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Case Report

Unusual Case of Pleural Effusion-Not Everything is Tuberculosis

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Abstract

Pleural effusion is a common disease entity in a country like India. A majority of the cases relate to Tuberculosis or Malignancy. Varied causes of Pleural effusion are reported in literature. Drug induced pleural effusion is a rare and important cause of pleural effusion. It is difficult to diagnose as there is no definitive diagnostic tool. Drug induced pleural effusion is diagnosed by ruling out common causes of pleural effusion along with having a strong suspicion of an offending drug causing the disease entity. We here present a very rare case of drug induced pleural effusion caused due to Valproic acid which was earlier treated a as Tubercular pleural effusion.

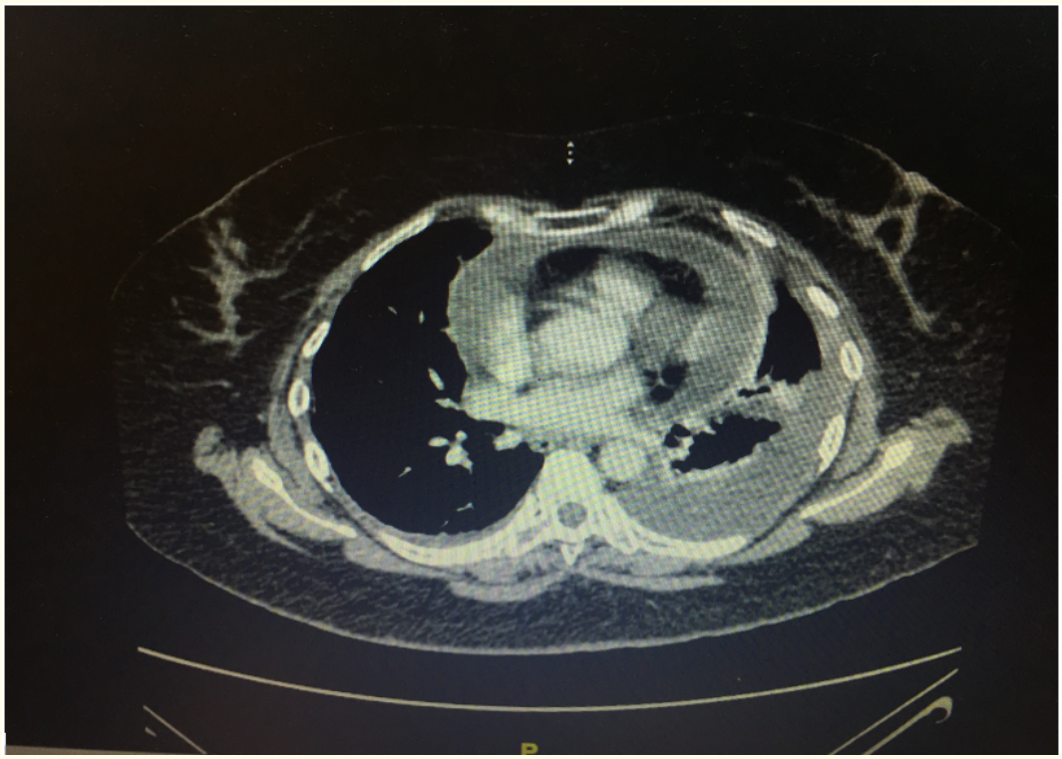
Keywords: *Pleural effusion; Tuberculosis; Valproic Acid*

Introduction

Valproic acid is one of the most widely used antiepileptic drugs(AED) drugs used for the management of epilepsy, mood disorders, bipolar disorders [1]. Drug induced effusion are rare and extremely difficult to detect and prove. Common drugs implicated in drug induced pleural effusion include amiodarone, nitrofurantoin, dantrolene, methysergide, fluoxetine and clozapine [2]. We hereby report a case of concomitant pleural and pericardial effusion in a patient with previous seizures undergoing valproic acid therapy which improved upon substitution of the drug with Levetiracetam.

