"Snuff Granuloma" of the Lung*

Report of a Case

T. Thomas, M.B., M.S.,** E. Thomas, M.D.,†
S. Prusty, M.S.†† and S. Annapoorna, M.B.B.S.‡

Manipal, India

Rare pulmonary lesions continue to be recorded in the literature. We have reported a case of rhinosporidiosis of the bronchus,† and a teratoma completely replacing the middle lobe,‡ where successful resection was done.

CASE REPORT

A 65-year-old retired professor of English was admitted to the Kasturba General Hospital with complaints of left sided chest pain, dry cough, general weakness and a low-fever of a month’s duration. The fever ranged from 99°F. to 101°F. For the past 16 years, he had attacks of respiratory difficulty which were thought to be "asthma." He was known to be diabetic for 15 years. He also mentioned that he was sensitive to penicillin.

Physical examination showed diminished vocal fremitus and vocal resonance and rales over the base of the left lung. Investigations revealed a total white count of 14,600 cells per cmm. with a differential count of 70 per cent neutrophil polymorphs, 20 per cent lymphocytes, 9 per cent eosinophils and 1 per cent monocytes. The erythrocyte sedimentation rate was 102 mm. in the first hour and 110 mm. in the second hour by the Westergren method.

The blood urea was 43 mg. per cent. A random blood sugar was 210 mg. per cent. Urine showed sugar ++. Repeated sputum examinations and bronchial washings were negative for tubercle bacilli and malignant cells. Other findings were not significant.

X-ray film of chest showed a somewhat dense shadow approximately 6 cm. in diameter, with irregular margins, situated in the superior segment of the left lower lobe. The left upper lobe and the right lung were clear. Bronchoscopy revealed only congested bronchial mucosa.

Diabetes was controlled by diet and insulin. The provisional clinical diagnosis was carcinoma of the lung. A left lower lobectomy was performed and he was discharged in good condition ten days after the operation. The histopathology findings were unexpected and interesting.

The resected specimen of left lower lobe weighed 215 gm. and cut section showed a greyish yellow fleshy mass measuring 7x6x6 cm. extending from the hilum to the pleura in the superior segment surrounding the segmental bron-

*From the Departments of Thoracic Surgery and Pathology, Kasturba Medical College Hospital. Presented at the Seventh International Congress on Diseases of the Chest, New Delhi, India, February 20-24, 1963.
**Professor of Thoracic Surgery, Kasturba Medical College.
†Chief, Division of Pathology, Kasturba Medical College Hospital.
††Reader and Junior Thoracic Surgeon.
‡Tutor in Surgery.

Figure 1: Resected specimen of left lower lobe showing a solid mass which measured 7x6x6 cm.

Figure 2: The fleshy area shows complete loss of architecture with a granulomatous infiltrate and occasional foreign body type of giant cells (see arrow) (H and E).
chus (Fig. 1). The lumen of the bronchus was blocked beginning at 2.5 cm. from the point of surgical resection and the distal part of the lumen of the bronchus was filled with the same fleshy mass. The demarcation between the fleshy area and the surrounding well aerated lung was clearly seen. There was a small cavity measuring 1.5 cm. in the center of this mass, with bronchial communication.

Microscopically the fleshy area showed complete loss of lung architecture. The lung tissue had been destroyed and was replaced by a granulomatous infiltrate (Fig. 2). The alveolar walls were thickened by fibrous tissue and chronic inflammatory cells (Fig. 4). The small cavity appeared to be a bronchus with ulceration of the wall (superior segmental bronchus). The lumen contained acute inflammatory exudate. The cavity was lined in places by respiratory epithelium and in other places by clusters of mononuclear cells. Occasional eosinophils, numerous plasma cells and foamy macrophages were seen (Fig. 3). Foreign body type of giant-cells with two to ten nuclei were seen in the solid area as well as in the ulcerated area of the bronchus (Fig. 3). A few giant cells showing somewhat large and bizarre nuclei were seen in the floor of the ulcer. Small clusters of hyperplastic epithelium were seen. There was no evidence of malignancy. One hilar lymph node showed no lesion. Frozen section on a piece removed from the solid area of the lung showed numerous fat laden macrophages staining bright red with Sudan IV. Gridley's stain for fungus was negative. No acid-fast bacilli were found. Under the polarising microscope the fleshy areas showed minute doubly refractile particles, the exact nature of which could not be established.

**DISCUSSION**

The firm mass showed a granulomatous infiltrate, destruction of lung tissue, areas of lipoid pneumonia, fat necrosis, foreign body reaction, as well as chronic pneumonitis and diffuse interstitial fibrosis.

There was no obvious explanation for these lung changes. The findings were not consistent with bronchiectasis or lung abscess. It was difficult to label the lesion. A probable clue was obtained when the patient was carefully questioned again after the operation. He was addicted to the use of large quantities of snuff every few minutes throughout the night and day for the last 40 years. The patient's son stated that the father was using snuff 70 times or more in 24 hours. He would even wake up numerous times in the night to use snuff.

It was difficult to postulate that snuff by itself had produced this lesion, but on detailed inquiry, the patient explained that the snuff he used was prepared by frying tobacco leaves in ghee, then powdering it and adding small quantities of slaked lime. Camphor is also added to the snuff by some manufacturers to improve the odor. We feel that the changes in the lung could have been produced by the various constituents of snuff which are ghee, slaked lime, tobacco leaves and sometimes camphor.

