Introduction

A 70-year old man who was found to have generalized lymphadenopathy in neck, axilla and groin during physical examination. There were no B symptoms, focal signs of infection or palpable spleen. Serologic tests for viral hepatitis and HIV were negative, and serum lactate dehydrogenase level was normal. The patient underwent excisional biopsy of cervical lymph nodes. Microscopic examination revealed effacement of the architecture by myriads of variable-sized follicles. The follicles were crowded, lacked the normal polarization pattern and the presence of tingible-body macrophages and showed permeation of the lymph node capsule. The inter-follicular area was expanded by small cleaved lymphocytes. The follicles were composed of numerous centrocytes and moderate amount of centroblasts. Immunohistochemical study showed the follicles were positive for CD20, PAX5, Bcl2, Bcl6 and CD10. CD21 highlighted irregular FDC meshwork inside follicles. The overall features were diagnostic of grade-II follicular lymphoma. Of note, most of the neoplastic follicles exhibited one or more of Warthin Finkeldey cells (WFC). On low-power view, they appeared dark, hyperchromatic cells, mainly located at the periphery of follicles and occasionally in the center. The number of nuclei ranged from 3 to as many as 16. The nuclei were round, larger than lymphocytes and exhibited vesicular chromatin and a small central nucleolus. They arranged in grape or chain-like patterns. Careful examination of PAX5 immunohistochemical stain showed negative nuclear reaction in these
Comment
WFC is a type of multinucleated giant cells that arise in lymphoid tissues in certain conditions. It was first described by Drs Aldred Scott Warthin and W. Finkeldey in 1931 after examining tonsils removed from children with measles. More studies revealed WFCs appearing in lymph nodes and even appendix of measles patients, creating a strong relationship between them. However, later reports identified WFCs in various benign and malignant lymph node diseases such as HIV-lymphadenopathy, Kimura disease and neoplastic lymphoid proliferations like Hodgkin lymphoma as well as B and T-cell lymphomas. WFC is characterized by a large size and numerous nuclei arranged in a grape-like cluster. The number of nuclei can be in dozens. The cytoplasm and cell membrane are indistinct by light microscopy. The cells are mainly located in germinal centers, but can appear in interfollicular areas. The origin of WFCs remained enigmatic for decades, until it was recently found they express follicular dendritic cell (FDC) markers by immunohistochemistry. The pathogenesis of its formation is uncertain, but it is hypothesized to result from fusion of FDCs. They were first described by Drs Aldred Scott Warthin and W. Finkeldey in 1931. Historically, they were notorious for their strong relationship with measles infection, but later reports described them in other conditions such as HIV-lymphadenopathy, Kimura disease and Hodgkin lymphoma. This case brings the light to the possible appearance of WF cells in follicular lymphoma which was not described previously. It also carries an important massage to the community of pathologists that the presence of follicular lesion in a lymph node with numerous WFCs does not indicate, by default, a reactive viral disease.

References
Figure 1: (A) Low and (B+C) high power views of neoplastic follicles that are predominantly composed of small cleaved cells and lack tingible-body macrophages, characteristic of follicular lymphoma. Note the presence of peripherally and centrally located Warthin-Finkeldey cells (Hematoxylin and Eosin stain, 200X, 600X, inset 1000X).

Figure 2: (A) CD21 immunohistochemical stain highlights follicular dendritic cells in the neoplastic follicle. Note the membranous positivity in Warthin-Finkeldey cell (inset). (B) PAX5 immunohistochemical stain is positive in nuclear pattern in neoplastic lymphocytes but negative in Warthin Finkeldey cell. (C) CD3 highlights reactive T-lymphocytes, but it is negative in Warthin-Finkeldey cells.