



Journal Homepage: -www.journalijar.com

INTERNATIONAL JOURNAL OF ADVANCED RESEARCH (IJAR)

Article DOI:10.21474/IJAR01/11560
DOI URL: <http://dx.doi.org/10.21474/IJAR01/11560>



RESEARCH ARTICLE

A RARE CASE OF GIANT EMPHYSEMATOUS BULLAE IN LEFT LUNG DUE TO ALPHA 1- ANTI-TRYPsin DEFICIENCY

Priya Kushwah¹, Akhilesh Patel², Sunil Gujar², Yogeshwar P. Shukla¹, Jyotsana Goyal¹, Sneha Ninama¹ and Manoj Kumar Chaudhary²

1. Surgical Oncology Resident, Aiiims Bhopal, Madhya Pradesh, India.
2. General Surgery, Senior Resident, Aiiims Raipur, Chhattisgarh, India.

Manuscript Info

Manuscript History

Received: 25 June 2020
Final Accepted: 30 July 2020
Published: August 2020

Key words:-

Alpha-1-Antitrypsin Deficiency, COPD,
Vanishing Lung Syndrome,
Emphysematous Bullae

Abstract

Introduction: Alpha-1-antitrypsin deficiency (AATD) is a genetic disorder that manifests as pulmonary emphysema, liver cirrhosis and, rarely, as the skin disease panniculitis, and is characterized by low serum levels of AAT, the main protease inhibitor (PI) in human serum. The prevalence in Western Europe and in the USA is estimated at approximately 1 in 2,500 and 1: 5,000 newborns. Environmental factors such as cigarette smoking, and dust exposure are additional risk factors and have been linked to an accelerated progression of this condition. Cirrhotic liver failure may occur around age 50. The diagnosis can be established by detection of low serum levels of AAT and isoelectric focusing.

Case Report: A 22 years old male presented with complaint of Breathlessness since 6 month, Pain over left chest since 4 months. Patient was chronic smoker from past 7 years and used to smoke 12 cigarettes daily. Past history suggested of Pulmonary Tuberculosis 6 years back for which he took Anti-tubercular treatment category I for 6 Months. CT chest was suggestive of middle sections of the left lungs contains gigantic bullae over ½ of hemithorax volume. Pulmonary parenchyma in lower sections was preserved, but emphysematous and Fibrotic Patch and Similar Emphysematous Bullae on right side. Serum Alpha-1-antitrypsin level was 0.2g/L. Antero-lateral skin incision was taken a large Emphysematous Bullae found and excision of that part of lung lobe was done. one month follow up xray was done in which there was expansion of left lung was seen. patient kept under regular follow up and even after two year lung showed expansion with no recurrence of bullae.

Conclusion: In conclusion, surgical resection of giant emphysematous bullae and appropriately prescribed therapy (drug treatment and hygiene regime) allowed us to achieve a positive effect and maintain the patient's life quality for a long time.

Copy Right, IJAR, 2020. All rights reserved.

Corresponding Author:- Akhilesh Patel

Address:- General Surgery, Senior Resident, Aiiims Raipur, Chhattisgarh, India.

