Recurrent spontaneous pneumothorax in a patient Wilson disease who is on long term D-penicillamine. Case report

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Case Report  

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Abstract

Background

Recurrent spontaneous pneumothoraces (PSP) in association with liver disease is well known to occur with alpha 1 antitrypsin deficiency (AATD). Wilson disease (WD) association to recurrent PSP is not a known entity.

Case presentation

A 42-year-old nonsmoker man with a history of recurrent PSP admitted with large right pneumothorax. Following intercostal chest drain (ICD) patient's breathing improved and the lung expanded. Despite that, he continued to have a small residual pneumothorax (< 2cm). Twelve years ago, he was diagnosed to have WD. Patient was on treatment with D-penicillamine. After 3 years to the diagnosis of WD, patient had developed left sided recurrent PSPs where he ended up with left-pleurectomy in 2015. For the current event, initially expectant management was done for residual pneumothorax. All the possible causes for PSP were excluded. On follow up, he continued to be symptomatic. Thoracic surgical referral was arranged for Video-Assisted Thoracoscopic Surgery (VATS) and redo-pleurectomy. Safety of future treatment with D-penicillamine is not concluded as there is no convincing evidence to prove it as a culprit agent for PSPs. Multidisciplinary discussion arranged and consideration of treatment with alternative copper chelating therapy was emphasized.

Conclusions

Though rare, it is important to observe for occurrence of PSP in WD patients. This case report will be an eye opening for association of lung disease and WD and related treatment.

Background

Wilson disease (WD) is an autosomal recessive disorder with liver disease and neurological sequale. Well known clinical manifestations include cirrhosis, neurological manifestations and renal manifestations [1]. Lung diseases association to WD is sparsely reported in literature.

Treatment with D penicillamine is in high-profile to cause varied adverse events of respiratory system including pleural based diseases and rarely pleural effusions [2].

Recurrent spontaneous pneumothoraces in association with either Wilson disease or D-penicillamine have not been documented in the medical literature. In this case report we publish a very rare co-occurrence of recurrent PSP in a patient with WD.
Case presentation

A 42-year-old non-smoking male with history of multiple spontaneous pneumothoraces (which had been treated with pleurectomy) was referred to our tertiary center with sudden onset difficulty in breathing and right sided pleuritic chest pain. He was found to have a large right sided pneumothorax and managed initially with intercostal chest drain (ICD). Following the drain insertion, patients breathing had improved and the lung had expanded. Despite that, he continued to have a small residual pneumothorax (< 2cm) (Fig. 1a & b).

Twelve years ago, he has been evaluated for tremors and ataxia where he was diagnosed to have WD with positive ATP7B gene homozygous mutation, very low serum ceruloplasmin level. Additionally, his MRI brain showed giant panda sign and positive Kayser- Fleischer (KF) rings (Fig. 2). Since then the patient was on treatment with D-penicillamine.

After three years to the first diagnosis of WD, patient had developed left sided recurrent PSPs (Fig. 1c & d), where he ended up in video assisted thoracoscopic (VATS) guided left side pleurectomy in 2015. Since then, he was stable until the current presentation.

There was no similar history in the family and there was no evidence of significant exposures, neurocutaneous diseases, and interstitial lung diseases. He was a lifetime non-smoker and had not used any other substances.

Examination revealed normal vital signs, reduced chest expansion and absent breath sounds on the upper zone of right chest.

Immediate antero-poterior chest radiograph revealed right side mild (< 2cm) pneumothorax and high-resolution chest-tomography revealed an uncomplicated right-side pneumothorax without associating sub pleural blebs, cystic/bullous lung disease. The parenchyma and the mediastinum were otherwise normal. His pulmonary function test found to be normal. The results of routine blood investigations were essentially normal including retroviral screening.

Evaluation for possible causes of primary spontaneous pneumothorax (PSP) work up was done including tuberculosis, Marfan syndrome, alpha 1 antitrypsin deficiency (AATD), Interstitial lung disease, neurocutaneous syndromes and cystic lung diseases.

