Periodic Peritonitis, Amyloidosis and Colchicine

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Periodic peritonitis, an hereditary disease, recurs at nearly precise or at unpredictable intervals of days, weeks or months. Episodes of febrile illness, sterile peritonitis, and at times pleuritis and arthritis, last several days. Episodes recur for decades in otherwise healthy persons. Occasionally, long remissions or spontaneous cessations occur. Turks, Jews, Armenians and Arabs are affected predominantly, but all races are susceptible. Many patients had exploratory surgery and much medication before a correct diagnosis was made. The terms paroxysmal peritonitis, familial recurring polyserositis and variants thereof had been applied to the entities, but the Index Medicus lists periodic peritonitis (PP) in the group of periodic diseases. More than 1,000 cases are on record since introduction of the entity in 1945 and 1948. Ten years later, confusion began when the same disease was regarded as a separate entity and called familial Mediterranean fever (FMF). Yet, they are the same clinically, Colchicine therapy suppresses episodes in both and serves as a diagnostic aid. According to reports by some Israeli investigators, FMF differed in two respects. One was the high incidence (26 percent) of complicating amyloidosis ending fatally in all cases. The other was that regular periodicity did not occur. According to other observers in Israel, amyloidosis ensued in only 12 percent of patients the rest lived for many years. Elsewhere among Jews, Arabs and Armenians, the incidence ranged from zero to 17 percent. Only one of Siegal's 42 Jewish patients had renal amyloidosis. Amyloidosis ensued in 32 percent of the Turkish patients. Evidently Turks and some Jews have traits for PP and an unusually effective gene for the development of amyloidosis. Valid statistics depend upon careful search for the complication.

More confusion arose from theories that PP resulted from an inborn error of metabolism, an endocrinal disturbance, an allergy or infection, that etiocholanolone was causal or that a low-fat diet was palliative. Another idea was offered regarding the cause that an underlying biorhythm is apparently present in all humans. In rare, genetically sensitive persons, it becomes overt by provoking PP at the crest of its cycles. Probably, the hypothalamus is stimulated to provoke PP and minor autonomic responses as well. Salivation, flushing, erythema and urticaria concur at times. To date, no better explanation has been proposed.

The striking periodicity of episodes noted by many patients unfortunately impresses few physicians. Episodes in some patients can be predicted to the day, once a week, every other Wednesday or once a month, enabling them to arrange their activities accordingly.
Amyloidosis and Periodic Peritonitis

Several theories account for amyloidosis as a complication of PP. One is that it is an integral component and often the sole manifestation of the disease. Another is that it results from an immunologic disturbance. However, measurements of HL-A (human leukocyte locus-A) antigens and other immunologic factors yielded no clues. A third theory is that a defective leukocytic function exists.

A more likely explanation follows. Blood proteins seem to be derived from leukocytes and endothelial cells. They increase in amount as a teleologic function. Hyperproteinemia, especially composed of globulins and fibrinogen, characterizes PP as it does chronic tuberculosis, leprosy, osteomyelitis and multiple myeloma. Amyloidosis occasionally ensues in each. Amyloid is a protein substance immunologically identical to a circulating serum constituent. When hyperproteinemia is prolonged, excessive amounts can no longer be disposed and accumulate as amyloid deposits.

Effect of Colchicine

The advent of colchicine therapy answered some questions. The palliative effect of the drug probably depends less on its direct action of leukocytes than on the suppression of the inflammatory episodes that account for hyperproteinemia, as suggested. If the cause is removed, hyperglobulinemia ceases, amyloid no longer forms and its deposits may be resorbed. That has occurred in other circumstances. Experimentally, colchicine therapy blocked the induction of amyloid in mice caused by prolonged injections of casein. Such may be expected in PP. Evidence of a reduction of proteinuria, gradual remission of nephrosis and of amyloidosis in colchicine treated patients already has been observed. Recent publications, however, should have included measurements of blood globulins. Hyperglobulinemia seems to be the key to the problem of secondary amyloidosis.

References