Introduction:-

Alpha-1-antitrypsin deficiency [AATD] was first reported in 1963 by Carl-Bertil Laurell and Sten Eriksson who noted a link between low plasma serum levels of alpha-1-antitrypsin and symptoms of pulmonary emphysema [1]. Since these first cases were described, an understanding of the biochemical mechanisms and genetic abnormalities involved has developed [2], and alpha-1-antitrypsin deficiency is now thought to be one of the most common hereditary disorders worldwide, comparable in frequency to cystic fibrosis [3,4]. The protein alpha-1-antitrypsin is a 52 kDa molecule produced primarily in hepatocytes and released into the blood circulation by the liver [5]. The protein is present in all body tissues but appears to have its primary physiologic significance in the lungs, where it protects the healthy but fragile alveolar tissue from proteolytic damage by enzymes like neutrophil elastase [6]. Alpha-1-antitrypsin is an acute phase protein which means that production by the liver is subject to various stimuli, including inflammatory mediators induced by fever [2]. Therefore, protein levels in the circulation may vary depending on the medical condition of an individual. The normal serum concentration may range between 1.5 to 3.5 g/L (or 20 to 48 μ M) [2]. Among clinicians and patients some confusion may arise about the clinical significance of deficiency in alpha-1-antitrypsin. The first cases described by Laurell and Eriksson were related to a very low serum concentration of the protein and subsequently it was discovered that these patients had a particular gene defect (defined as Z deficiency) in both alleles of the chromosome making them prone to the development of lung and liver disease. Later in time it was discovered that various other gene defects exist and most of them cause their own range of serum concentrations below the normal range [5]. A serum concentration below 0.5 g/L (11 μ M) is considered a reason for further analysis. In addition, individuals who carry a genetic defect in only one allele of the chromosome (heterozygotes) may also have a reduced serum concentration. Often, when patients with emphysema are told that they are deficient of alpha-1-antitrypsin, they fear that their deficiency will cause the clinical events described by Laurell and Eriksson. However, as described below, it will be explained why in contrast to heterozygous MZ type, in most cases only the homozygous Z type of deficiency, as well as some very rare Null phenotypes with absent alpha-1-antitrypsin serum levels result in clinical significant disease.

Case Presentation:

A 22 years old male presented with complaint of Breathlessness since 6 month, Pain over left chest since 4 months. Patient was chronic smoker from past 7 years and used to smoke 12 cigarettes daily. Past history suggested of Pulmonary Tuberculosis 6 years back for which he took Anti-tubercular treatment category I for 6 Months. Physical examination revealed an expiratory wheeze and fine crackles during forced expiration. Radiographically, giant thin-walled bullae were detected in left lungs, characteristic of vanishing lung syndrome [5–7]. Chest X-ray was suggestive of Emphysematous Bulla in left lower lung with underlying compressed lung with mediastinal shift to right side [FIGURE 1A]. CT chest was suggestive of middle sections of the left lungs contains gigantic bullae over $\frac{1}{2}$ of hemithorax volume. Pulmonary parenchyma in lower sections is preserved, but emphysematous and Fibrotic Patch and Similar Emphysematous Bullae on right side [FIGURE 1B]. Serum Alpha-1-antitrypsin level was 0.2g/L. Routine blood investigation was done and it was normal in limit. Pre operative preparation was done. Antero-lateral skin incision was taken a large Emphysematous Bullae was found and excision of that part of lung lobe was done (lobectomy) [FIGURE 2]. After operation patient was not able to maintain the SpO₂ over one lung, which was also compromised hence patient kept in ICU and tracheostomy was done. Patient kept on mechanical ventilation for 12 days. Weaning off from ventilator was done gradually and under higher antibiotic coverage to avoid lung infection. Once patient got use to one lung ventilation, he was shifted to ward from ICU. ICD drain was removed on 14TH post operative day once drain fluid become serous and 48hrs drain output was less than 100ml. After one month follow-up X-ray of left lung suggested of expansion of left lung [FIGURE 3]. After two year expanded lung with no recurrence of bullae.

