

B-cell lymphoma in a tubular adenoma with high-grade dysplasia: a rare extramedullary manifestation of high-grade diffuse large B-cell lymphoma

B-cell lymphomas represent about 90% of all non-Hodgkin lymphomas (NHLs). Almost all express pan B-cell antigens including CD19, CD20, and PAX5. Most patients with NHL present persistent painless peripheral lymphadenopathy. Staging tests do not include colonoscopy. Here we present a rare case of synchronous occurrence of a high-grade diffuse large B-cell lymphoma (DLBCL) initially presenting in a tubular adenoma of the large bowel and subsequently in the bone marrow.

A 73-year-old woman was referred to our hospital because of leukopenia (minimum $0.6 \times 10^9/L$), anemia (hemoglobin 83 g/L), dyspnea, and B symptoms. Previously, 27 years earlier, the patient suffered from a pluriform differentiated mucinous breast carcinoma (pT3 pN0 M0) treated with radiation (46 Gy high dose) after mastectomy.

A computed tomography (CT) scan of the abdomen detected few enhanced para-aortal lymph nodes, and routine laboratory analysis showed elevated values for lactate dehydrogenase (maximum 2892 U/L), C-reactive protein (312 mg/L), liver enzymes, ferritin (6334 ng/mL), and CA 12–5 (160 U/mL). Colonoscopy revealed a 2-cm tubular adenomatous sigmoid polyp, which was completely removed by endoscopic resection (● Fig. 1). Histological examination and appropriate immunohistochemical staining showed high-grade intraepithelial neoplasia and focal infiltration of the stroma by highly proliferative lymphoid blasts positive for CD20 and PAX5. Bone marrow immunocytology displayed a monoclonal B-cell lymphocytosis. Subsequent bone marrow biopsy revealed an interstitial and diffuse infiltration by a DLBCL with positivity for CD20, bcl2, and PAX5, negativity for TdT, CD10, and CD34, and a proliferation index of 80% (MIB1 staining). Infiltration by the previously diagnosed breast carcinoma was excluded by negativity for the pan-keratin markers A/E1–3 and MNF116.



Fig. 1 Endoscopic view of the polyp at the rectosigmoid junction. Note the smooth contour of the mildly protruding lesion as well as the bleeding, which occurred even with gentle endoscopic manipulation.

Finally, molecular genetic analysis detecting the rearrangement of the FR3a region of the immunoglobulin heavy chain was performed, and identical monoclonal amplicates of approximately 248 base pairs were detected in both manifestations, demonstrating malignancy and clonal association of the lymphoma infiltrates in the adenoma and the bone marrow (● Fig. 2). The ileocecal area and ileum are the regions most frequently affected by primary small-intestinal and large-intestinal NHL, and most of such cases are DLBCL [1–3]. Synchronous diagnosis of colorectal malignancy and lymphoma is rare [4]. Colorectal lymphoma is extremely infrequent, representing less than 0.5% of all primary colorectal neoplasms [5]. B-cell lymphomas should be included in the differential diagnosis of polypoid lesions in patients suspicious for malignancies. Endoscopy with complete histological analysis may be important in the diagnosis of high-grade DLBCL of the lower gastrointestinal tract.

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E. Roeb¹, M. Rummel², W. Blau², B. Etschmann³, S. Gattenlöhner³

¹ Division of Gastroenterology, Department of Internal Medicine, University Hospital, Justus Liebig University, Giessen, Germany

² Division of Hematology, Department of Internal Medicine, Justus Liebig University, Giessen, Germany

³ Institute of Pathology, University Hospital, Justus Liebig University, Giessen, Germany

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Corresponding author

E. Roeb, MD

Division of Gastroenterology
Department of Internal Medicine II
Justus Liebig University Giessen
Clinic Street 33
D-35385 Giessen
Germany

