LYMPHOMA, A BENIGN TUMOR REPRESENTING A LYMPH GLAND IN STRUCTURE.

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PLATES XXVI AND XXVII.

There is little uniformity of opinion among authorities to satisfy the critical student concerning the word "lymphoma" and the conception conveyed by it. In conformity with oncological nomenclature, the term is, in a strict sense, applicable only to new growths made up of lymphoid tissue, but in the course of time it has come to include a variety of pathological conditions.

Kaufmann (1) and Orth (2) classify lymphomata into leukæmic, aleukæmic and malignant. Klebs (3), following Virchow, Birch-Hirschfeld (4) and Ziegler (5), emphasize the fact that in many instances inflammatory processes have monopolized the use of the term. Langhans (6) many years ago stated that "in pseudo-leukæmia there are two forms of lymphomata;" and Warren (7), in enumerating the conditions denoted by the word "lymphoma," mentions "simple hypertrophy of the lymphatic glands, due to some of the above causes (tuberculosis, syphilis and other infective diseases), to which the term lymphoma has been applied." Warren advocates dropping the term lymphoma, since "those cases which were supposed to occupy an independent position under the name of lymphoma or lymphadenoma can now be classified under some one of the other headings." The objection to this by Birch-Hirschfeld is that if the term lymphoma is limited to the infectious enlargements of lymph glands to which it has so far been mainly applied, there remains nothing by which to designate a benign lymphomatous tumor.

Most unsatisfactory is the definition of Stengel (8), who defines lymphoma as "a more or less malignant form of new growth affecting

the lymph glands or other lymphadenoid tissues." Unna (9) evidently considers a lymphoma to be simply a collection of leucocytes, for he says, "we shall not go far astray if we regard this very obstinate form of leukæmic cutaneous nodule also as a granuloma and not as a collection of leucocytes—a lymphoma."

With gratifying clearness Senn (10) defines lymphoma as "a benign tumor formed of lymphoid tissue produced from a matrix of lymphoblasts;" further (11), as "an encapsulated tumor which manifests no tendency to implicate adjacent glands and which is never complicated by affections of the blood-forming organs." That this conception of a lymphoma was largely theoretical in its deduction is evidenced by the admission of the author that "it is easier to say what a lymphoma is not, than what it is." The reason for this last statement obviously lies in the absence from medical literature of any observations of growths which would conform to such a definition, *i. e.* a true tumor, benign, atypical in structure, yet representing lymphoid tissue and not due to any inflammatory process. Not even Senn refers to any such observations; he remarks further, "In no department of surgical pathology do we meet with more confusion than in the difference between benign and malignant tumors and inflammatory swellings of the lymph glands." This confusion is due not so much to a lack of knowledge of the inflammatory affections of lymph glands nor to an ignorance of the nature and characteristics of malignant tumors but to the great rarity of benign new growths of lymph glands.

I am indebted to Dr. J. B. Murphy for the opportunity to examine a small tumor, which, I became convinced from a careful study, represented a benign, non-inflammatory, new-growth of lymph nodes; in other words, a lymphoma according to Senn, a benign lymphoma according to Ziegler and others.

The tumor was located in the left groin and had attained the size of a pigeon's egg by a very gradual growth extending over a period of fifteen years. The inguinal canal was not patent and there was no enlargement of the adjacent glands nor of those of the opposite side. The man was in good general health; there were no similar

tumors elsewhere on the body, and there has been no recurrence of any growth since its removal three years ago.

When examined in the fresh condition the tumor presented an oval, flattened shape not very unlike a small kidney (Plate XXVI, Fig. 1). On section, light reddish surfaces were exposed which were studded with areas the size of millet seeds and resembling closely the Malpighian bodies of the spleen. These minute areas were very uniform in their distribution; there was apparently no difference in this respect between the cortical and the more central portions, these two regions being quite similar in color. Although a fibrous capsule surrounded the growth, there were no coarse trabeculae entering the tissue. The blood-vessels exposed in a number of sections were all small. There were no spots of softening or hæmorrhage nor any special features which would point to an inflammatory process.