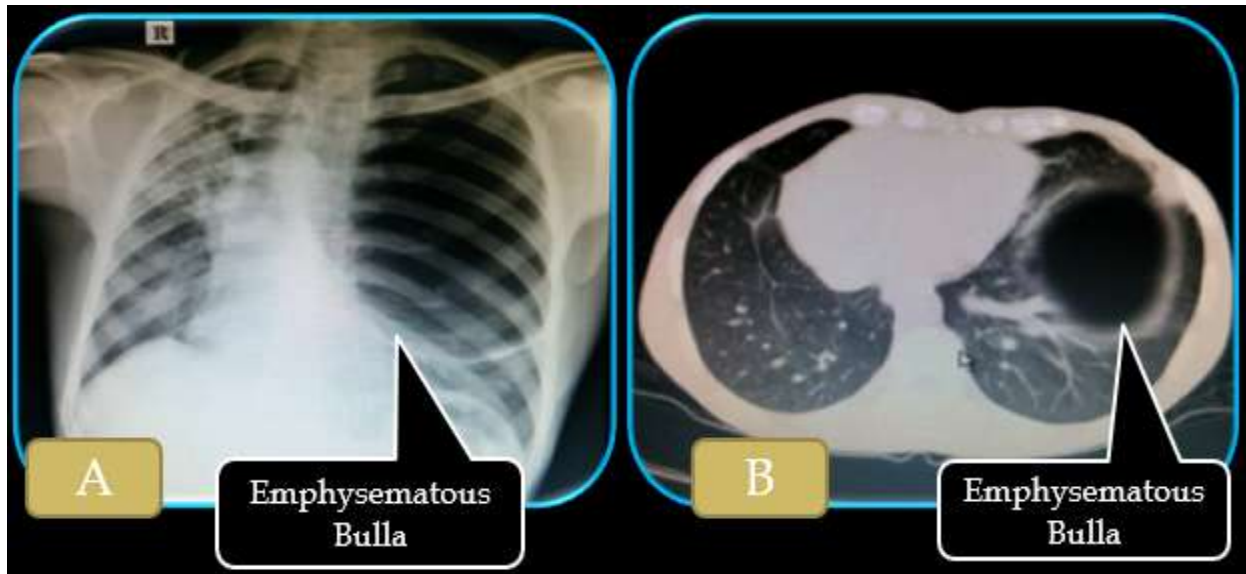


Figure 1:- Chest X-Ray showed emphysematous bulla in left side lung with underlying collapse lung, B- CT chest showed well defined emphysematous bulla in left side lung.