As our patient was asymptomatic with residual small pneumothorax, initially expectant management was done. But on follow up visits he continued to have no improvement, thoracic surgical referral was arranged for video-assisted thoracoscopic surgery (VATS) and redo- pleurectomy. Safety of future treatment with D-penicillamine is not concluded in this patient as there is no convincing evidence to prove it as a culprit agent for PSPs. Multidisciplinary discussion with the treating neurologist, pulmonologist, patient and the family was arranged and considering of treatment with alternative copper chelating therapy was emphasized.
Discussion

Wilson disease, which is also known as hepatolenticular degeneration, is an autosomal recessive disorder with dysfunctional copper metabolism. ATP7B mutation is the primary pathology which cause dysfunctional biliary copper metabolism [3]. As a result, free copper is accumulated inside the mitochondria of liver, limbus of the cornea, basal ganglia and kidneys. These will manifest as cirrhosis, KF rings, neuro-psychiatric manifestations, and renal tubular disorder [3].

Co-existing liver and lung diseases is well known to occur in patients with AATD. Though, recurrent pneumothoraces in association with AATD has been reported in the literature, association with WD is not yet reported. The exact mechanism by which the pneumothorax occurs remains unclear.

D-penicillamine which is a chelating agent for copper, a high-profile cause for various multisystemic side effects. By the immunosuppressive mechanism of action, it can cause blood dyscrasia, dermatitis, nephrotic syndrome, myasthenia gravis and systemic lupus erythematosus (SLE) [4]. Moreover, it is well known to cause respiratory system related side effects such as bronchospasms [5], bronchiolitis obliterans [6], Good pasture's syndrome and interstitial pneumonitis [7]. D-penicillamine induced SLE can be associated with pneumonitis, alveolitis and pleural effusions [8]. However, very few cases of pleural based diseases were reported with direct association to D-penicillamine. Single case has been reported with pleural effusion who has received twelve years of D-penicillamine treatment [2].

Our case demonstrates a very rare occurrence of recurrent pneumothoraces in a patient diagnosed with WD who is on long term D-penicillamine therapy. To the best of our knowledge, this is the first case report with recurrent pneumothoraces in association to WD or D-penicillamine treatment.

Conclusions

Given the rarity of recurrent pneumothoraces association with Wilson disease and usage of D-penicillamine, it is truly important to observe for occurrence of such complications in these group of patients. This case report will be an eye opening for association of recurrent pneumothorax and WD.

List Of Abbreviations

AATD (Alpha-1 antitrypsin deficiency)

FLAIR (Fluid-attenuated inversion recovery)

PSP (Primary spontaneous pneumothorax)

SLE (Systemic lupus erythematosus)

VATS (Video assisted thoracoscopic surgery)
WD (Wilson disease)

Declarations

Ethics approval and consent to participate.

Not relevant

Consent for publication

Written informed consent was obtained from the patient for publication of this case report and any accompanying images. A copy of the written consent is available for review by the Editor-in-Chief of this journal.

Availability of data and materials

Not relevant

Competing interests

The authors declare that there is no conflict of interest regarding the publication of this paper.

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Author's contributions

Gunathilaka MDN, Bandara LMH, Kularatne WNS and Handagala S were involved actively in the management of the patient. Gunathilaka MDN drafted the manuscript. All the others provided valuable inputs and guidance during the preparation of the manuscript. Bandara LMH and Kularatne WNS was responsible for overall management of the patient and supervised the writing critically. All authors read and approved the final manuscript.

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References


Figures
Figure 1

(a & b) illustrates the current presentation with right side residual pneumothorax in CXR (white arrows) and in HRCT of chest (Red arrows). Figure 1 (c & d) illustrate past left sided pneumothorax in CXR (yellow arrows) and HRCT (Black arrow)
Figure 2

(a) White arrows indicate the KF rings of anterior chamber of eye. (b) MRI of brain FLAIR sequence showing the face of giant panda sign. Green arrow shows increased signal intensity in the midbrain, yellow arrow shows preservation of signal intensity of pars reticulate of substantia nigra.