Microscopic Examination.—The tumor was hardened in alcohol. Sections stained by ordinary methods show the tissue to be distinctly lymphoid in character and to contain many lymph nodes (Plate XXVI, Fig. 2). In serial sections the largest diameters of one of average size were 112 by 88 μ . A very large node measured 160 μ in its longer diameter by 116 μ in the shorter. The cells composing these nodes are arranged in a very striking and peculiar manner. Around the periphery they form encircling rows which extend for one-third or, in rare instances, one-half of the circumference (Plate XXVII, Fig. 4). The arrangement in rows is more perfect in some nodes than in others, but when serial sections are examined it is found to occur at some point and to some degree in every node. Frequently these rows are double; or three or four rows form a band, which, extending around the node for some distance, breaks up to anastomose with similar bands or single rows. Between these rows and bands are cleft-like spaces (Plate XXVII, Fig. 4) which are more marked in some preparations than in others, and in some are undoubtedly to be ascribed to shrinkage. The rows are most perfect at the periphery, so that the edge of the node is usually well defined. This is, however, not invariably the case, for some nodes fuse gradually with the inter-nodal tissue, while short tangential rows shoot out into the surrounding

tissue, obscuring the distinctness of the margin. The cells themselves which form these rows are small, 4 to 5 μ in diameter, with a nucleus which occupies almost the entire cell, leaving only a narrow margin of cytoplasm (Plate XXVII, Fig. 6). The nuclei are round, with a deeply staining nuclear membrane. The chromatin frequently forms an irregular lining for the nuclear membrane and usually two or three centrally located large granules.

The reticulum supporting these cells is very scanty in the outer zones of the node. Here it forms delicate strands which extend between and parallel to the rows. Toward the centre it is more dense and forms heavier bands. It is always greater in amount and, in carefully pencilled preparations, is found to produce a finer meshed network around the blood-vessels.

Blood-vessels can be found in every node by the study of serial sections, and there are generally one or two in the majority of the sections from any one node. The vessel enters obliquely and frequently divides after its entrance. In such cases its further course is not easily followed. These vessels are evidently arterioles; they possess thick hyaline walls. In case the blood-vessel is cut directly across, the row formation is very perfect; row after row or layer upon layer surround the vessel throughout the entire nodule. When the vessel is cut obliquely the row arrangement is more regular at the periphery, the remainder of the node consisting of the same small darkly staining cells grouped in a dense mass and devoid of any formation of rows. Figure 3 of Plate XXVI shows the rows of lymphoblasts about one of the larger internodal blood-vessels.

Each node is found to possess at some point a group of cells which afford a marked contrast to those just considered. This group is generally central in its location but in some sections is nearer to one pole of the node (Plate XXVI, Fig. 2, and Plate XXVII, Fig. 4). The cells forming these groups are large, 8 to 10 μ in their long diameter, and like the others consist mainly of nuclei. But these nuclei are oblong and irregular or notched and stain faintly with the exception of the nuclear membrane. In examining successive sections one reaches the conclusion that these groups of pale cells occur at or near

the point where the arteriole breaks up to form capillaries, and, further, that the individual cells resemble in size, shape and staining those which line the blood-vessels. The division into capillaries results in a denser reticulum which, with the large faintly staining cells, forms an area differing very much from the densely packed, darkly stained cells which surround it. When, as exceptionally is the case, a rather large arteriole passes into a node and immediately divides into a number of small branches, the resulting pale centre is quite large.

Thus it is seen that the light areas resembling the Malpighian corpuscles of the spleen, observed when the tumor was first cut, are lymph nodes which are remarkable for their extraordinary size and the extreme regularity in the arrangement of the cells forming them; also that these nodes are formed around blood-vessels or at points where the blood-vessels divide to form capillaries.

The internodal tissue is loose and shows considerable stroma, which supports small cells similar to the darkly staining cells of the nodes. There is no particular arrangement of these except that they are more numerous at the edges of the spaces formed by the reticulum, the centres of such spaces being empty. The reticulum of this internodal tissue, stained by Van Gieson's stain (Plate XXVII, Fig. 5), picro-nigrosin or the iron-haematoxylin method and in carefully pencilled sections, shows no nuclei which can be positively said to be a part of the stroma in spite of the fact that the nuclei of the cells lining the spaces often appear as though they belong to the reticulum, as though in fact the reticulum were connected with cells. The blood-vessels in the internodal tissue are larger than any found within the nodes. The arteries possess thick hyaline walls with two, three or more elastic sheaths and occasional isolated elastic fibres (Plate XXVII, Fig. 7). The thickening in the walls of the arteries and arterioles has affected only the tunica media. As the vessel becomes smaller its wall becomes more and more homogeneous and hyaline in character, until finally no nuclei can be seen in its middle coat. The veins are easily recognized by their thin walls; they show no changes. Blood is quite generally absent from the vessels, a small amount occurring in the

largest. There are no heavy bands of stroma which extend in from the capsule. The capsule itself is thin, largely fibrous, with few nuclei.

The similarity of the nodes, which form the greater and more interesting part of this tumor, to the "secondary nodules" of lymphoid tissue described by His, Flemming and others is very apparent.

