



## EBV-positive mucocutaneous ulcer within colonic diverticulitis mimicking diffuse large B cell lymphoma

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Dear Editor,

An 84-year-old immunocompetent woman underwent sigmoid resection for acute colonic diverticulitis (Fig. 1a). Histologically, mucosa and submucosa of two inflamed diverticula showed a dense infiltrate of medium- and large-sized cells (Fig. 2a), some with an Hodgkin-like morphology (Fig. 1b), admixed with plasma cells. The base of the lesion was sharp and rimmed by a band-like infiltrate of small T lymphocytes, CD3 and CD8 positive. The atypical cells were diffusely positive for CD30 (Fig. 1c) and B cell markers as CD20 (Fig. 2b) and CD79 $\alpha$ , with variable staining for PAX5, MUM1/IRF4, BOB1, and OCT2. CD15, BCL6, CD10, and HHV8 were negative. Ki67 proliferative index was high up to 80% (Fig. 2c). A diffuse positive staining for EBV by in situ hybridization for EBV-encoded RNA (EBER) was present (Fig. 2d). Clonal immunoglobulin gene (Ig) rearrangement was identified. T cell receptor (TCR) rearrangement was negative. Staging procedures were negative. Epstein-Barr virus (EBV)-positive mucocutaneous ulcer (EBVMCU) arising in colon diverticulitis was diagnosed.

This case represents the second report of EBVMCU occurring within colonic diverticula [1], and the first identified at this site mimicking an aggressive B cell lymphoma. EBVMCU can be a diagnostic pitfall, leading to patient's overtreatment.

EBVMCU was initially described in 2010 as sharply circumscribed ulcers of skin, oropharynx, and gastrointestinal tract, occurring in conditions of immunosuppression related to either therapy or advanced age and it has been included, as a provisional entity, in the current World Health Organization (WHO) classification of lymphoproliferative disorders [2, 3]. Recently, its clinicopathologic spectrum turned out to be wider than initially described [4]. Lesions can be single or multiple, but usually confined to a unique anatomic area [4]. Histologically, EBVMCU can mimic either classical Hodgkin lymphoma (cHL), when showing a polymorphic pattern, or diffuse large B cell lymphoma (DLBCL), if displaying a monomorphic, diffuse pattern of growth [4]. We recently reported a case of EBVMCU occurring within colonic diverticulitis, in an elderly patient with immunosuppression related to both advanced age and long-term methotrexate therapy [1]. EBVMCU involved just one colonic diverticulum and histologically resembled cHL [1].

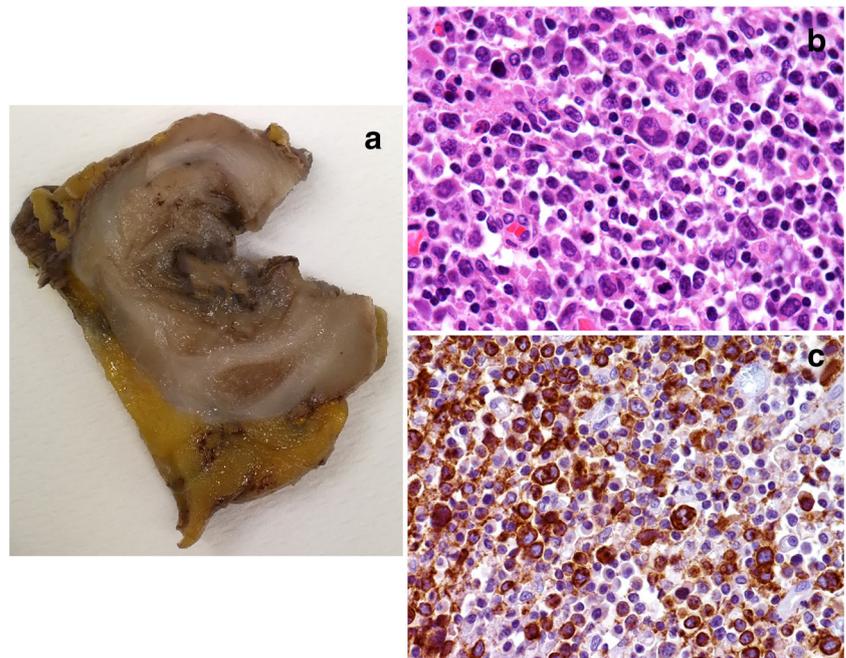
In the present case, main risk factor for developing EBVMCU was represented by the patient's advanced age. EBVMCU was multifocal, being identified within two colonic diverticula and histologically closely simulated an aggressive B cell lymphoma, showing a diffuse pattern, large B cell lymphoma-like. We believe that the local irritative stimulus caused by colonic diverticulitis can represent an additional factor favoring EBVMCU occurrence.

The correct recognition of EBVMCU, even in the recently reported setting of colonic diverticulitis, is very important for subsequent patient's management.

