Easier Detection of Amyloid in Systemic Accumulation

Key words: amyloid, amyloidosis, phenol congo red, reticulin fiber

Primary amyloidosis is a metabolic disorder, in which abnormal proteinous material deposition occurs in the mesenchyma of various organs. Since Bonet’s first description of lardaceous tissue of spleen in the 17th century, this enigmatic pathological condition became familiar because of its unique macroscopic “waxy”, or “lardaceous” hard texture. An excellent historical review is well documented in the literature (1).

Through a series of discoveries, the physical properties of this deposit became clear: 1) protein in nature that are of fibril (2-4) or no fibril (5) and 2) can be positively identified by using Congo red staining (6), and these deposits appear as an apple green color under a polarizing microscope. 3) The X-ray refraction analysis reveals β-pleats conformation of these deposits, eventually leading to the modern concept of β-fibrillosis (7). On the other hand, the accumulation of clinical evidence has provided a basis for knowlege on the causative profiles: the high incidence in patients with plasmacytic disorders (8) or with long-term suffering of rheumatism and chronic inflammation.

A paper, published in this periodicals p400-416 is a valuable presentation on an improved technique for amyloid confirmation with minimal tissue damage. For the histological confirmation of amyloid, the classical alkaline Congo Red method and the Dylon staining have been hitherto widely used: these are more popular than the sophisticated amyloid antibody method. The latter has been used to identify the subtype, the former two have target to the common property of the material. In any method, however, we often fall into the indefinite judgement. The phenol Congo Red (PCR) method can make up for these weak points in staining quality and could be an excellent and simple means of analysis. I highly recommended the PCR method.

Additionally combined with trypsin (9) or potassium permanganate KMO, treatment (10), it becomes possible to differentiate AA amyloid from AL amyloid, and is becoming relatively more popular than the sophisticated immunohistological method (11). Before World War II, a clinical category of amyloidosis was given by Lubarsch (12) and Reimann (13) et al. Essentially, it is not so different from our current classification. It is not agreeable to put the local type of amyloid deposition in heart, brain, diabetic pancreas islet and lichenoid skin in the same category of systemic amyloidosis as seen in the present classification (14).

Recently, the diagnosis of amyloidosis is not so difficult from the physicochemical analysis. Nevertheless we are still confronting a serious clinical enigma, because of the following questions: 1) why amyloidogenic fibrile combines so uniquely to reticulin fiber with a high affinity, presumably as a result of local increase of proteolytic activity, 2) why the distribution is so heterogenous, that is not easily predictable, and it correlates with the nosographical features at low coefficient.

With regard to 1), deposits are uniquely observed along the reticulin network (14). Although this fiber is biochemically identical to collagen and elastin fiber, these three show a heterogenous configuration with regard to three-dimensional molecular structure. It is often distributed along the vascular adventitia in various organs in one group of patients. In another group, the pulmonary alveolar septa, cardiac parenchyma, renal glomeruli and vascular rays in renal medulla become rather vulnerable sites, and in the more diffuse type, the reticular framework of the mucosa, spleen, lymph nodes, thyroid gland, hepatic sinusoidal wall, and musculature of the tongue and skeleton are extensively involved.

Regarding 2), some reports (15) have attempted to determine correlating factors, but only in a very low correlation was found. This heterogeneity manifests largely not only in predisposing favorite sites, but also in the deposition pattern in the same organ. For example there are six different patterns of splenic deposits: vascular, marginal of the white pulp, mantle zone, germinal center, follicular (sago spleen), and diffuse red pulp (ham spleen) (16).

Not so rare, rapid progression may occur after diagnosis, as if a sleeping lion, when stepped on the tail, wakes up, having no effective therapeutic means for eliminating the dissolved substance. This rapid progression is one of the characteristic profiles of this disease. The deposit occurs slowly at first, then suddenly accumulates at an accelerating rate, eventually leading to the death of the patient.

The DMSO (dimethyl sulfoxide) administration, which is capable to dissolve amyloid from the tissue, could lead to acute renal failure. The high concentration of amyloid easily leads to the deposition in the glomerular basement membrane (spinula formation) (17).

The early detection of amyloid deposition is very crucial not only in the diagnosis, but the therapeutic strategy of systemic amyloidosis. In the early stages, treatment with DMSO is very effective for the management of the systemic
amyloidosis. However, if the diagnosis is made in the late stage of the disease, DMSO treatment plus plasma-exchange would be favorably used in order to avoid renal failure.

The improvement of detection method of amyloid, that is both very sensitive and easily performed, is very important for medical praxis, because early treatment is so important in treating this serious condition. The phenol Congo red method is much more sensitive than the conventional alkaline Congo red method for the amyloid detection.

As the general principle of “early detection and rapid therapeutic introduction” holds a high value in all diseases, it is worth saying that it is also valid a principle in the management of patients of amyloidosis. Therefore, the paper, published in page 400–416 is of high value in medical practical significance.

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References