Hoyer (12), in describing the cells in lymph glands, referring to the pale centres of the germinal areas, speaks of "the cells described by Flemming with large nuclei which give the centres of the germinal areas their pale color."

Hoehl (13), in a good description of the reticulum of lymph glands, states that the connective tissue surrounding the germinal areas is arranged in a tangential direction as regards the periphery of the nodes, and Flemming (14) says that in the germinal areas it must be that there is a form of slow centrifugal pressure whereby the younger cells are pressed toward the periphery and driven out through the spaces of the reticulum. It can be seen from these citations and from the structure of the tumor that cells were produced in these pale centres and pressed toward the periphery, but lacking a normal exit through lymph sinuses into the circulating blood were accumulated in the growth and produced not only a remarkable formation of rows around such germinal centres, but also extremely large nodes. Concerning the formation of lymph nodes about blood-vessels, Flemming (15) finds that "the view that the arrangement of the lymph node about the blood-vessel originates in the germinal area, is perfectly acceptable." Also Ribbert (16) has noted that lymphomata occur on blood-vessels without any increase in the number of leucocytes in the blood.

Hansemann (17), in a consideration of the tumors which may develop from lymph glands, specifies three varieties of cells from which they may originate, viz.: the lymphocytes which form the parenchyma proper, the endothelial cells and the cells which form the framework (Gitterzellen). The existence of the last is positively denied by Hoehl (18), who says "the reticulum is entirely devoid of nuclei."

Senn (19) tells us that in true lymphoma "the follicular structure

(nodes) is well preserved," and that "the lymphoblasts produce lymph corpuscles which are not transformed into leucocytes but remain in the reticulum of the tumor as the essential cell elements."

It is well to note the resemblance in structure of the nodes in this tumor to the corpuscles of the spleen, for Albrecht (20) has reported a case in which numerous dislocated spleens were scattered over the peritoneal surfaces. Their number was estimated at about four hundred, and they varied in size from those which were strictly microscopic to some the size of a walnut. The greater number were found in the upper left quadrant of the abdominal cavity and on the posterior surface of the greater omentum. But they were found also in Douglas's pouch and on the upper one-third of the rectum. Eight were examined microscopically and found to resemble splenic tissue in every respect. They contained large quantities of blood and blood pigment, and in one of the larger examples typical splenic follicles were found about the blood-vessels.

The absence of blood pigment, as well as the scanty amount of blood and the lack of coarse trabeculae would, in themselves, be sufficient to prevent a conclusion that the above-described growth represents or has sprung from displaced splenic tissue. The pale germinal areas present in the nodes of the lymphoma and absent from splenic follicles afford another striking difference. Albrecht also found accumulations of round cells about the masses of blood pigment, whereas the absence of any of the histological features of inflammation in this growth constitutes one of the main reasons for concluding that it is a true lymphoma.

Freund (21) has called attention to the resemblance between the accumulations of cells around the blood-vessels in periarteritis nodosa and lymphomata as follows: "Indeed one sees not seldom circumscribed areas of cells in the adventitia which have some similarity to lymphomata." In periarteritis nodosa, however, many vessels of the body and in different sites are the seat of such accumulations. The clinical picture is often that of a toxic neuritis or a toxic myositis and not only is the process in and around the vessel wall histologically an inflammatory one, but there are also changes in the organs due to obstruction of the vessels.

In concluding, this tumor seems to form a veritable confirmation of the words of Lancereaux (22), who in 1875 wrote: "It is indeed probable that this lymphoid tissue gives birth to young cells, and one can see how, under the influence of a mild irritant, the production of these cells becomes more abundant; the elements of the network multiplying at the same time, it results that tumors occur which have for their common characteristics a reticulated network in which the lymphoid elements are accumulated more or less abundantly. Such tumors or lymphatic growths are designated by the name—lymphoma."

DESCRIPTION OF PLATES XXVI AND XXVII.

PLATE XXVI.

Fig. 1. Photograph of lymphoma (exact size). The tumor has been cut open and from the right half portions have been removed for examination.

Fig. 2. Photograph of section showing lymph-nodes and internodal tissue. Low power.

Fig. 3. Formation of lymphoblasts about one of the larger internodal blood-vessels.

PLATE XXVII.

Fig. 4. Photograph of centre of a node showing the pale germinal area.

Fig. 5. Reticulum of the internodal tissue. Pencilled section; Van Gieson's stain.

Fig. 6. Cells of the rows of lymphoid tissue.

Fig. 7. Cross-section of one of the larger internodal vessels showing the elastic sheaths. Orcein stain.

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FIG. 1.

FIG. 3.

FIG. 2.

FIG. 4.

FIG. 5.

FIG. 6.

FIG. 7.