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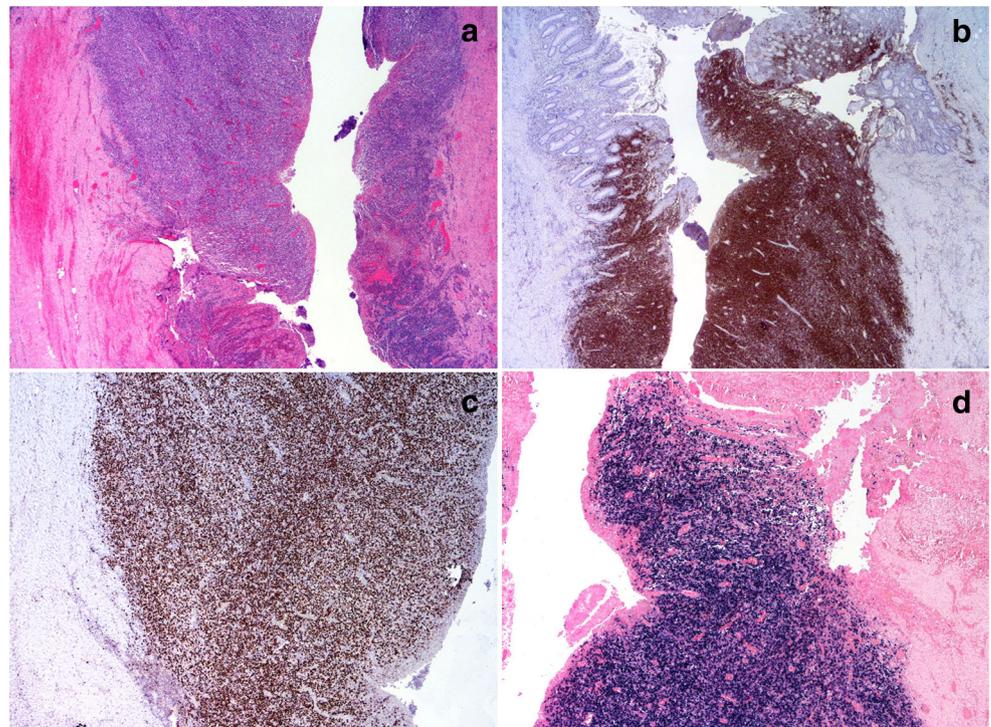
**Fig. 1** **a** Gross section of a sigmoid diverticulum. **b** High-power view highlighting medium- and large-sized atypical cells, some with an Hodgkin-like appearance (HE  $\times 20$ ). **c** Diffuse positivity for CD30



Despite histological alarming features as an elevated proliferative fraction and the identification of clonality, either of Ig or of TCR reported in about one third of cases, clinical course of EBVMCU is mostly indolent [2–4]. It is a self-limiting disease resolving spontaneously or upon reduction of immunosuppressive therapy [2,

3]. The localized and superficial nature of the lesions and the sharp deep margin rimmed by small T lymphocytes are considered helpful clues to recognize this entity, avoiding misdiagnosis with much more aggressive disease like DLBCL or cHL and consequent patient's overtreatment [2–5].

**Fig. 2** **a** Low-power view of the diverticulum with a diffuse infiltrate involving mucosa and submucosa (HE  $\times 2$ ). **b** Low-power view showing diffuse positive staining for CD20. **c** High proliferative index (Ki67). **d** Epstein-Barr virus diffuse positivity in variably sized cells of the infiltrate, by in situ hybridization for EBV-encoded RNA (EBER)



## Compliance with ethical standards

**Conflict of interest** The authors declare they have no conflict of interest.

**Ethical approval** Local ethics committee (Comitato Etico dell'Area Vasta Emilia Nord, Italy) ruled that no formal ethics approval was required in this particular case.

**Informed consent** Written informed consent was obtained from patient for publication of this case report and any accompanying images. A copy of the written consent is available for review by the Editor-in-Chief of this journal.

## References

- Zanelli M, Mengoli MC, Valli R, Froio E, Bisagni A, Zizzo M, De Marco L, Ascani S (2019) Primary classic Hodgkin lymphoma of the ileum and Epstein-Barr virus mucocutaneous ulcer of the colon: two entities compared. *Virchows Arch* 474(1):117–123. <https://doi.org/10.1007/s00428-018-2451-9>
- Dojcinov SD, Venkataraman G, Raffeld M, Pittaluga S, Jaffe ES (2010) EBV positive mucocutaneous ulcer. A study of 26 cases associated with various sources of immunosuppression. *Am J Surg Pathol* 34(3):405–417. <https://doi.org/10.1097/PAS.0b013e3181cf8622>
- Swerdlow SH, Campo E, Harris NL, Jaffe ES, Pileri SA, Stein H, et al. (eds.) WHO classification of tumours of haematopoietic and lymphoid tissues, WHO classification of tumours, revised 4th edition, ed. IARC: World Health Organization; 2017
- Prieto-Torres L, Eraña I, Gil-Redondo R, Gómez de la Riva I, Manso R, Pajares R, Córdoba R, Machan S, Ara M, Requena L, Piris MÁ, Rodríguez-Pinilla SM (2019) The spectrum of EBV-positive mucocutaneous ulcer: a study of 9 cases. *Am J Surg Pathol* 43(2):201–210. <https://doi.org/10.1097/PAS.0000000000001186>
- Gratzinger D, Jaffe ES (2016) Mucocutaneous ulcer: a mimic of EBV+diffuse large B-cell lymphoma. *Leuk Lymphoma* 57(8):1982–1983. <https://doi.org/10.3109/10428194.2016.1166492>

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