presentation with secondary spontaneous pneumothorax [10] published by Becker et al. This publication had a second case of IPPFE which had a persistent pneumothorax after a VATS biopsy, as in our case. Both the cases published by Redondo et al. [8] were complicated by a pneumothorax post CT guided biopsy. It has been suggested that the increased deposition of elastin fibres in the lung is responsible for the easy development of pneumothorax. In an excellent comparison with IPF which is a close clinical differential for IPPFE, as in our case, Enomoto et al. [11] elucidated a lower incidence of the fine crackles, more pneumothoraces, a higher proportion of never-smokers, and lower body mass indices in patients with IPPFE. Our patient does have all these characteristics.

The largest series published so far (12 cases), in 2012 by Reddy et al. [12] and the recent series with literature review by Rosenbaum et al. [3], contend the etiology in the cases of PPFE usually

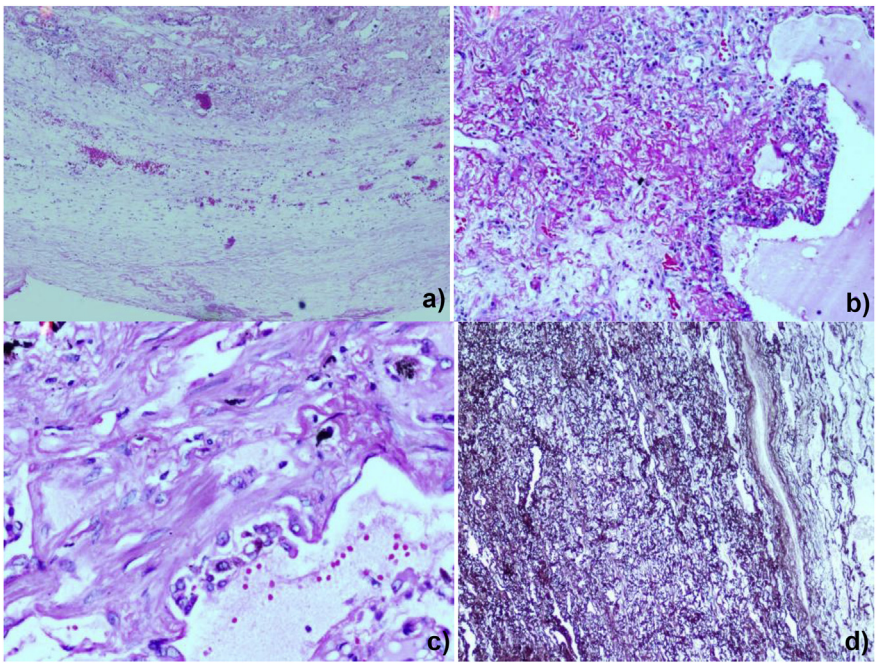

Fig. 2. (a) Subpleural fibrosis and elastosis with extension into the pulmonary parenchyma; H&E 50x. (b) Interstitial fibrosis with elastosis and type 2 pneumocyte hyperplasia; H&E 200x. (c)Interstitial fibrosis with elastosis; H&E 400x. (d) Orcein stain showing numerous elastic fibres in the pleural tissue extending into the adjacent parenchyma. 50x.

reported as idiopathic. The etiological factors proposed based on various cases are genetic, familial, autoimmune, recurrent infections and drug induced including chemotherapeutic agents. A review published in 2013 by von der Thusen [13], looked at 78 cases of PPFE published till then. The etiology in just over half of these patients was either post lung transplantation or bone marrow transplantation highlighting the commonest cause of PPFE. In the other half of these patients who have been thought to have IPPFE,

Table 1
Survival details of all patient with IPFFE published so far.

Sl. No.	Author	Duration from onset of symptoms to time of report or death		Alive(A) or Dead(D) at time of report
		Years	Months	
1.	Frankel et al. [1]	12	0	A
2.		7	0	A
3.		7	0	A
4.		2	0	D
5.		5	0	D
6.	Piciucchi et al. [14]	3	0	A
7.	Reddy et al. [12]	2	0	A
8.		4	0	A
9.		6	4	D
10.		2	7	A
11.		3	6	D
12.		3	0	A
13.		5	0	A
14.		6	0	D
15.		4	0	A
16.		8	0	A
17.		4	0	D
18.		5	5	D
19.	Kusagaya et al. [9]	1	0	A
20.		0	6	A
21.		3	8	A
22.		0	10	A
23.		1	4	A
24.	Noh et al. [6]	3	1	A
25.	Cuppens et al. [7]	2	6	A
26.	Rosenbaum et al. [3]	1	2	D
27.		7	0	A
28.		2	0	A
29.		9	0	D
30.	Redondo et al. [8]	7	10	A
31.	Our case	1	3	D

the above mentioned etiological uncertainties remain.

The review by von der Thusen [12], also set out separate HRCT and pathological criteria for PPFE and classified them as 'definite' and 'consistent with'. Our patient would classify into 'definite PPFE' based on HRCT findings of upper lobe pleural thickening, subpleural fibrosis and less marked involvement of the lower lobes. The differential diagnosis for these HRCT features would usually include asbestosis, advanced chronic fibrotic sarcoidosis and drug induced lung disease. The histopathology is crucial is concluding the diagnosis of PPFE. Rosenbaum et al. [3] in a more recent publication, in addition to proposing that PPFE is secondary to chronic lung injury rather than a separate entity, have laid down proposed diagnostic criteria, based on their series of 5 cases and few of the earlier reports. These are: (1) Fibrous interstitial pneumonia with >80% fibroelastic changes in nonatelectatic (collapsed) lung, (2) Subpleural and/or centrilobular distribution, (3) Overall inflammation absent to mild, (4) No specific lobe predilection, typically multilobar and (5) Rare or no granulomas. These are different from those followed so far, and are yet to be validated and considered by others.

The definitive treatment for IPPFE is lung transplantation. Most patients are tried with steroids [3] and some have tried other immunosuppressants in addition. In our patient, we also tried Pirfenidone due to the clinical possibility of Idiopathic Pulmonary Fibrosis. Prognosis of patients with IPFFE is variable. Piciucchi et al. [14] observed that there could be two forms of IPFFE, looking at the cases published between 2004 and 2008. These they termed as a sporadic form and a familial form, the latter being more aggressive. But this has not been talked of since. We have tabulated (Table 1) the survival details of all the patients published so far, as mentioned in each of the reports. Six of the 36 patients did not have details on the duration of symptoms.

4. Conclusion

IPPFE is a rare IIP, but more cases have been reported in the last few years. It is being debated if there are specific etiologies in these cases. Newer diagnostic criteria are being proposed and need validation and acceptance. Treatment options are limited and prognosis is poor. We report this case of PPFE of probably idiopathic origin, the first of its kind from India, which will add to number of global cases reported and will help in establishing the above, more definitely.

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