

ANGIOFOLLICULAR HYPERPLASIA OF AN ABDOMINAL LYMPH NODE

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In 1956 Castleman, Iverson and Menendez¹ described a hitherto unrecognized form of localized mediastinal lymph node hyperplasia. This was characterized by large lymphoid follicles in the centres of which were structures which bore some resemblance to Hassal's corpuscles of the thymus. Although obviously very rare, further reports suggested that a similar if not identical form of hyperplasia of lymphoid tissue could occur retroperitoneally or in the soft tissues of the shoulder region^{2,3} although an anterior mediastinal location was more common. In a recent study Lattes and Pachter⁴ concluded that there was insufficient evidence to regard the lesion as originating in lymph nodes, and preferred to label their cases as 'benign lymphoid masses of soft tissue'. They also suggested that the lesions were of hamartomatous nature.

It is the main purpose of this paper to support Castleman's original contention that this rare condition can indeed arise within a lymph node. Additional observations on its possible histogenesis are also presented.

CLINICAL MATERIAL

The patient, a Coloured male of 29 years, was admitted to hospital following a stab wound of the abdomen. During a laparotomy a mass, which was evidently solitary, was removed from the mesentery. There was nothing of apparent significance in the past history or general clinical examination of the patient. He made an uneventful recovery.

Gross Pathology

The excised specimen was an ovoid structure measuring $3 \times 2 \times 1.4$ cm. and showing at one pole a stubby tongue-like process projecting from the surface (Fig. 1). On section the entire specimen was faintly yellow in colour with whitish rounded foci 1-2 mm. in diameter dotted over the surface. The macroscopic appearance seemed similar to that of case 2 of Harrison and Bernatz⁵ and case 1 of Lattes and Pachter.⁴

Histology

The projection arising from the main mass proved to be normal lymphoid tissue, the reticulin stain confirming that this was unquestionably the remaining portion of the lymph node in which the lesion had arisen (Fig. 2). The pattern of peripheral sinuses, lymphoid follicles and medullary cords was not unusual, and there were no other distinctive features apart from a mild sinus hyperplasia.

The greater part of the ovoid mass was composed of lymphoid tissue showing the features of the condition originally described by Castleman *et al.*¹ and subsequently labelled 'angiofollicular hyperplasia' by Harrison and Bernatz.⁵ The most striking feature was the presence of numerous large follicles throughout the section. In their most characteristic

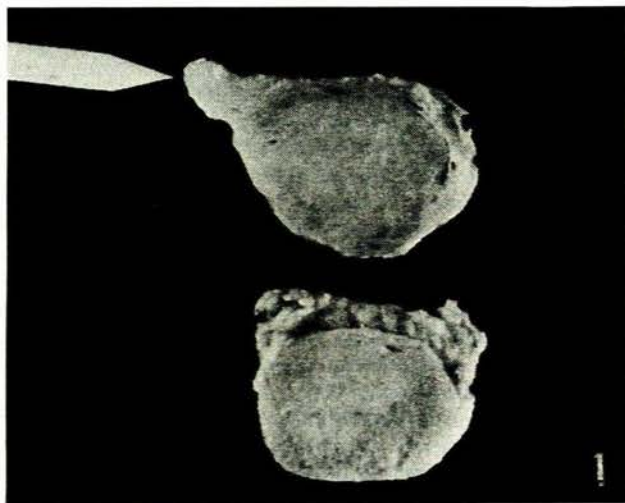


Fig. 1. The surgical specimen. The arrow points to the remaining normal part of the lymph node (approximately full size).

form they were composed of masses of lymphocytes arranged concentrically around a central group of closely packed cells, hereafter referred to as pseudo-corpuscles, which sometimes resembled a Hassall's corpuscle. All of the follicles did not present such a characteristic picture. Some merely contained

