Parafollicular lymphoid tissue in follicular lymphoma: nodal versus extranodal

To the Editor:

In nodal follicular lymphoma (NFL), neoplastic follicles are formed upon the presence of parafollicular lymphoid tissue (PLT), and postcapillary high endothelial venule (HEV) of the paracortex constitutes the main histological component of the PLT [1,2]. Unlike lymph nodes, however, the paracortex with HEV is not readily recognizable in many extranodal lymphoid tissues, unless it is associated with chronic inflammation as in the tertiary lymphoid tissue [3]. Thus, in the primary follicular lymphoma of extranodal origin, which is not associated with inflammation, it is likely that PLT would appear different from that of NFL.

The gastrointestinal tract is the most common site of extranodal lymphoma, accounting for 40% of extranodal lymphomas. However, follicular lymphoma constitutes only 1%-3% of primary gastrointestinal lymphomas, and the most frequent site of involvement is the duodenum [4].

Duodenal-type follicular lymphoma (DFL) resembles NFL with respect to morphology, expression of immunohistochemical markers for the germinal center, and harboring of t(14;18)(*IGH-BCL2*) translocation [5]. However, DFL is distinct from NFL on account of (1) the involvement being limited to the mucosal/submucosal layers in DFL, whereas spread to the muscularis/serosa is common in NFL; (2) neoplastic follicles lacking the follicular dendritic cell network in DFL, with dendritic cells restricted to the periphery of the follicles (duodenal pattern) in contrast to the nodular pattern of NFL; (3) $\alpha 4\beta 7$ integrin and CD27 being expressed in DFL, which are both negative in NFL; (4) there being a loss of activation-induced cytidine deaminase in DFL, which is positive in NFL [5-7].

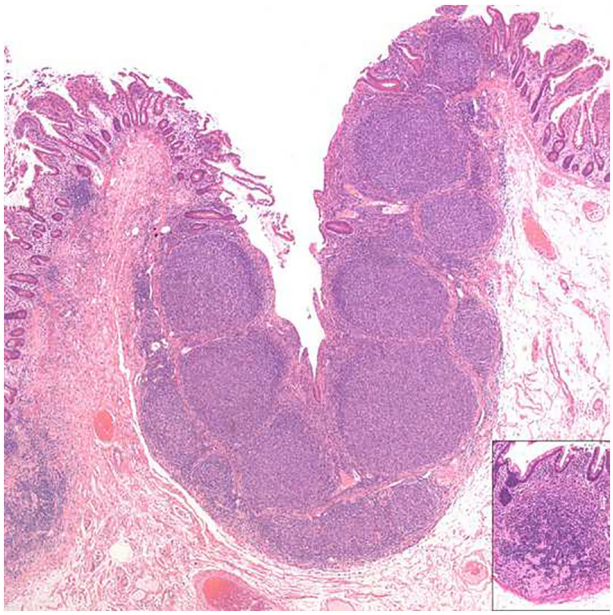

Fig. 1 Duodenal-type follicular lymphoma with a group of neoplastic follicles confined to the mucosa. Inset, Some vessels of the follicles are hyalinized, giving rise to a feature reminiscent of hyaline vascular Castleman disease.

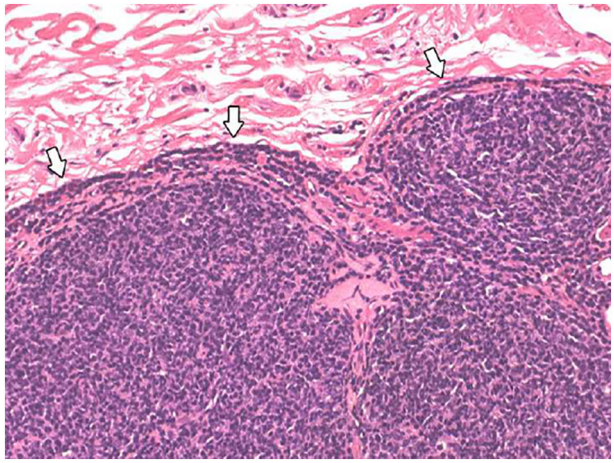

Fig. 2 Neoplastic follicles are bordered by stromal lymphocytes, frequently arranged in rows, some of which are accompanied by hyalinized membranous wall (arrows).

Neoplastic follicles of DFL are usually confined to the mucosa (Fig. 1) and are bordered by stromal lymphocytes, frequently arranged in rows, with some accompanied by hyalinized membranous wall (Fig. 2). Some vessels within the follicles are hyalinized, giving rise to the feature reminiscent of hyaline vascular Castleman disease. To evaluate the extent of HEV involvement, we studied the reactivities of the MECA-79 antigen for nodal HEV and MECA-367 for extranodal vessels [8,9].

