

The “hallmark” cells

Presence or lack of anaplastic lymphoma kinase (ALK) rearrangement and ALK protein labels the anaplastic large cell lymphoma (ALCL) into ALK-positive (ALK+) and ALK-negative (ALK-) categories but with comparable morphological and phenotypic features. A morphological feature seen in all types of ALCL is the presence of “hallmark” cells (HCs) as described by Benharroch *et al.* in 1998. These cells are so named because they can actually be detected in all the morphological variants of ALCL which also includes the small cell and the lymphohistiocytic types.^[1]

Histologically, these cells are large pleomorphic cells with abundant cytoplasm. The nuclei are eccentric, “horseshoe or kidney” shaped and often usually contain multiple small basophilic nucleoli [Figure 1a].^[2] A hand-drawn corresponding picture is illustrated in Figure 1b. An eosinophilic region may frequently be seen near the nucleus, which probably represents a prominent Golgi apparatus [Figure 1a arrow].^[1] Occasionally, some cells on histological sections may appear to contain nuclear inclusions which in fact are not true inclusions. These cells, termed as “doughnut cells,” appear so depending on the plane of section, rather than true invaginations

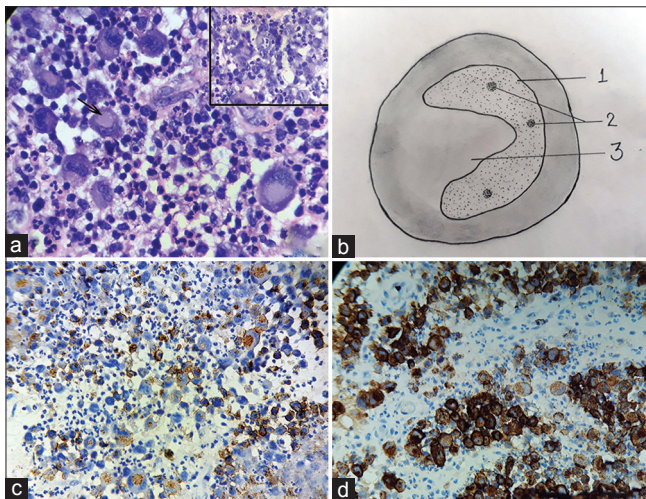


Figure 1: (a) Photomicrograph of H and E section showing sheets of large cells showing pleomorphic hallmark cells with horseshoe-shaped nuclei, amphophilic cytoplasm and eosinophilic area probably representing Golgi region (arrow). A large kidney-shaped cell is shown in the inset ($\times 400$). (b) A hand-drawn picture of hallmark cells showing horseshoe-shaped nuclei (1), multiple prominent nucleoli (2) and adjacent Golgi zone (3). (c and d) Photomicrographs showing diffuse epithelial membrane antigen and CD30 positivity (immunohistochemistry)

of the nuclear membrane.^[3] Figure 2 illustrates different appearances of nuclei of HCs depending on the plane of section. Other variant is cells with lobulated nuclei often called “embryo” cells.^[4] Multinucleated cells may appear similar to Reed–Sternberg (RS) cells; however, as compared to the nucleoli seen in the RS cells, the nucleoli of HC are often less prominent.

Immunohistochemistry plays an important role in the establishment of phenotype of the cells. Epithelial membrane antigen (EMA) and CD30 are helpful and stain the cell membrane and Golgi region of the HCs [Figure 1c and d]. S100 and cytokeratin are negative.^[5] Based on ALK positivity or negativity, ALCL is subcategorized. These cells are consistently negative for Epstein–Barr virus (EBV, i.e. for EBV-encoded small RNA and latent membrane protein-1),^[3] and CD15 immunoreactivity is observed rarely. These both may be exploited in cases where HCs morphologically resembles RS cells and give a diagnostic challenge. Perivascular pattern of the neoplastic cell infiltration may prove fruitful in addition to ALK protein and EMA positivity and lack of CD15 in differentiating ALCL from ALCL-like Hodgkin’s disease.^[1]

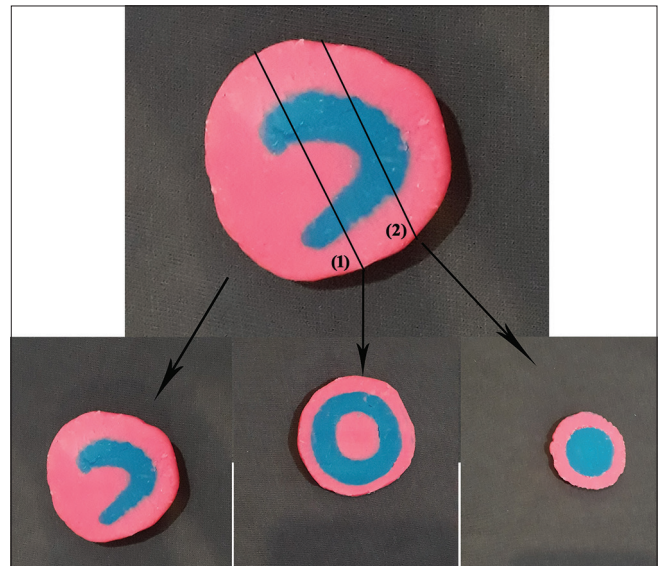


Figure 2: Illustration of different appearances of the nuclei of hallmark cells depending on the plane of section using playing dough; when sectioned from the center, they appear as doughnut cells (1) and as smaller cells with rounded nuclei when sectioned from the end (2)

Thus, identification of HCs of ALCL and their distinction from alike cells is important as ALCL has a grave outcome. Further immunophenotypical subcategorization of ALCL into ALK+ and ALK- cases is equally important as ALK- ALCL has poorer prognosis.

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Conflicts of interest

There are no conflicts of interest.

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REFERENCES

1. Benharroch D, Meguerian-Bedoyan Z, Lamant L, Amin C, Brugières L, Terrier-Lacombe MJ, *et al.* ALK-positive lymphoma: A single disease with a broad spectrum of morphology. *Blood* 1998;91:2076-84.
2. Falini B. Anaplastic large cell lymphoma: Pathological, molecular and clinical features. *Br J Haematol* 2001;114:741-60.
3. Swerdlow SH, Campo E, Harris NL, Jaffe ES, Pileri SA, Stein H, *et al.* WHO Classification of Tumours of Haematopoietic and Lymphoid Tissues. Revised 4th ed. IARC: Lyon 2017.
4. Jairajpuri ZS, Rana S, Khetrpal S, Talikoti MA, Jetley S. Extranodal anaplastic large cell lymphoma mimicking sarcoma: A report of an interesting case. *Int J Appl Basic Med Res* 2014;4:S50-2.
5. Ng WK, Ip P, Choy C, Collins RJ. Cytologic and immunocytochemical findings of anaplastic large cell lymphoma: Analysis of ten fine-needle aspiration specimens over a 9-year period. *Cancer* 2003;99:33-43.

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