

Excipient Lung Disease- An Under recognized Cause of Sudden Death in Young Adults: An Autopsy Case SeriesT. Subachitra¹, R. Sathyalakshmi², C. Arun Prabhakaran³, Yogambal Muthureddy⁴¹Associate Professor of Pathology, Stanley Medical College, Chennai, Tamil Nadu²Associate Professor of Pathology, Stanley Medical College, Chennai, Tamil Nadu³Assistant Professor of Pathology, Stanley Medical College, Chennai, Tamil Nadu.⁴Associate Professor of Pathology, Government Villupuram Medical College, Chennai, Tamil Nadu.

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Abstract:

Aim and Objectives: Sudden death in young adults can occur due to many reasons including myocardial infarction, Arrhythmias, Myocarditis, Pulmonary embolism etc. Excipient lung disease is an under recognized cause of sudden death in young adults which is characterized by multiple granulomas around the pulmonary vessels in intravenous drug abusers especially who misuse crushed oral tablets for intravenous injection. This study describes the pathological features of excipient lung disease and the importance of postmortem assessment to know the exact cause of death

Keywords: Excipient, Pulmonary Granulomas, Drug Abuse.

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Introduction

In India, 8.75 million population use cannabis, two million use opiates and 0.6 million use sedatives or hypnotics. 17 to 26% of these people are dependent and require urgent treatment. Cannabis, opiates and heroin are the drugs commonly misused in India. Heroin, Buprenorphine and proxyphene are the most commonly injected narcotic drugs.

2.8% are cannabis users, 1.08% use sedatives (non-medical use), 2.06% use opiates. 8.5 lakh people are injecting drugs as per National Centre for drug abuse.

Oral narcotic drugs and sedatives are frequently misused as intravenous injections but underreported. The fillers which are insoluble inert particles called excipients bind to protect the active drug and also helps in swallowing [1-3]. Starch, Crospovidone, talc, microcrystalline cellulose are the excipients used. [2,4,5,6,7]

Case series

We report a series of 12 cases of young adults with sudden death with features of excipient lung disease. All the cases had the history of crushed oral medications injected intravenously. None of the patients were diagnosed ante mortem as Excipient lung disease.[3] of them had the needle tracks in forearm. Invariably all the 12 cases in histopathology sections showed angiocentric granulomas in the lung parenchyma concentrated around the pulmonary vessels. (Figure 1-3) 5 cases had basophilic material in the pulmonary vessels and in the granulomas. Thrombophlebitis were noted in 2 cases where cubital veins were separately received for analysis. (Figure 4) special stains PAS, Congo red were used to find out the fillers used. In one case congo red was positive in the basophilic material. (Figure 3)

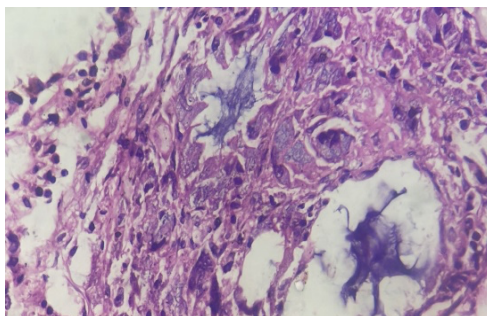


Figure 1: Low power view showing pale gray material surrounded by foreign body giant cell reaction

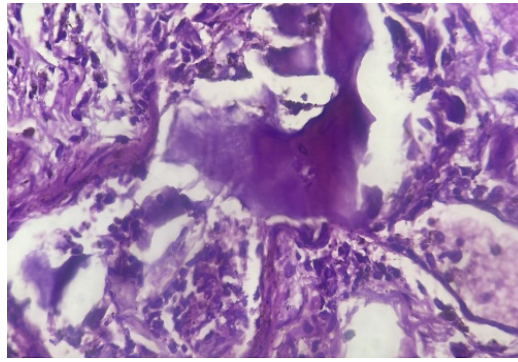


Figure 2: PAS special stain highlights the foreign material adjacent to blood vessel

