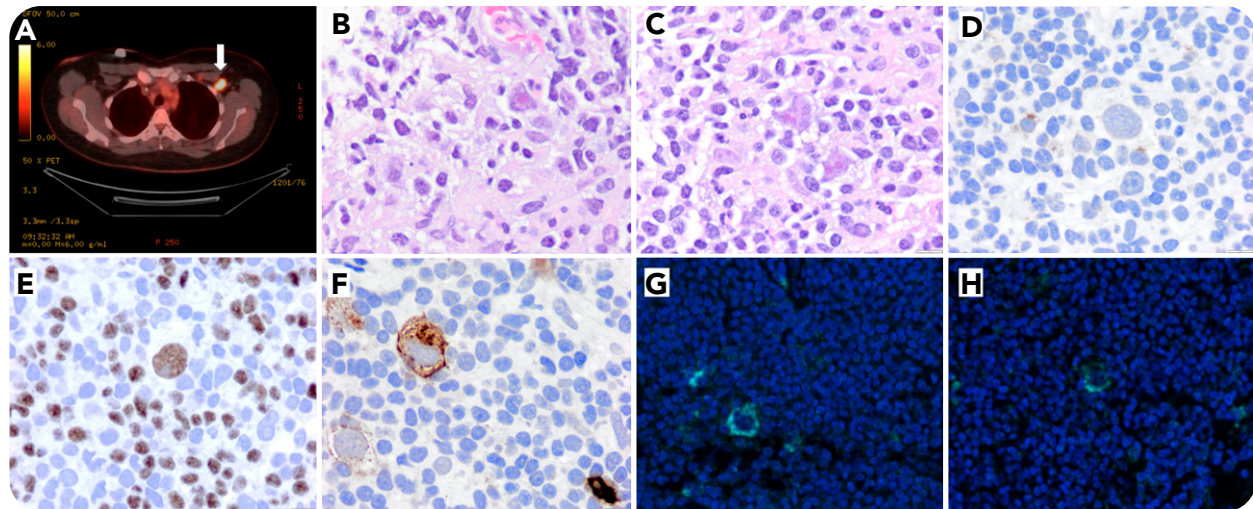


Relapsed classic Hodgkin lymphoma with decreased CD30 expression after brentuximab and anti-CD30 CAR-T therapies

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A 40-year-old woman was diagnosed with classic Hodgkin lymphoma (CHL) in 2016. At that time, the neoplasm was positive for CD30 as expected for a CHL. The patient was treated with 6 cycles of ABVD (Adriamycin [doxorubicin], bleomycin, vinblastine, dacarbazine) without radiation. The tumor relapsed in 2017 and was treated with nivolumab and later brentuximab vedotin (BV) and is receiving chimeric antigen receptor T cells (CAR-T) against CD30 since March 2021. Recent positron emission tomography scan showed chest wall/axillary lymph nodes with a standardized uptake value of 8.1 (arrow; panel A). Histologic section revealed few scattered, large, atypical cells with prominent eosinophilic nucleoli in a background rich in small lymphocytes (panels B-C; hematoxylin-eosin stain, objective magnification $\times 100$) with areas of fibrosis. The neoplastic cells were negative to weakly positive for CD30 (panel D;

immunohistochemical stain [IHC], objective magnification $\times 100$), weakly positive positive for PAX-5 (panel E; IHC, objective magnification $\times 100$), and positive for CD15 (panel F; IHC, objective magnification $\times 100$). They were negative for CD20 and CD45. More sensitive immunofluorescence testing using tyramide signal amplification (TSA) confirmed low-level expression of CD30 in tumor cells (panels G-H; objective magnification $\times 40$).

To the best of our knowledge, decreased expression of CD30 in CHL after BV or CAR-T treatment has not been reported. Negative to very weak positive CD30 by IHC and background rich in small lymphocytes created diagnostic difficulties; previous history of CHL, the presence of atypical large cells positive for PAX-5 and CD15 but negative for CD45 by IHC and positive for CD30 by TSA helped to establish the diagnosis.