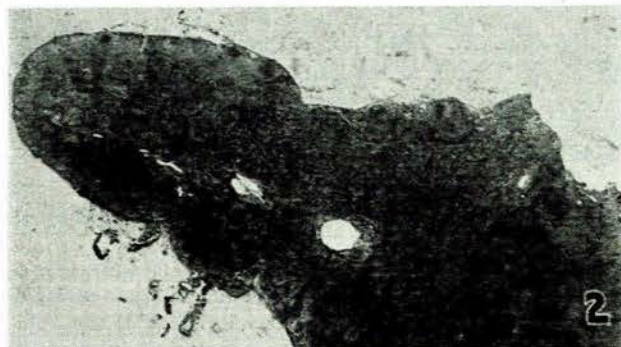


Fig. 2. The projection on the surface of the specimen. Normal lymph node structure is seen on the left and a small part of the hyperplastic tissue on the extreme right. The central portion is the intermediate zone (reticulin x 8).

a normal central capillary. Others showed changes which were thought to represent steps in the evolution of the pseudo-corpuscle, but reactive germinal centres of the ordinary variety were absent. In what was regarded as the earliest stage, cells with large pale vesicular nuclei, prominent nucleoli but scanty cytoplasm, were aligned along the course of a capillary which entered the centre of a lymphoid follicle (Fig. 3.) The reticulin stain showed that while many of these cells were merely activated endothelial cells, some were clearly situated just external to the basement membrane, though still in intimate contact with it. These perivascular cells gradually increased in number as the centre of the follicle was approached and eventually became continuous with the central mass of cells. With the acquisition of a more abundant pale eosinophilic cytoplasm and a tendency for the cells to arrange themselves in a whorled manner, the pseudo-corpuscle assumed its most characteristic form (Figs. 4 and 5). At this stage it was still sometimes possible to demonstrate an intact capillary in the pseudo-corpuscle by means of a reticulin stain, although the lumen was often largely occluded by endothelial cells and rarely contained erythrocytes. The direct continuity between the cells of the mature pseudo-corpuscle and the perivascular cells which occasionally formed a sleeve around the tangentially situated capillary, is especially well seen in Fig. 6, although the vessel itself has been obscured by the surrounding cells. Reticulin fibres penetrated between the cells of the pseudo-corpuscle. Collagen eventually replaced the reticulin and in the oldest lesions the fibrosis all but obliterated the centres of the follicles (Fig. 7).

The lymphoid tissue between the follicles included moderate numbers of reticulum cells and many eosinophils. Necrosis was absent. A variable amount of reticulin formed an irregular interfollicular network but the follicles themselves contained

little. Many capillaries with prominent endothelial cells were also seen, arranged in an entirely haphazard way.

Separating the small remaining normal part of the lymph node from the hyperplastic portion was an intermediate zone, the latter term being used in a topographical sense. This merged imperceptibly with the normal tissue on one side and, although partly demarcated from the hyperplastic area on the other by a slender band of compressed reticulin, elsewhere it was also in direct continuity with it. As its main feature it showed a remarkable number of slender columns of cells bridging the medullary sinuses. These structures were all arranged parallel to each other and extended between a trabeculum and the surrounding medullary cords, only some, however, apparently entering the cords themselves. The columns were composed of a double layer of cells of endothelial type but only rarely did the finding of an isolated red cell, wedged between the cells, suggest that the otherwise solid columns were acquiring lumina. The reticulin stain displayed a highly characteristic palisaded arrangement of the fibres which appeared to form a scaffolding for the endothelial columns (Fig. 8).

A narrow rim of non-reactive lymphoid tissue, continuous with the normal portion of the node, extended around the periphery of the hyperplastic area. In several sections this could be seen as a thin compressed layer of lymphoid tissue separated from the enclosed central hyperplastic area by a 'capsule' of condensed reticulin. In this case it was, therefore, clear that the zone of angiofollicular hyperplasia was entirely contained within a lymph node, and formed an integral part of it.

DISCUSSION

Because of their inability to demonstrate the normal reticulin pattern of peripheral lymphatic sinuses in the hyperplastic tissue, Lattes and Pachter rejected the original concept of Castleman *et al.* that the lesion arose in lymph nodes. This is not unexpected, for current accounts of the condition, including that of Lattes and Pachter, have been concerned with the fully established hyperplasia at a stage when the normal lymph node structure is obliterated. Examination of the entire specimen in the present case, however, has dispelled any doubt that angiofollicular hyperplasia can arise within a lymph node. It is not suggested that this is always the mode of origin, for similar lesions have been encountered at sites where there are normally no lymph nodes, e.g. in muscle and subcutaneous tissues.