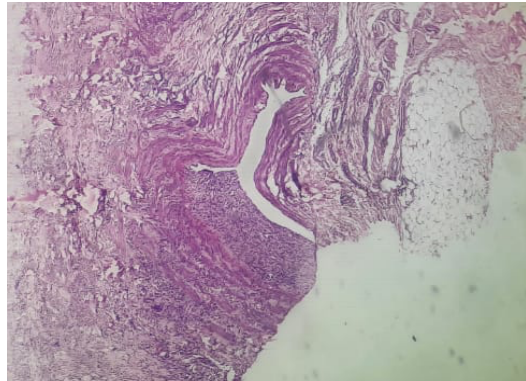


Figure 3: Congo red stain showing foreign body material

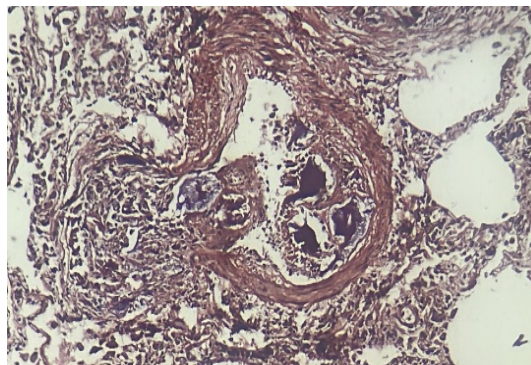


Figure 4: Low Power View Showing Thrombophlebitis Of Blood Vessels

Discussion

Initially methadone tablets were used by heroin addicts with talc as excipient[8]. Analgesics and other tablets such as antihistamines were also used for intravenous injection[2,8]. Amphetamine, Pentazocine, Barbiturates are the other tablets which contain talc and misused intravenously.[9,10]. Cospovidone and Starch were combined and used with other excipients.

Clinically patients with excipient lung disease usually asymptomatic and in severe cases patient may present with shortness of breath and cough. Patients under medication for chronic illnesses such as malignancies, migraine, psychiatric diseases were prone for dependency and addiction later on leading to excipient lung disease due to drug misuse. [11,12]. In our case series 2 cases had history of seizure disorder on medication.

Among the excipients Starch was removed quickly from lung and causes less reaction. Cospovidone will cause thrombosis and foreign body granulomatous reaction. Microcrystalline cellulose and talc will elicit foreign body granulomas both in intravascular and perivascular regions of lung. Radiological appearance in CT shows centrilobular micronodules exhibiting tree in bud pattern which closely mimics the bronchiolar diseases like mycobacterium infection, bronchiectasis and consolidation [12]. Also enlarged pulmonary vessels suggesting pulmonary hypertension. Features of centrilobular micronodules and pulmonary hypertension should rise the suspicion of excipient lung disease. Sometimes the micronodules coalesce to form conglomerate masses and fibrosis mimicking malignancy.

Histopathology

In our cases histopathology sections stained with hematoxylin and eosin revealed multiple granulomas which are angiocentric distributed in and around the pulmonary vessels with or without basophilic material. Arterial inflammation and enlarged vessels are also seen in few cases suggesting pulmonary hypertension. [13,14,15]

Talc particles in Hematoxylin and Eosin stain appears clear to pale yellow in color. Starch granules appear as round with maltase cross pattern under polarized light. Microcrystalline cellulose is colorless, translucent and appear pale blue to gray color in Hematoxylin and eosin staining. Crospovidone is deeply basophilic irregular coral like and not birefringent[11]. In our case series one appeared pale gray probably microcrystalline cellulose (figure 2) and 3 cases deeply basophilic suggesting crospovidone (figure 3). These inert particles which are insoluble elicit severe foreign body reaction. Excipient lung disease usually is a chronic and progressive disease but it can present as sudden death due to severe pulmonary hypertension. [10,15] Clinicians and pathologist can misdiagnose this rare condition for mycobacterium and other fungal infections. To conclude high index of suspicion is needed to diagnose this condition which needs early diagnosis and prompt treatment.

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