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LETTER TO THE EDITOR

ALK-positive anaplastic large cell lymphoma expressing membranous D2-40 immunopositivity and mimicking seminoma: potential diagnostic pitfall

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Dear editor:

Morphology of anaplastic large cell lymphoma (ALCL) varies from common pleomorphic large cell pattern, Hodgkin-like, lymphohistiocytic, signet-ring-cell carcinoma-like, or sarcoma-like to small cell pattern. Besides anaplastic lymphoma kinase (ALK) and CD30 immunopositivity, ALCL commonly expresses epithelial membrane antigen (EMA) and cytotoxic granule-asociated proteins, with variable positivity for T cell or natural killer cell antigens. CD45, most commonly used lymphoid marker in the initial differential diagnosis of tumors of uncertain histogenesis, is frequently negative [1]. Monomorphic large cell pattern especially when occurring in the mediastinum can mimic seminoma, which can occur in the same age group. We present a case of predominantly mediastinal ALCL resembling seminoma by morphology and immunohistochemical membranous D2-40 positivity, creating a potential diagnostic pitfall.

The patient was a 9-year-old boy and presented with cervical lymphadenopathy and anterior mediastinal mass. He underwent cervical lymph node biopsy, which showed partially effaced architecture, with malignant cells growing within the sinuses, around residual follicles, and in diffuse sheets (Fig. 1a). Tumor cells were round to oval and fairly uniform, with open vesicular nuclei, mildly prominent nucleoli, and lightly eosinophilic to clear cytoplasm. Small nonneoplastic lymphocytes were intermingled with the tumor cells (Fig. 1b). Typical "hallmark cells" were hard to find, but they were present. The case was treated as a rush biopsy and broad panel of antibodies was applied, including B- and T cell and germ cell markers. The tumor cells were negative for CD45 (anti-LCA, Clone 2B11&PD7/26, Diagnostic BioSystems, 1:100), CD20 (Clone L-26, Biogenex; 1:50), CD3 (Clone PS1, Diagnostic BioSystems; RTU), CD7 (Clone C21-Q, DB Biotech; 1:100), CD4 (Clone 4B12, Biogenex; RTU), CD8 (Clone P17-V, DB Biotech; 1:100), CD15 (Clone BRA4F1, Biogenex; 1:100), PLAP (Clone PL8-F6, Biogenex; RTU), and CD117 (c-kit, polyclonal, Dako; 1:300) and showed positivity for EMA (Clone E29, Diagnostic BioSystems; 1:100), CD30 (Clone HRS-4, Biogenex; RTU), keratin cocktail (Clone AE1/AE3, Biogenex; 1:50), as well as cytotoxic proteins perforin (Clone 5B10, Novocastra; 1:20) and TIA (Clone TIA-1, Abcam; 1:50). CD5 (Clone SP19, NeoMarkers; 1:100) was focally positive and strong nuclear, cytoplasmic, and membranous ALK positivity was detected (CD246, Clone ALK1, Dako; 1:30). D2-40 (Clone D2-40, Dako; 1:100) positivity was present as strong membranous staining in all tumor cells (Fig. 1c). Residual follicular dendritic cells served as internal positive control. ALK gene translocation, confirming the diagnosis of ALCL, was proven by break apart FISH (Poseidon Repeat-free ALK (2p23) Break; Kreatech) (Fig. 1d).

D2-40 is a monoclonal antibody against podoplanin and originally was reported as a specific marker of lymphatic endothelium. Subsequently, D2-40 expression was noticed in a wide spectrum of normal and neoplastic tissues (reviewed excellently by Kalof and Cooper [2]), including mesothelial cells and mesotheliomas, follicular dendritic cells (FDC) and FDC tumors, various vascular lesions with lymphatic differentiation (e.g., Kaposi sarcoma), adrenal cortical carcinoma (helping in distinction from renal cell carcinoma), schwannoma and malignant peripheral nerve sheath tumors, primary skin adnexal carcinomas (metastatic carcinomas are negative), ependyma and ependymomas, or myoepithelial cell (useful in breast pathology). Moreover, D2-40 expression by tumor cell or stromal cells, mostly in

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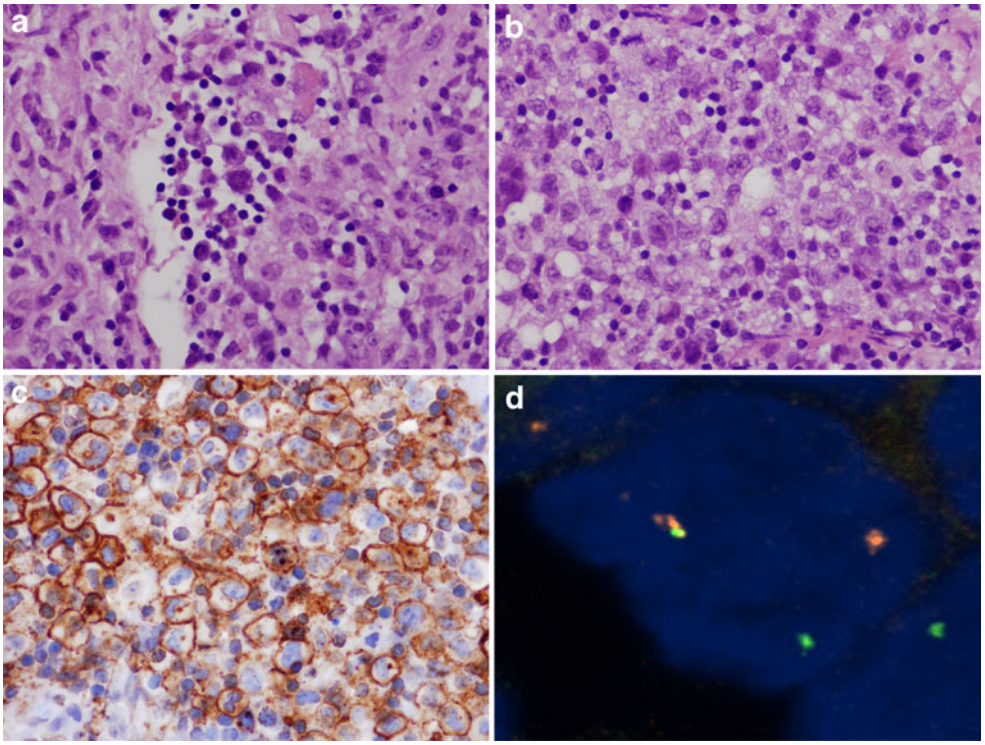

Fig. 1 **a** Neoplastic cells involving the sinus in a metastasis-like pattern (HE, ×400). **b** Monomorphic large cells intermingled with small lymphocytes, resembling seminoma (HE, ×400). **c** Strong membranous D2-40 positivity in all neoplastic cells. **d** ALK gene translocation proved by break apart FISH (break was present in 75 from 100 analyzed cells)

squamous cell carcinomas in various locations, has been linked to prognosis or progression [3–7].

It has been shown that diffuse membranous D2-40 positivity is a very useful marker of seminoma and helps to distinguish between seminoma and other germ cell tumors as well as metastatic neoplasms [8, 9]. In the English literature, only one case of ALCL with focal nonspecific cytoplasmic D2-40 positivity can be found [8]. To the best of our knowledge, this is the first case of ALCL with specific membranous positivity in the majority of neoplastic cells, which when limited panel of antibodies are used can lead to incorrect diagnosis. The distinction of ALCL from seminoma or other D2-40 positive tumors should therefore be based by the use of broader panel of antibodies.

Conflict of interest statement The authors declare that they have no conflict of interest.

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