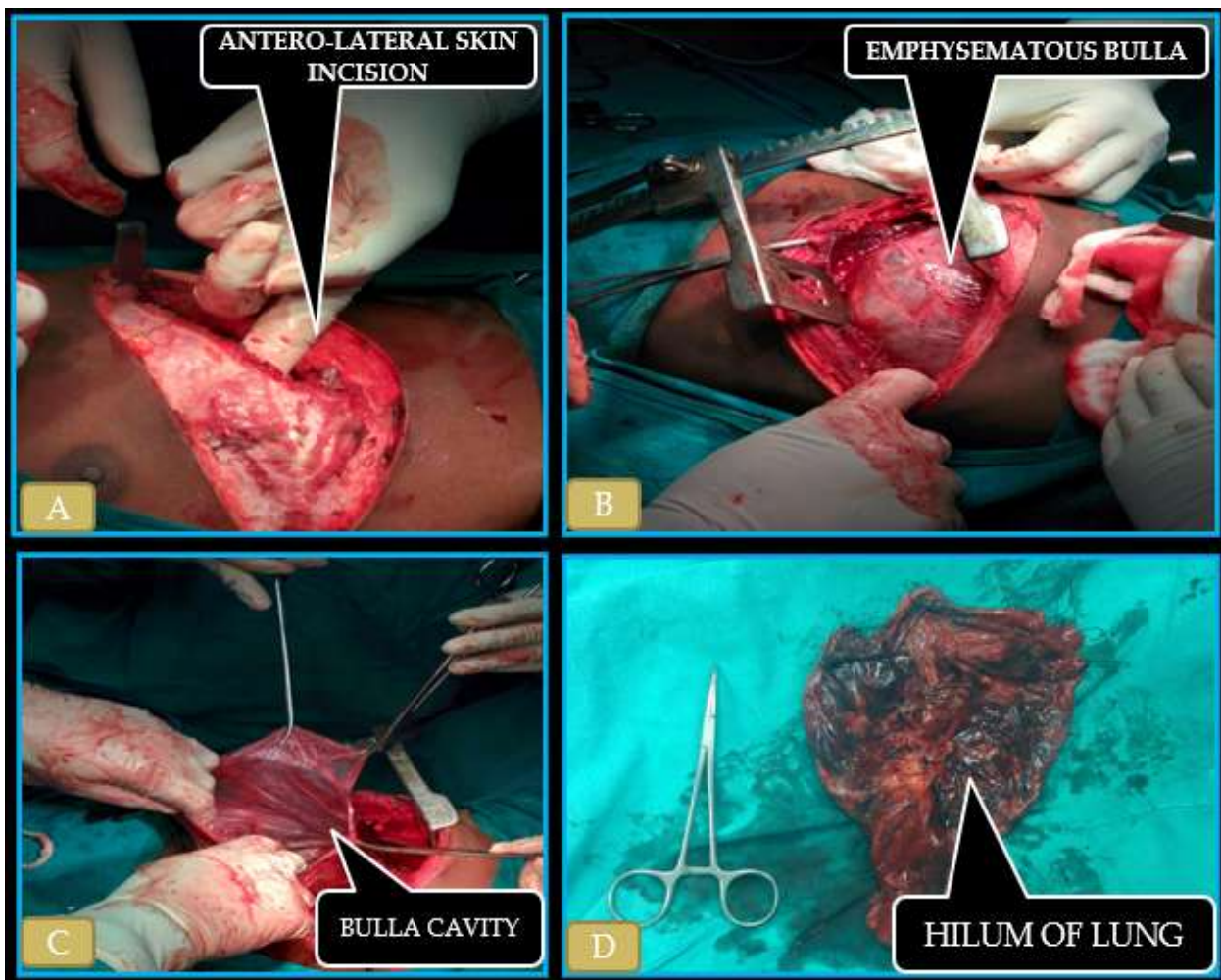


Figure 2:- Operative steps, A- Anterolateral incision, B- Bulla, C- Bulla cavity, D- Excision of cyst with hilar lung.

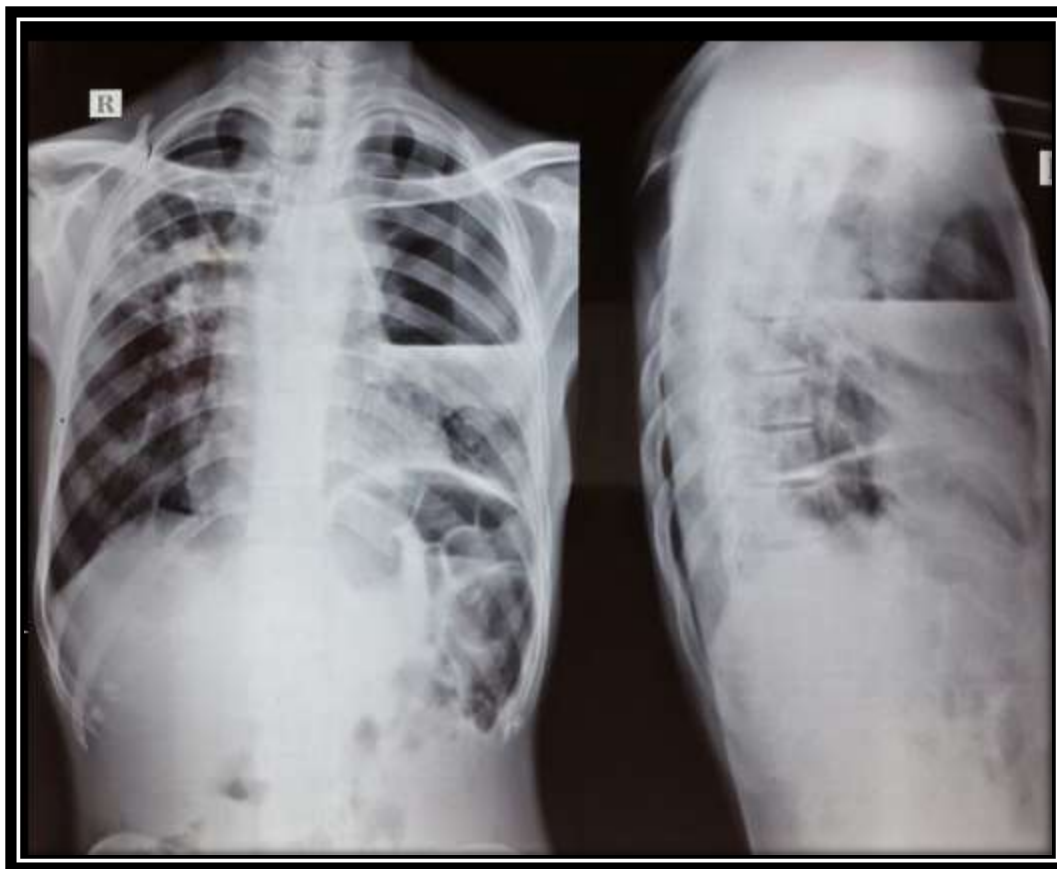


Figure 3:- Chest X-ray of left lung suggested of expansion of left lung.