Case Report

A 46-year-old female was admitted to the internal medicine department of our hospital due to breathlessness and dry cough since past one month. Her previous history was unremarkable except that she had epilepsy that was being treated for past one year with valproic acid 1250 mg/day. Physical examination of the chest revealed decreased breath sounds at the left side of the left hemithorax and faint heart sounds. Chest x-ray and Computerized Tomographic Thorax (Figure 1) was done which revealed left pleural effusion with moderate pericardial effusion. Pleurocentesis was done which revealed exudative effusion (protein: 5.4 gm/dL) with high total counts (12500 cells/mm^3) with lymphocytic predominance and low ADA (20 IU/L). Patient was then referred to the Department of Pulmonology for further evaluation and management. Further laboratory investigation, including thyroid hormones, Anti-nuclear antibody and anti-neutrophil cytoplasmic antibody tests were negative. Renal, liver, thyroid function tests, and serum electrolyte levels were found to be normal. Pleural fluid cytology, amylase, triglycerides and cholesterol were within normal limits. On revisiting her clinical reports, test and whole history, regular use of valproic acid was suspected to be the cause of the effusion. Neurology opinion was taken and Valproic acid was substituted with Levetiracetam. Patient improved with the substitution of the drug confirming our diagnosis.



Discussion

Valproic acid is known to have a wide spectrum of anticonvulsant activity against different seizure types, hence it is increasingly suggested that it acts through a combination of several mechanisms. Valproate is known to increases GABA synthesis and release, thereby potentiating GABAergic functions in some specific brain areas, such as substantia nigra which is thought to be involved in the regulation of seizure generation and propagation. It also seems to reduce the release of the epileptogenic amino acid γ-hydroxybutyric acid and attenuate neuronal excitation induced by NMDA-type glutamate receptors [3].

Possible adverse effects of Valproic acid include, sedation, weight gain, hair loss, gastrointestinal symptoms, derange live functions. Serious adverse events include agranulocytosis, encephalopathy and fetal hepatotoxicity [4].

Pleural effusion has rarely been reported in literature with Valproic acid [2-9]. The effusion may be eosinophilic or lymphocytic, may be unilateral or bilateral and may improve within days if discontinuation of the offending drug. Pericardial effusion after drug therapy has been reported in literature with chemotherapeutic drugs. Pleural effusion may appear within hours to upto 12 years after a drug is initiated Antiepileptics induced pericardial effusion has been reported previously with clozapine [5]. Most of the cases in literature have isolated Pleural effusion which is either lymphocytic or eosinophilic as the complication [6]. Our case is rare as it is associated with simultaneous pleural and pericardial effusions. Only two previous cases of pleuro-pericardial effusion with valproic acid have been reported after searching through literature [7,8]. An interesting one describing a case of bilateral transudative pleural effusion has also been described in literature where the patient had been receiving the drug for a year and presented with fever, dry cough, dyspnea and unilateral pleural effusion [9].

After all other causes of pleuro-pericardial effusion have been excluded, can a diagnosis of valproic induced pleuro-pericardial effusion can be made. A complete drug history should hence be sought in undiagnosed cases of pleural/pericardial effusions. He mechanisms underlying drug induced effusion include acute hypersensitivity reaction, drug-induced inflammation in the pleural space, a direct dose-related toxic effect, or mesothelial cell injury [10]. The probability of the drug causing the effusion has to be based on clinical judgment and can be proved after stopping the offending drug.

This case is probably the only third case in literature with valproate causing concurrent pleura and pericardial effusion.

Conclusion

Valproic acid induced pleura-pericardial effusion is an extremely rare condition which can be difficult to detect but relatively easy to treat in the form of substitution of the drugs. Physicians should be aware of the various unusual causes of pleuro-pericardial effusions and should keep drug induced effusion in mind while investigating a case of undiagnosed pleura-pericardial effusion.

Support

Nil.

Conflicts of Interest

None declared.

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