Both the naked-eye and microscopic features indicated that the hyperplastic area had evolved from only part of a node, while the rest had still retained its normal architectural characteristics. The close similarity between the specimen described in the present paper, and that of Lattes and Pachter (case 1)⁴ and Harrison and Bernatz (case 2),⁵ is immediately apparent, but these authors do not specifically state whether the histological examination of

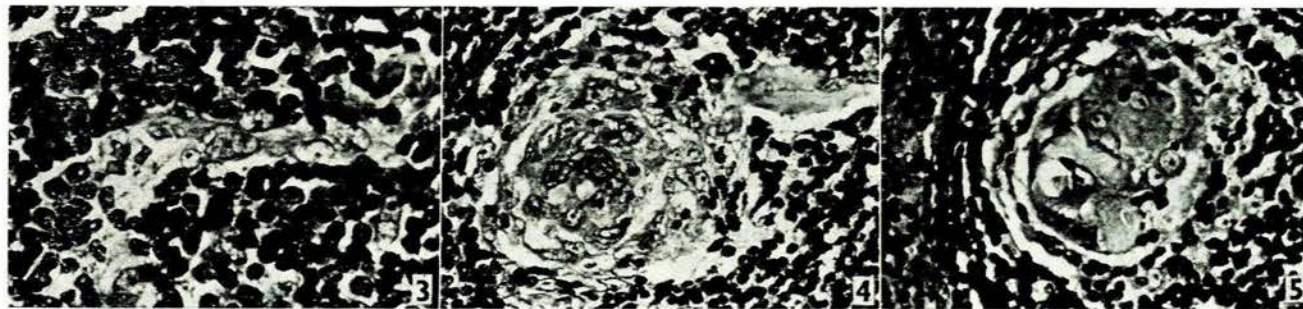


Fig. 3. A capillary entering the centre of a lymphoid follicle. The large reticulum-like cells are just external to the basement membrane. The large cell towards the lower left-hand corner has acquired some cytoplasm (H. & E. x 1020).

Fig. 4. A fairly mature pseudo-corpuscle showing the whorled arrangement of the cells and a capillary entering the mass on one side (H. & E. x 640).

Fig. 5. The pseudo-corpuscle in its most characteristic form. On one side the lymphocytes are arranged in concentric rows of cells (H. & E. x 640).

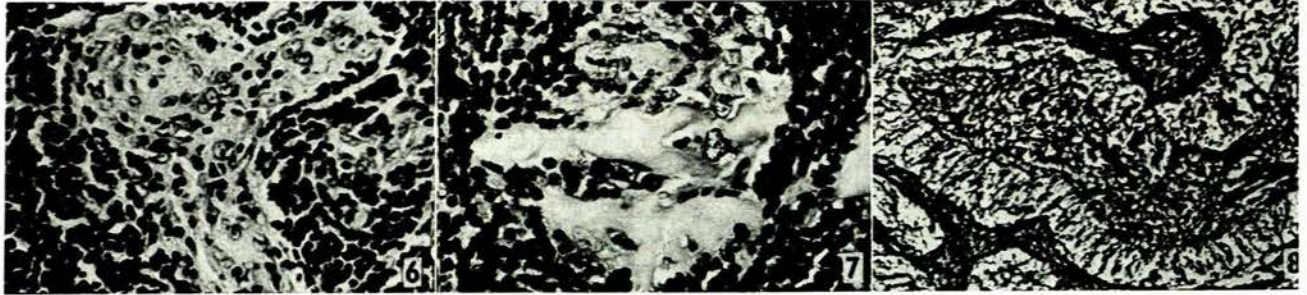


Fig. 6. Here a pseudo-capsule is seen to be continuous with a sleeve of cells around a capillary at its periphery (H. & E. x 510).

Fig. 7. The pseudo-capsule being replaced by hyaline fibrous tissue (H. & E. x 640).