Discussion:-

The lung manifestations of AAT deficiency include emphysema and chronic obstructive pulmonary disease (COPD) [8]. Emphysema usually develops by the third to fourth decade in affected individuals who smoke cigarettes and may appear in the fifth or sixth decade in individuals who have never smoked. It is currently hypothesized that two mechanisms contribute to the development of lung disease, in particular to emphysema. First, the serum level of alpha-1- antitrypsin appears to be important. It is observed that cigarette smokers who produce no alpha-1-antitrypsin at all in their liver or in monocytes, defined as individuals with the very rare homozygous Null variant, develop emphysema at younger age than subjects with the homozygous Z allele related deficiency [9]. Under appropriate circumstances, cigarette smoke recruits inflammatory cells in the lung which may release proteolytic enzymes in alveolar areas. For the development of emphysema, plasma levels of alpha-1-antitrypsin are important in the protection against proteolytic damage of alveoli in the lung, in particular by neutrophil elastase activity [10,11].

Diagnosis for alpha-1-antitrypsin deficiency? First of all, all newborns with a bleeding disorder or prolonged neonatal jaundice should be tested [8]. Secondly, all individuals with a history of asthma or chronic obstructive lung disease, particularly below the age of 40 [8]. Thirdly, all siblings of index cases [8]. Finally, all individuals with unexpected liver cirrhosis should be tested [2]. With respect to lung disease, individuals should not start cigarette smoking or should stop urgently when smoking already started. This is the only available effective treatment to reduce the progression of decline in lung function. There is consensus in the scientific community on how to test, expressed in an ATS/ERS Statement on the diagnosis and treatment of alpha-1-antitrypsin deficiency [8]. This important document states that a physician should start with the detection of a serum level of alpha-1-antitrypsin. If reduced below the reference value of the laboratory, physicians should obtain a genotype or phenotype of alpha-1-antitrypsin. There are now commercial kits that test for presence of Z and S alleles in the gene [12]. If the serum level of alpha-1-antitrypsin is low, but the genotype test does not reveal a Z or S deficiency, isoelectric focusing of serum may reveal rare Null variants of alpha-1-antitrypsin which can be further characterized by genotyping. Once new cases of alpha-1-antitrypsin have been detected, it is recommended by the Alpha1 International Registry (AIR) [13] to contact the national representative for alpha-1-antitrypsin deficiency matters to submit the clinical phenotype

of the patient to the database of AIR and to obtain a plasma sample and DNA sample for future scientific studies and potential participation of the newly detected patient in future clinical trials for new drugs. Differential diagnosis Often physicians diagnose patients with emphysema at age 30 to 40 but who have no alpha-1-antitrypsin deficiency. There are no known other genetic deficiencies that are as strongly related with emphysema as Pi ZZ alpha-1-antitrypsin deficiency. These include viral infection, hemochromatosis, Wilson's disease and autoimmune hepatitis. The formation of rapidly progressing giant emphysematous bullae is often associated with COPD progression [14, 15–17], and if combined with a FEV1 decrease to less than 25%, may be an indication for lung transplantation [18]. Significant progressive reduction of spirometry indications and reduced exercise tolerance accompanied with dyspnea are characteristic to patients with vanishing lung syndrome (VLS). Surgical treatment is possible and effectively reduces dyspneic symptoms and significantly lowers the risk of spontaneous pneumothorax in patients with VLS [18]. Despite the associated risks of bulla recurrence, VATS bullectomy significantly improves patient respiratory function and reduces risks of serious complications associated with giant emphysematous bullae. Our case reports shows, that within a two year follow-up period it is possible that no recurrence of giant bullae manifests, which underlines the efficacy of surgical treatment of patients with VLS. VLS in patients with COPD is complicated by significant reduction in healthy lung tissue, and is often accompanied by severe respiratory function morbidity. VATS giant bulla resection should be accompanied by proper pharmacological therapy and strict respiratory exercise regimen. Surgical excision of giant bullae significantly reduce the ratio of pleural cavity to lung volume, so we recommend gradual expansion with controlled pneumoperitoneum to reduce risk of postoperative complications and spontaneous pneumothorax.

