Unusual Pulmonary Vascular Lesions after Intravenous Injections of Microcrystalline Cellulose

A Complication of Pentazocine Tablet Abuse

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Summary. We present the morphological features of a case of fatal pulmonary granulomatosis from illicit intravenous injections of microcrystalline cellulose derived from pentazocine tablets. Extensive foreign body granulomas were found in the lumena and walls of pulmonary vessels and in the pulmonary interstitium. Previously unreported gaps containing foreign material were found in the walls of medium-sized muscular pulmonary arteries. This peculiar finding is discussed in the light of the possible mechanisms involved in the removal of embolized foreign material.

Key words: Cellulose - Drug abuse - Foreign body reaction - Pentazocine - Pulmonary artery

Introduction

Since 1950 at least 33 reports have documented a whole spectrum of pulmonary lesions due to the intravenous (iv.) injection of unfiltered aqueous suspensions of pharmaceutical preparations that are intended for oral use (Spain 1950; Siegel 1972; Tomashefski and Hirsch 1980). Embolized insoluble particulate material such as talc (magnesium trisilicate) cornstarch or microcrystalline cellulose, used as fillers and binders in tablets and capsules may cause pulmonary foreign body granulomatosis and angiothrombosis. After injection of abundant foreign material, vascular changes indicative of pulmonary hypertension may be seen. Talc containing preparations, known to cause these pulmonary lesions include methadone hydrochloride (Vevaina et al. 1974), propoxyphene hydrochloride (Butz 1969), methylphenidate (Hahn et al. 1969; Lewman 1972; Arnett et al. 1976) and tripelemamine hydrochloride (Wendt et al. 1964; Szwed 1970). Cornstarch is added to barbiturates (Johnston and Waisman 1971) and to pentazocine, a potent analgesic. The latter drug is manufactured in the form of tablets also containing microcrystalline cellulose (Houck et al. 1980; Tomashefski et al. 1981).
In this communication we describe peculiar pulmonary lesions observed in an individual who was a known abuser of pentazocine tablet taken intravenously. To our knowledge, this is the first published case of a death related to injections of dissolved pentazocine tablets reported from a country other than the USA (Zeltner and Nussbaumer 1982).

**Case Report**

A 40-year-old white male nurse was found dead in the bathroom of his apartment in the vicinity of Berne, Switzerland. A syringe was discovered on the floor containing residues of pentazocine tablets. He had been suffering from back pain for several years and had been treated with pentazocine tablets for at least one year.

Six months before his death he started to complain of exertional dyspnoea and fatiguability. No medical examination was performed. About the same time pentazocine dependence was suspected, but the actual amount of drug taken is not known. An autopsy was performed.

**Gross Findings**

Multiple recent and old punctures were found on the left forearm and the antecubital fossa. The lungs were heavy and oedematous. The pulmonary cut surface presented a gritty texture due to the presence of numerous firm, greyish nodules measuring up to 1 mm in diameter. The heart weighed 390 g. The right atrium, ventricle and the tricuspid valve ring were dilated, but without ventricular hypertrophy. The left cardiac chambers and the endocardium were unremarkable. The liver showed signs of both acute and chronic congestion. There was no hepatitis.

The other organs showed no further important gross changes.

**Histopathological Findings**

In the lungs, the most impressive finding is the presence of numerous foreign body granulomas, filling up to 75% of every ten power microscopic field. About 40% of the granulomas are located in pulmonary vessels; 60% are found in the perivascular interstitium. The granulomas consist of macrophages and foreign body giant cells and often have a rim of small lymphocytes and a few plasma cells. Neutrophils are almost absent. The granulomas contain grey to green, birefringent, needle- or rod-shaped crystals that disclose the typical histochemical properties of microcrystalline cellulose:

Microcrystalline cellulose stains pale to dark violet with PAS stain and is diastase resistant. It is a deep black after staining with methenamine silver and is brilliantly orange with the Congo Red stain, showing a yellow to green birefringence in polarised light (Tomashefski et al. 1981).

No cornstarch nor other foreign material can be detected. Cellulose particles often occlude the lumina of smaller pulmonary arteries. The latter are frequently thrombosed, the thrombi being in various stages of organisation. The term “angiothrombosis” has been used for the description of these lesions (Tomashefski and Hirsch 1980). Vascular dilatation is a prominent feature of involved muscular arteries. In the dilated segments the elastic laminae are focally or totally absent and the muscular wall is often destroyed and replaced by fibrous tissue. An additional tortuosity of these vessels sometimes produces angioama-like structures. In older lesions the intravascular foreign material is laterally displaced by canalisation of the occluding thrombi. Foreign material and foreign body granulomas are found in medial layers of inflicted vessels and in perivascular locations (Fig. 1).

Perivascular foreign body granulomas are preferentially located around dilated tortuous vessels with a destroyed wall (Fig. 2).

Medial hypertrophy is seen in muscular pulmonary arteries. Complete occlusion of major muscular pulmonary arteries is seldom found. In contrast, partial obstruction with foreign body granulomas or intimal hypercellularity is a frequent finding. The elastic laminae and the muscular wall beneath these lesions are often intact. However these partial occlusions often are found near the site of ramification of small arteries or arterioles that arise perpendicularly or somewhat oblique