Fig. 8. The intermediate zone, which shows the palisaded arrangement of the fibres crossing the medullary sinus. This is an exaggeration of a pattern encountered in some normal lymph nodes (reticulin x 150).

the two specimens referred to included the projections which in both cases appear to arise from the main mass. It seems quite possible that these protruberances would also have proved to be remnants of lymph nodes.

The centres of the lymphoid follicles have been described as though each represented a different stage in the sequence of development of the pseudo-capsule. This may be an erroneous conclusion, the different appearances possibly resulting from the section passing through varying planes of a structure essentially similar in all the follicles. But even if this were true, the appearances undoubtedly still suggest that the pseudo-capsule arises mainly by a proliferation of cells, originally found along the capillary coursing through the centre of a lymphoid follicle. It is hard to assess the extent to which the endothelial cells have participated in the formation of the pseudo-capsule and this is largely due to the difficulty of always identifying the basement membrane of the capillary among the other reticulin fibres present. Where this can be done, however, the extracapillary origin of most of the cells has become obvious. No mitoses were seen and the bulk of the pseudo-capsule seemed as much the result of acquisition of cytoplasm by the cells, as of an increase in their number. The relationship between the cells of the pseudo-capsule and those situated perivascularly, as seen in Fig. 6, is a very intimate one, and they resemble one another closely in their large pale vesicular nuclei of reticulum-cell type. They differ from one another principally in the amount of cytoplasm they possess and they may well have a common origin. Even acknowledging the pitfalls of attempting to visualize transitional forms, it was possible to trace gradations between the swollen perivascular cells and those eventually forming the pseudo-capsule. It is probable that the cells in question are of reticulo-endothelial origin. This is supported by the appearance of reticulin and ultimately of collagen between the cells. Their distinctive character, however, is emphasized by the fact that they generally persist as a closely-knit ball of cells quite unlike the dividing cells of a reactive germinal centre in which the cells tend to form a much less compact mass, while they have not shown any phagocytic activity.

The significance of the palisaded columns of cells in the intermediate zone was not immediately apparent, if only because of the uncertainty concerning their histogenesis. Although probably of reticulo-endothelial or endothelial origin, their vaso-formative potentiality remained in some

doubt because of the failure to demonstrate clear-cut vascular lumina. It is not clear whether the changes of the intermediate zone preceded the development of the angio-follicular hyperplasia or merely developed subsequently in the remaining nodal tissue. However, if the first possibility should prove to be the correct one, then it is not inconceivable that the sinusoidal columns may represent the earliest phase of the vascularization of the inter-follicular tissue and the follicles. Lattes and Pachter and others have commented on the rich vascularity of this zone, the vessels frequently possessing swollen endothelial cells. In itself this is a non-specific phenomenon, occurring as it does, though less impressively, in unrelated hyperplastic and neoplastic states of lymph nodes.

The basic nature of the condition must remain unsettled. The statement by Iverson⁶ concerning the finding of a similar, though less pronounced, type of reaction in a lymph node from a case of bronchogenic carcinoma casts doubt on the supposed hamartomatous nature of the process and suggests that it is more likely a non-specific form of hyperplasia. In addition, its proven occurrence in a lymph node as seen in the present case eliminates one of Lattes and Pachter's major objections to the original concept proposed by Castleman *et al.* In view of the apparent significance of capillaries and perivascular cells in the formation of one of the most characteristic features of the lesion, i.e. the pseudo-capsule, the term angiofollicular hyperplasia therefore seems more suitable than that introduced by Lattes and Pachter.⁴

SUMMARY

A mass found incidentally in the mesentery during a laparotomy proved to be a lymph node which showed the features of angiofollicular hyperplasia. This was characterized by the formation of Hassal's-like corpuscles in the centres of lymphoid follicles. A small part of the node was uninvolved by this process. The cell masses in the follicle centres arose mainly by a proliferation of perivascular reticulum-like cells. Occasionally these cells surrounded a capillary for some distance from the centre of the follicle. Eventually the cell masses were obliterated by hyaline fibrous tissue. The lesion is thought to be an unusual type of hyperplasia rather than one of hamartomatous origin.

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