Case Report Section

Xanthogranuloma as a Coin Lesion of the Lung*

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Isolated pulmonary xanthomatous nodules which present as coin lesions are uncommon. The gross resemblance of the lesion to a neoplasm and the peculiar microscopic characteristics, especially as seen in frozen sections, may lead to diagnostic errors. The following two cases are similar to those classified as xanthomas and reported by Scott, Morrow, and Payne in 1948 and by Ford, Thompson, and Blades in 1950. The lesion appears to be identical with the xanthogranulomas in the retroperitoneal region as described by Oberling in 1955.

Case 1: (11087) A 10-year-old white boy was admitted to the National Jewish Hospital at Denver because an asymptomatic round mass was found in the upper lobe of the right lung by x-ray film six months before (Fig. 1). He was treated with streptomycin and para-aminosalicylic acid on the assumption that it was a solid tuberculous focus. Physical examination was negative. The x-ray picture remained unchanged, and the tuberculin, histoplasm, and coccidioidin skin tests were negative. Laboratory procedures were negative; blood lipid studies were not done. At thoracotomy, a discrete nodule was shelled from the upper lobe of the right lung. As frozen sections showed a highly cellular lesion, this lobe was then resected. Recovery was uneventful.

The specimen consisted of a soft resilient pale yellow unencapsulated nodule which measured 2.5 x 3 cm. The right upper lobe appeared to be normal except for a cavity in the apical segment from which the lesion had been enucleated. Microscopically, the mass consisted of sheets of spindle-shaped and oval cells in fascicular arrangement with small blood vessels interspersed (Figs. 2 and 3). The nuclei were relatively large and vesicular with one or two nucleoli. Some nuclei were hyperchromatic. The cytoplasm was pale with faint minute vacuoles. Some syncytial-like groups of larger cells were scattered throughout, but typical reticulated xanthoma cells and giant cells were not observed. Occasional eosinophils and lymphocytes were present. Scharlach R. fat stain unexpectedly revealed large amounts of lipid within the great majority of both the spindle and oval cells. Reticulum fibers outlined the many small blood vessels, and, in some fields, coarse parallel fibers were present among the cells containing lipid. The elastic fiber Van Gieson stain failed to reveal mature collagen or elastic tissue. The Weil and Bodian stains showed no nerve fibers. The margin of the lesion in the separately resected right upper lobe consisted of a fairly discrete zone of granulation tissue with many foam cells, neutrophils, plasma cells, nodules of lymphocytes, and relatively little collagen. The mucosa of an apical segmental bronchial branch was involved in the reaction.

Case 2: (89366) A 17-year-old white boy entered Colorado General Hospital for resection of a round lesion in the right lower lung field just above the diaphragm, which was found in a routine radiograph. Physical examination and routine laboratory studies revealed no abnormality. Blood lipid levels were not obtained. At thoracotomy, a sharply circumscribed spherical nodule, unrelated to bronchi, was shelled from the lower lobe of the right lung. His postoperative course was uneventful.

The specimen consisted of a gray-yellow, homogeneous, soft, slightly bosselated spherical nodule measuring 1.8 cm. in diameter. Microscopically, it was composed of compact fasciculated spindle-shaped or oval cells with finely vacuolated cytoplasm. The nuclei were plump, pale or darker, with fine evenly distributed chromatin. Lymphocytes, plasma cells, and larger histiocytes were scattered throughout. Typical

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large xanthoma cells were numerous in several fields (Fig. 4). The reticulum stain outlined many small blood vessels throughout the lesion, but fibers between cells were rare. Mature collagen was present only in occasional patchy peripheral foci.

Discussion

These discrete soft pale yellow nodules were composed predominantly of spindle-shaped cells which resembled fibroblasts. For this reason the diagnosis of a fibroblastic tumor was suggested. However, stains for connective tissue revealed only rare foci of collagen. One of the lesions contained intercellular reticulum; reticulum fibers were generally confined to walls of the many small blood vessels. It is of interest that a significant component of collagen was absent in the lesion of a previously reported case. The abundance of lipoid material was recognized only with the use of the stain for fat. The phagocytic character of the cells might have been suspected from the fine foamy cytoplasmic vacuolation of most of the cells. Typical xanthoma cells were present in a few fields in Case 2; giant cells were absent. Leukocytes were present in varying numbers. The pulmonary framework was destroyed; the mucosa of a bronchial branch was partly replaced with granulation tissue.

