Etiology, pathogenesis and differential diagnosis of lung granulomatosis. An update

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Slowly dissolving or even insoluble particles or organisms generally cause the formation of granulomas in the lung as elsewhere in the body. These might enter the lung by inhalation or by circulation via blood vessels. Living organisms or organic and inorganic particulate matter might cause granuloma formation. This can both be driven and regulated by immune mechanisms or by the older phylogenetic mechanism of phagocytosis and lysosomal degradation, with few or no participating lymphocytes.

The granuloma is defined as a nodular, well-circumscribed inflammatory lesion composed of either histiocytes (histiocytic granuloma), epithelioid and giant cells (epithelioid cell or sarcoïd granuloma), Langerhans' cells (Langerhans' cell granulomatosis, histiocytosis X), foreign body giant cells (foreign body granuloma), or fibroblasts with hyalinization (hyalinizing granuloma), respectively. These granulomas can have an additional mixture of neutrophils, eosinophils, or lymphocytes. Additional structural features might be encountered, such as vasculitis or necrosis.

Formation of granulomas by immune mechanisms can either progress along a T-helper l-lymphocyte profile, ruled and regulated by cytokines such as tumor necrosis factor-α (TNF-α), interleukin (IL)-3, IL-12, interferon-γ (IFN-γ), or by a T-helper 2-lymphocyte profile, ruled and regulated by cytokines, such as IL-4, which are secreted by macrophages and probably also by a few bypassing lymphocytes, necessary for giant cell formation by fusion and/or nuclear division, with the process of granuloma formation not being regarded as immunologic. Phylogenetically, this mechanism can already be found in primitive multicellular organisms. A wide variety of inhaled materials can be found and are most often food. Material entering the lungs through the blood stream can be shedded particles from dialysis membranes or other medical devices, and inorganic chemicals like talcum in drug abusers.

Foreign body granulomas are also seen in different forms of pulmonary amyloidosis and in the very early phases of some pneumocooniosis (silicosis, asbestosis, and hard metal lung disease). Pulmonary microthlasis is a very rare disease causing foreign body granulomatis. In this condition, many large and small alveoliths can be found, surrounded by foreign body giant cells, sometimes forming granulomas. Some of the alveoliths may be free in the alveoli, but most of them are within the alveolar walls.

The characteristic features of hyalinizing granulomas are their sharp delineation and their acellular centers. Usually a dense yinphycotic and plasmocytic infiltration is seen at the rim of the hyalinized nodules, but also within the nodule. Most patients are either children or patients in their second decade of life. The typical features of collagen fibers can be seen under polarized light.

References


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Pulmonary emphysema revisited

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Despite the number of publications generated from the 1950s to the 1960s, the interest of pathologists and clinicians in the pathology of pulmonary emphysema seems to have dissipated over the years. Several reasons can account for this. Pathological lesions are well enough defined to explain the clinical, functional and radiological findings. The study of pulmonary emphysema is based on large surgical or postmortem specimens usually by means of rather complicated and “uncomfortable” techniques. The pathological studies rendered data accurate enough to understand and classify experimental emphysema as well as the forms of emphysema associated with inherited metabolic diseases.

However, it is likely that now pathology must be required to update morphological findings and the anatomicoclinical correlations within a new scenario involving the introduction of new imaging techniques, namely CTS and high resolution CT scan, the new definition of emphysema, and the need for clearly defined criteria to identify early stages of the disease. Most of these questions were previously formulated by early investigators, but a reconsideration would probably useful. For example, the following should be taken into account when considering the current definition of emphysema:

i) What can be termed “normal size” in alveolar sacs and alveolar ducts? Distal air spaces change in size along fetal, early and late postnatal life. In addition, differences in size between alveoli from upper and lower segments have been described. Therefore, a precise definition of what can be considered normal in the adult lung is necessary. Likewise, a reformulation of the term “ductectasia” must be undertaken.

ii) What are the criteria for destruction? Commonly admitted criteria include the presence of alveolar fenestrae and vascular strands or baffles. Both are easily seen by light microscopy when severe and extensive. However, small size early fenestrae, which precede larger ones, and the development of vascular strands require more sophisticated anatomical techniques and probably the help of quantitative methods.

iii) Is the premise of no fibrosis valid in the current definition of emphysema? It is evident that by definition scar-related irregular emphysema has a component of fibrosis. It is also common that paraseptal emphysema have a component of fibrosis and that most cases of cenbroilobular emphysema also have some fibrous proliferation. This can be important data on the interpretation of imaging techniques.

Current knowledge allows the identification of emphysema in surgical or postmortem specimens, its classification, its quantification and a acceptable correlation with functional studies. These provide a useful tool to investigate the epidemiology of the disease in different countries, and to follow up the prevalence of the disease in the autopsied population. However, these could be considered only marginal aspects in the investigation of the disease. Future prospects of research on emphysema point mainly toward not only the epidemiology but the pathogenesis and prevention. In summary, the pathologist will play a role in developing cooperative work with the radiologist to correlate and gain structure, function and radiology to validate transversal and longitudinal studies on the prevalence and evolution of emphysema in selected population groups, to clarify and correlate the morphological facts with the molecular, immunohistochemical and clinical studies as far as the elastase-antielastase hypothesis is concerned, and to apply all the results to the prevention of the disease.

References