Fax: +49-641-98542339

Elke.Roeb@innere.med.uni-giessen.de

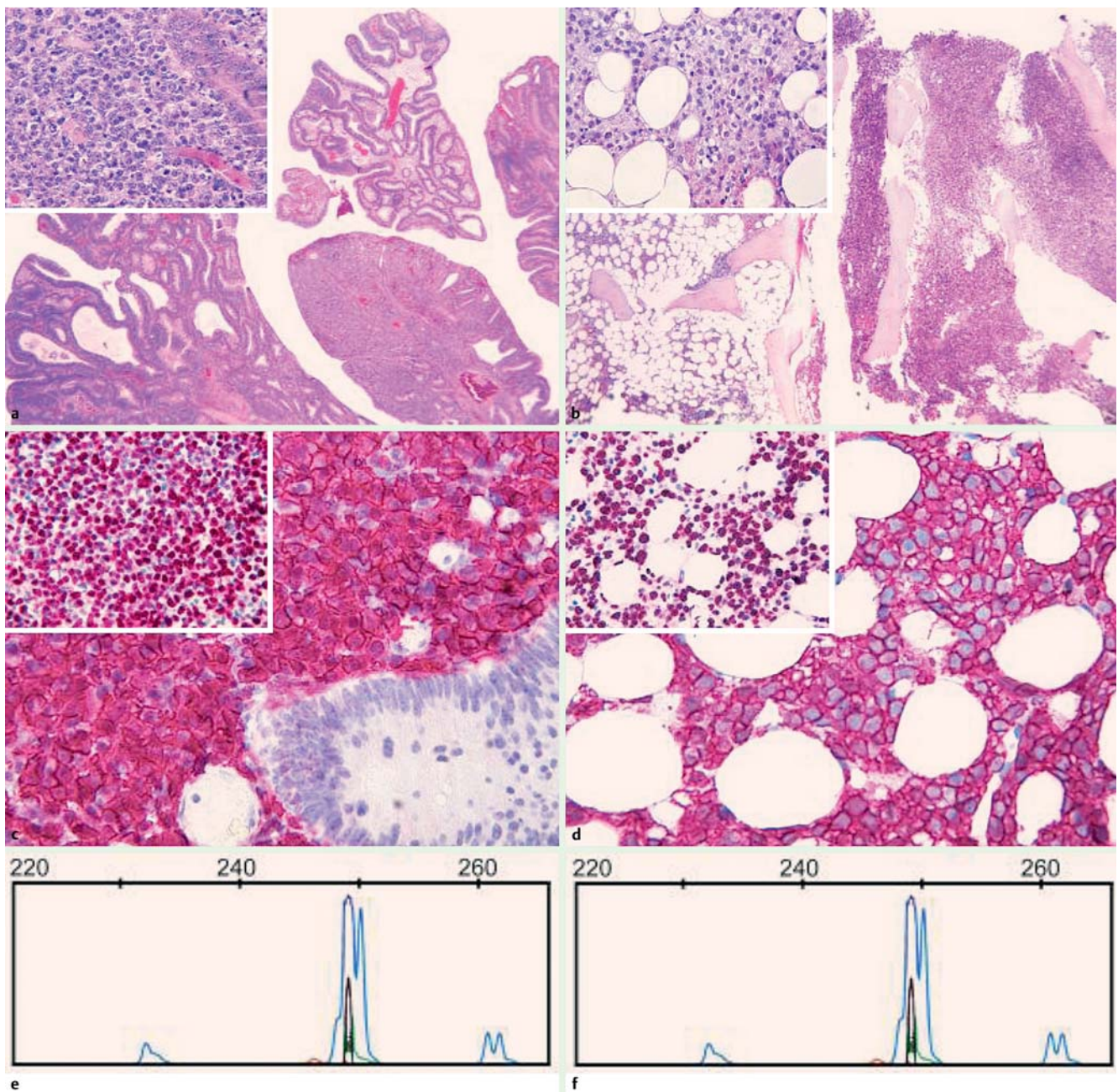


Fig. 2 Histochemical and molecular genetic analysis of lymphoma infiltrates in: **a, c, e** the colonic adenoma; **b, d, f** bone marrow biopsy. Lymphoid blast infiltrates in the adenomatous stroma (**a**, circle and inset) and the bone marrow (**b**) are strongly positive for the B-cell marker CD20 (**c** and **d**) and show proliferation rates > 80% with the MIB1 stain (insets **c** and **d**). Molecular genetic analysis detecting the rearrangement of the FR3a region of the immunoglobulin heavy chain (IgH) demonstrates mono-clonal amplificates for both lymphoma infiltrates, showing mono-clonal peaks (**e** and **f**) with a so-called slight poly-clonal background in the colonic adenoma (**e**), representing the reactive non-neoplastic B-cells in the surrounding tissue.