We have classified these lesions as xanthogranulomas because they appeared to represent a genuine granulomatous reactive process, basically identical with that described by Oberling in three retroperitoneal lesions. The relationship of the pulmonary form of the disease with the retroperitoneal lesions was pointed out by Stout who studied material from Case 1. Stout noted the occurrence of xanthogranulomas in the mediasti-
num and mesentery as well as in the lung and retroperitoneal region. Although the term xanthogranuloma does not emphasize the pseudoneoplastic quality of the process, we prefer it to others which have been used. The term xanthoma indicates a uniform proliferation of characteristic foam cells. Fibroxanthoma or xanthofibroma seem to be less appropriate terms as they imply a neoplastic origin, and collagen fibers also are sparse in the nodules.

Oberling stated that xanthogranulomas are frankly inflammatory, consisting of more or less extensive infiltrations of macrophages, lymphocytes

Figure 2 (Case 1): Bundles of spindle-shaped cells. H. & E. ×100.—Figure 3 (Case 1): The foamy character of the cytoplasm of the elongated cells is shown. H. & E. ×400.
and plasma cells, areas of sclerosis, and invariably foam cells containing neutral fat and cholesterol. One of his three cases exhibited a pseudosarcomatous pattern. He related the disease to that of Hand-Schuller-Christian and noted that such isolated granulomas had been described in bones, lymph nodes, the stomach, and elsewhere. He considered them to be distinctly different from the xanthomas of skin, tendon sheath, and joints which were associated with jaundice, diabetes, or generalized disturbances of fat metabolism. They were not simply a reaction to lipid such as occurs in Niemann-Pick's disease. They also differed from the xanthomatous transformation of nerve sheath tumors. Oberling further believed that local irritative inflammation and derangement of cholesterol metabolism were both significant factors in pathogenesis. In his cases as in ours no clue to a specific infective agent was noted.

More recently, Umiker and Iverson added three intrapulmonary postinflammatory "tumors" to the literature and included those of Scott et al., Ford et al., Csermely's case of xanthofibroma, and Childress and Adie's plasma cell tumor in a review of the problem. They considered that all of these lesions were inflammatory on the basis of microscopic appearance or history. If one cell predominated, they simulated xanthoma, fibroxanthoma, neurofibroma, vascular tumor, or plasma cell tumor. These nodules were similar to three nonxanthomatous lesions of the pleura described by Brown and Johnson. We believe that the lesions we have called xanthogranulomas are the same as several of the postinflammatory "tumors". Nevertheless, as the xanthomatous feature was dominant, the

FIGURE 4 (Case 2): Field of typical xanthoma cells. H. & E. × 400.
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more specific descriptive diagnosis of xanthogranuloma appears to have merit, at least in certain cases.

The sclerosing hemangiomas of the lung reported by Liebow and Hubbard also showed xanthomatos elements. These vascular lesions, regarded as analogous to those of the skin, exhibited hemorrhages, papillary infoldings, and obliteration of air spaces with atypical proliferation of lining cells. The authors concluded that the relationship to the so-called xanthomas or postinflammatory "tumors" must be considered tentative.

Two cases of a peculiar xanthomatous nodule of the lung have been reported because their superficial resemblance to a neoplasm offers a diagnostic problem and because they probably will be observed more frequently with the increasing tendency to extirpate coin lesions. They are termed xanthogranulomas because of the basic granulomatous nature of the cellular proliferation, the heavy lipoid content of the constituent cells, and the similarity to the lesion as seen in other locations. These two cases appear to be either variants or identical with the other seven cases in the literature which have been called postinflammatory "tumors" by Uímker and Iverson. The inflammatory origin seems to be common to all. Oberling believed local inflammation and a derangement of cholesterol metabolism were important. Association with a general disturbance of lipoid metabolism has not been noted in any of the cases, although sufficient laboratory investigations have not been made to exclude this possibility. As yet there is no certainty that the lesions are related to Hand-Schuller-Christian disease as considered by Oberling or to eosinophilic granuloma of the lung. The prognosis appears to be good, and symptoms are either absent or mild.

REFERENCES

4 Stout, A. P.: Personal Communication.