BRONCHOCENTRIC GRANULOMATOSIS

At his presentation of the J. Burns Amberson Lecture in 1972, Averill A Liebow [61] described a unique clinicopathologic entity, previously unrecognised, characterised mainly by focal granulomatous and destructive lesions of bronchi and bronchioles. Since then, several series and case reports have further characterised this disorder, bronchocentric granulomatosis (BCG) [50,54,58.]

Males and females are affected equally. The age distribution is broad, with the exception of those patients who have associated bronchial asthma (approximately one third), who are younger on average. Although some patients may present with an abnormal x-ray without symptoms, most will have fairly longstanding complaints of malaise, cough, fever, dyspnoea, chest pain, sweats or haemoptysis. It is chronicity of symptoms and the x-ray appearance, often suggesting a tumour or chronic suppurative process that eventually results in surgical resection and the diagnosis of BCG by histologic examination of the resected tissue.

The pathology [61] is characterised grossly by thickened bronchial walls and inspissated yellowish viscous material lying within bronchial lumens that are often dilated and saccular in appearance. Microscopically, in some larger bronchi, focal shallow ulcerations lined by palisading epithelioid cells or granulation tissue are seen. Cartilagenous invasion by large numbers of plasma cells may lead to extensive necrosis of the bronchial walls. Masses of mucin that contain neutrophilic debris and in asthmatics, eosinophils, may occupy the bronchial lumens. Occasionally, epithelioid granulomas of the sarcoid type may be observed in the sub-epithelial tissue. The parenchyma between bronchi is often involved as the inflammatory process, which is comprised of plasma cells, lymphocytes and eosinophils (mainly in asthmatics), extends outwards from bronchi and bronchioles. Necrotic areas, resembling fibrocaseous tuberculosis and containing various cell remnants as well as Charcot-Leyden crystals (mainly in asthmatics) may also be observed. The bronchioles appear to be more diffusely involved with marked penetration of the epithelium by palisaded epitheliod cells, which may completely fill the lumen; scattered giant cells of either Langhan's or foreign body type are also commonly present (Fig 3). Beyond obstructed bronchioles, distal air spaces become filled with fat-laden macrophages producing areas of "golden", "lipid" or "endogenous cholesterol" pneumonia. Both bronchi and bronchioles often are "cuffed" by plasma cells and lymphocytes and adjacent blood vessels may be involved by contiguous spread of the process from the bronchi. This extensive mixture of histologies, highlighted by intense granulomatous inflammation and mucus impaction with varying degrees of fibrosis, accounts for the radiological appearance of mass and nodular densities that may mimic those of neoplasms, tuberculosis, or chronic suppurative lung disease.

The following represents information regarding the association of BCG and *Aspergillus* from three reported series [50,54,58] and eight case reports [8,17,19,20,35,36,62,116.] Four of 15

patients (27 per cent) with bronchial asthma and BCG had precipitating antibodies against *Aspergillus*, while none of 19 patients with BCG but without asthma had precipitating antibodies. Aspergillus hyphae were seen, on appropriate staining in resection tissue in 18 of 24 patients (75 per cent) who had BCG and asthma. These organisms were found in 6 of 21 (29 per cent) of BCG patients who did not have bronchial asthma. Cultures of *Aspergillus* organisms were only occasionally positive from either the sputum or the resected tissue, whether asthma was present or not. From this data alone, it would be most difficult to assign conclusively an etiologic role to *Aspergillus* in the immunopathogenesis of BCG. It is important in diagnosis to rule out meticulously an infectious etiology [78] since almost identical pathology may be seen that is attributable to tuberculosis, [64, 78] histoplasmosis, [78] coccidioidomycosis, [62] blastomycosis, [78] and pulmonary echinococcus [19]. We have also recently observed histologic changes consistent with BCG attributable to the pulmonary aspiration of lentials. Reports of BCG in patients with seropositive [8] and seronegative [36] arthritis as well as eye involvement (scleritis) [116] raises some suspicion as to whether this condition may in some instances be part of a systemic disorder.

Spontaneous remission has been reported in BCG [54]. Corticosteroid therapy has, in general been quite effective treatment resulting in radiological clearing and subsidence of clinical symptoms in many patients. Unfortunately, relapse after discontinuation of corticosteroid therapy is not uncommon requiring reinstitution of treatment. The duration of therapy must be monitored on the basis of clinical and radiologic response.

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Bronchocentric granulomatosis and allergic bronchopulmonary aspergillosis.

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