Eight cases of DFL were stained and compared with 5 cases each of reactive hyperplasia of the lymph node (RH) and NFL. The MECA-79 staining was positive in the vessels of the interfollicular zone (IFZ) in RH as well as in NFL (Fig. 3A and B). However, positively stained vessels in NFL were longer and more complex than those in RH. The staining was totally negative in 6 DFLs (Fig. 2C), with rare microfoci of stain-positive vessels in the remaining 2. Thus, HEV appears to be minimally affected, if not entirely unaffected, by neoplastic follicle formation in DFL.

MECA-367 was weakly positive in some IFZ vessels of RH and NFL (Fig. 4A), whereas the staining was stronger in DFL (Fig. 4B), a feature suggestive of MAdCAM1 expression. Thus, it is not (MECA-79$^+$) PNAd but (MECA-367$^+$) MAdCAM1 that is involved in the extravasation of lymphocytes in DFL and may contribute to the formation of DFL. The endothelial height of these MECA-367$^+$ vessels was much lower (Fig. 4A) than that of MECA-79$^+$ HEV, and the number of MECA-367$^+$ vessels was much lower than that of MECA-79$^+$ vessels. If the height of endothelium reflects the traffic of lymphocytes [10], the traffic in DFL would not be as high as in NFL, so the MECA-367$^+$vessels are not tall enough to be called *HEV*.

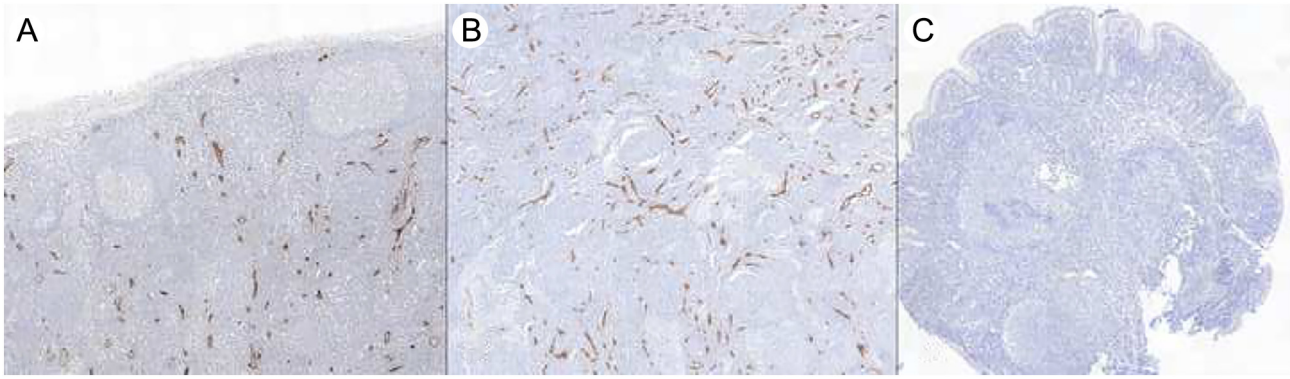

Fig. 3 MECA-79 staining of nonspecific RH (A), NFL (B), and DFL (C). The staining patterns in panels A and B are similar, showing positively stained vessels in the IFZ, with the only difference being that the positive vessels in panel B are longer and more complex than those in panel A. There are no positively stained vessels in panel C.

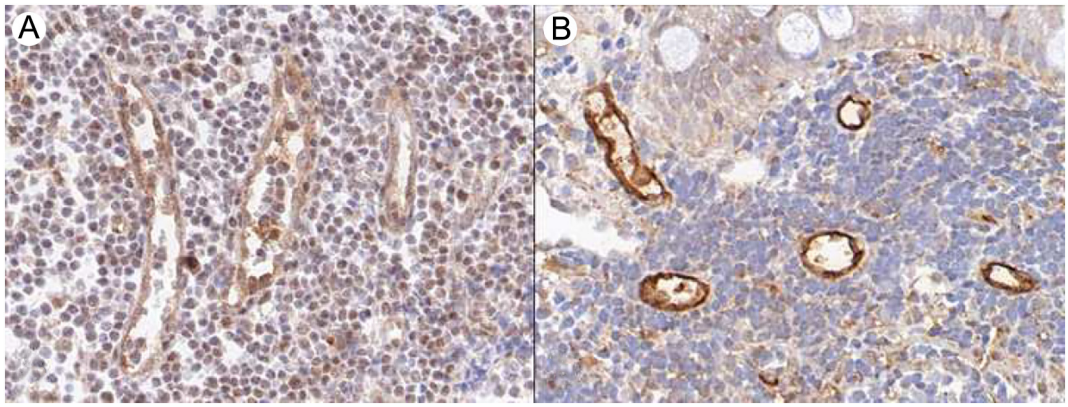

Fig. 4 MECA-367 staining of nonspecific RH (A) and DFL (B). A, Some IFZ vessels stained weakly. The endothelial height of these vessels is lower than that of the postcapillary HEV. B, The staining is stronger than that of RH or NFL.