_Ghee_: This is melted butter. Because of its good keeping qualities it is used universally in all Indian homes. It is well known that any oily material, when inhaled, acts as an irritant. Graef, Ikeda, and Walsh and Cannon observe that aspirated milk
and cream evoke an inflammatory response. Moran* found that acute cases show a mononuclear infiltrate and more chronic cases may show pneumonia, granuloma formation with giant cell reaction or abscess formation. Ghee, being a milk product, can produce the same changes.

Unsaturated oils are more toxic and oils with a larger free fatty acid content produce more reaction. Moore* and Pinkerton* state that chaulmoogra oil, with an acid value of 28, causes acute necrosis of the lung, while iodized sesame oil, which is innocuous, has an acid value of 2.5. Animal oils are known to be more irritating than vegetable oils, such as coconut oil. Mineral oil is quite bland and acts as an inert foreign body in the tissues.

The ghee present in snuff may explain the areas of lipoid pneumonia in this patient. No bronchogram was done and no radiopaque oil was administered at any time. He had never used nasal drops of any kind, or mineral oil as laxative.

A localized granulomatous mass has been known to occur when oil such as liquid petrolatum gains access to the bronchial tree. The late lesions of lipoid pneumonia are characterized by fibrosis, giant cells, and a granuloma-like formation which have been mistaken radiologically and at operation for bronchogenic carcinoma.

Camphor: Camphor belongs to the group of volatile oils and must have contributed to the lipoid pneumonia and to the irritation.

Slaked Lime: Slaked lime is prepared in this locality by heating crude sea shells. In this process, the calcium carbonate is converted into calcium oxide which is also known as quicklime. To this, water is added and slaked lime is formed. The chemical reactions may be represented as follows:

\[
\text{CaCO}_3 \quad \text{heat} \quad \text{CaO} + \text{CO}_2 \\
\text{CaO} + \text{H}_2\text{O} \rightarrow \text{Ca(OH)}_2
\]

Calcium hydroxide, since it is an alkali, has a mild corrosive action, which may have contributed to the tissue damage in the lung. In addition, there may be physical irritation of the lung by slaked lime particles by virtue of the sharp crystalline fragments, structurally damaging cells. Minute particles may be dissolved in tissue and cell fluid and act as protoplasmic poisons. It is also possible as has been postulated recently in silicosis that the damage is due to surface electric potentials. In silicosis, it is suggested that the particles carry powerful negative ionic charges, which, in contact with cells protoplasm, become hydrated at the expense of the protoplasm and disrupt the physicochemical state of the cells, leading to their death.

The calcium content of patient's lung and of snuff were carefully analyzed. A relatively normal area from the resected lung of this patient showed a calcium content of .5 gm. per cent. Snuff purchased from a local shop showed a calcium content of 3 gm. per cent. The area of granuloma in the patient's lung showed a calcium content of about 1 gm. per cent. Thus, the high content of calcium in snuff tallies with the increased calcium content of the granulomatous mass.

Tobacco leaves: The tobacco leaves are powdered by hand. We purchased some snuff from the local shops and found that fine gritty particles could be felt when a little snuff was rubbed between the finger tips. Since powdering is done by hand, some of the particles may be coarse and these may have excited the foreign body reaction.

Differential Diagnosis

Other varieties of pneumoconioses, beryllium granuloma, Wegener's granulomatosis, eosinophilic pneumonia, irradiation pneumonitis (Thomas and Forbus') Hamman-Rich syndrome, farmer's lung, cholesterol pneumonitis, rheumatoid pneumoconioses, etc. can all be ruled out in the absence of the characteristic history and microscopic findings of each disease. Also, in this case a localized mass was present and there was no involvement of the lung. Radiologically the other lung was normal.
Macrophages containing lipid may be present in the lung in pulmonary tuberculosis. Suppuration and near large infarcts. These conditions were also ruled out.

It may be argued that snuff is used all over the world and if it has irritant properties, we should be seeing many more similar cases. However, snuff may contain other substances than tobacco. We have already explained how the presence of slaked lime, ghee and camphor in local snuff can produce lung changes after prolonged use. The fineness of the powder may also vary. Crude preparations made by hand will naturally contain coarse particles which may act as irritants and set up a foreign body reaction.

Individual sensitivity may modify the reaction of the tissue to the snuff. This patient gave a history of sensitivity to penicillin. Guidry and others have observed that the relative infrequency of mineral oil granuloma despite the high incidence of mineral oil aspiration may be due to individual sensitivity or intolerance to the oil in the lung.

The tolerance of any tissue for foreign material depends on the presence or absence of infection. This patient was a proved diabetic, thereby increasing his chances of infection following the inhalation of the irritant substances in the snuff.

The almost fantastic frequency and duration of the habit may have been a powerful factor in this particular tissue response (70 times or more in 24 hours). During the postoperative period, when snuff was withheld, the patient felt somewhat miserable and repeatedly asked for it. A few other persons who were heavily addicted to snuff, when questioned, explained that they tended to use snuff more often when there was stress and strain in their personal life and the use of snuff gave them a sense of relief.

The location of the mass in the lower lobe is also suggestive of aspiration followed by gravitation into this area. In eight patients where pulmonary resection for mineral oil granulomas was done at the Mayo Clinic, Guidry3 and others observed that the lower lobe was most frequently involved. Only in three patients was there bilateral disease.

Another point which may be raised is that our patient developed respiratory symptoms only after 40 years of constant use of snuff. The duration of exposure to the offending material, required to produce the symptoms of pneumoconioses, is also astonishingly long.

ACKNOWLEDGMENT: We wish to thank Dr. B. K. Bachawat, Professor of Biochemistry at C.M.C. Hospital, Vellore and his staff for performing calcium estimations of lung tissues in this case.

References
9 Thomas, T. and Betts, R. H.: "Teratoma of the Lung," to be published.