Conclusion:-

In conclusion, surgical resection of giant emphysematous bullae and appropriately prescribed therapy (drug treatment and hygiene regime) allowed us to achieve a positive effect and maintain the patient's life quality for a long time. It is important to plan a surgical intervention with compensation of lung volume reduction (controlled pneumoperitoneum, pleural cavity draining), appropriate pharmacological therapy and respiratory exercises to maintain the positive effect of VLS treatment.

Funding:

None.

Availability of data and materials:

Data and material available upon request.

Consent for publication:

Informed consent for publication was obtained.

Competing interests:

None.

References:-

1. Laurell CB, Eriksson S: The electrophoretic pattern alpha1- globulin pattern of serum in alpha1-antitrypsin deficiency. *Scan J Clin Lab Invest* 1963, 15:132-140.
2. Fagerhol MK, Laurell CB: The polymorphism of "prealbumins" and alpha-1-antitrypsin in human sera. *Clin Chim Acta* 1967, 16:199-203.
3. World Health Organization: Alpha-1-antitrypsin deficiency: memorandum from a WHO meeting. *Bull World Health Organ* 1997, 75:397-415.
4. de Serres FJ: Worldwide racial and ethnic distribution of alpha1-antitrypsin deficiency: summary of an analysis of published genetic epidemiologic surveys. *Chest* 2002, 122:1818-1829.
5. Brantly M, Nukiwa T, Crystal RG: Molecular basis of alpha-1-antitrypsin deficiency. *Am J Med* 1988, 84:13-31.
6. Gadek JE, Fells GA, Zimmerman RL, Rennard SI, Crystal RG: Antielastases of the human alveolar structures. Implications for the protease-antiprotease theory of emphysema. *J Clin Invest* 1981, 68:889-898.
7. Sveger T: Liver disease in alpha1-antitrypsin deficiency detected by screening of 200,000 infants. *N Engl J Med* 1976, 294:1316-1321.

8. [ATSERS] American Thoracic Society, European Respiratory Society: American Thoracic Society/European Respiratory Society statement: standards for the diagnosis and management of individuals with alpha-1 antitrypsin deficiency. *Am J Respir Crit Care Med* 2003, 168:818-900.
9. Cox DW, Levison H: Emphysema of early onset associated with a complete deficiency of alpha-1 antitrypsin (null homozygotes). *Am Rev Respir Dis* 1988, 137:371-375.
10. Eriksson S: Pulmonary emphysema and alpha-1-antitrypsin deficiency. *Acta Med Scand* 1964, 175:197-205.
11. Kramps JA, Bakker W, Dijkman JH: A matched-pair study of the leukocyte elastase-like activity in normal persons and in emphysematous patients with and without alpha1-antitrypsin deficiency. *Am Rev Respir Dis* 1980, 121:253-261.
12. Bals R, Koczulla R, Kotke V, Andress J, Blackert K, Vogelmeier C: Identification of individuals with alpha-1-antitrypsin deficiency by a targeted screening program. *Respir Med* 2007, 101:1709-1714.
13. Alpha1 International Registry (AIR) [<http://www.aatregis try.org>]
14. Global initiative for chronic obstructive lung disease strategy for the diagnosis, management and prevention of chronic obstructive pulmonary disease: an Asia-Pacific perspective. *Respirology*. 2005;10(1):9-17Wiley; Available from: <https://doi.org/10.1111/j.1440-1843.2005.00692.x>.
15. Findlay JM. Radiological presentation of a giant bulla as a tension pneumothorax. *J Emerg Med*. 2012;3(43):e211-3. 11. Pearson MG, Ogilvie C. Surgical treatment of emphysematous bullae: late outcome. *Thorax*. 1983;2(38):134-7.
16. Schipper PH. Outcomes after resection of giant emphysematous bullae. *Ann Thorac Surg*. 2004;3(78):976-82.
17. Fishman RMS, Grippi MA, Elias JA, Fishman JA, Kotloff RM, Fishman AI Fishman's pulmonary diseases and disorders 5th edMcGraw-Hill Medical; 1. 2015.
18. Gian FM, Franca MA, Alfredo M, Antonio P. Treatment by VATS of giant bullous emphysema: results. *Eur J Cardiothorac Surg*. 1998;13:66-70.