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Pseudo-"solid pseudopapillary neoplasms" of the testis: in reality Sertoli cell tumors

Dear Editor,

We read with interest and concern 2 reports published in Human Pathology [1,2] concerning testicular neoplasms that were felt to be "testicular analogues" of the well-known "solid pseudopapillary neoplasm" (SPN) of the pancreas; albeit in 1 of the 2 articles; the authors preferred to designate the tumors as *primary signet ring stromal tumors* of the testis [1]. Although we acknowledge that the pseudopapillae in the SPNs may be limited in amount, their apparent absence, according to the descriptions of the microscopic findings in all of the 14 tumors in these 2 reports, struck us as unusual for a tumor the authors were placing in the SPN category.

The 14 tumors had foci of signet ring–type cells as well as solid, nested, and trabecular patterns of growth. They shared many immunohistochemical reactivities with SPNs, including nuclear β-catenin, CD10, CD56, and α-1-antitrypsin in the subset of cases studied by this method. The authors reported that they were negative for inhibin (0/12) and calretinin (0/12). Eleven analyzable tumors had exon 3 mutations in the *CTTNB1* gene that encodes β-catenin. In our estimation, these tumors fall within the Sertoli cell tumor, not otherwise specified (NOS) category of testicular tumors, and should not be regarded as SPNs.

Signet ring–type cells are a well-recognized feature of Sertoli cell tumor, NOS. They have previously been illustrated in Sertoli cell tumors by authorities in testicular pathology [3-7] (see p. 119, Fig. 5.18 [3]; p. 367, Fig. 5.39D [4]; p. 248, Fig. 6-20 [5]; p. 790, Fig. 12-79, and p. 791, Fig. 12-83 [6]; p. 716, Fig. 14 [7]), and they are almost certainly due to large fat vacuoles in the cytoplasm. One of us coauthored a large study indicating so, and in that series, they were seen in 26 (43%) of 60 cases [7]. The reactivity of Sertoli cell tumor, NOS, for a variety of antigens including nuclear β-catenin [8-10] and CD56 [11] is well established, as is their variable positivity for inhibin and calretinin. In 5 series, the rate of inhibin reactivity in Sertoli cell tumors varied from 25% to 90% [12-16], and a recent study showed calretinin reactivity in 43% [16]. Negative staining for inhibin and calretinin, therefore, does not exclude Sertoli cell tumor. We are not aware of studies that have looked for CD10 or

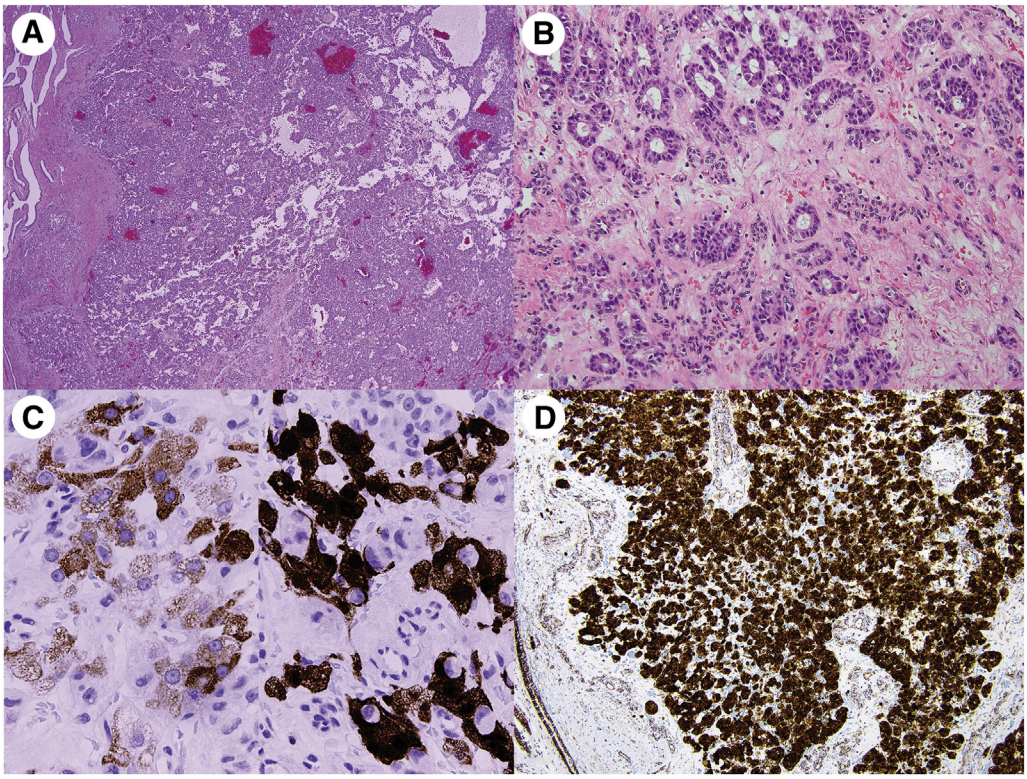

Fig. 1 Sertoli cell tumor from a 43-year-old man shows solid and trabecular growth with irregular spaces (A), prominent hollow tubules (B), patchy inhibin (left) and calretinin (right) positivity (C), and strong, diffuse nuclear and cytoplasmic reactivity for β-catenin (D).