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13. Geisler CH, Kolstad A, Laurell A, et al; Nordic Lymphoma Group. Long-term progression-free survival of mantle cell lymphoma after intensive front-line immunochemotherapy with in vivo-purged stem cell rescue: a nonrandomized phase 2 multicenter study by the Nordic Lymphoma Group. *Blood.* 2008;112(7):2687-2693.

14. Kolstad A, Laurell A, Jerkeman M, et al; Nordic Lymphoma Group. Nordic MCL3 study: 90Y-ibritumomab-tiuxetan added to BEAM/C in non-CR patients before transplant in mantle cell lymphoma. *Blood.* 2014;123(19): 2953-2959.

15. Desai P, Mencia-Trinchant N, Savenkov O, et al. Somatic mutations precede acute myeloid leukemia years before diagnosis. *Nat Med.* 2018;24(7):1015-1023.

16. Abelson S, Collord G, Ng SWK, et al. Prediction of acute myeloid leukaemia risk in healthy individuals. *Nature.* 2018;559(7714): 400-404.

17. Young AL, Tong RS, Birmann BM, Druley TE. Clonal haematopoiesis and risk of acute myeloid leukemia. *Haematologica.* 2019;104(12): 2410-2417.

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TO THE EDITOR:

EBV^{+} diffuse large B-cell lymphoma associated with chronic inflammation expands the spectrum of breast implant–related lymphomas

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Breast implant–associated anaplastic large cell lymphoma (BI-ALCL) has emerged as a new provisional entity in the revised 2016 World Health Organization classification of lymphoid malignancies.[1] BI-ALCL is a rare T-cell lymphoma arising adjacent to breast implants and composed of large atypical CD30^{+} cells frequently confined to the peri-implant seroma fluid and adjacent capsule, more rarely forming a solid infiltrating mass.[2,3] So far, only exceptional cases of lymphomas other than BI-ALCL have been reported to occur in the vicinity of breast implants, including miscellaneous B-cell lymphomas.[4-7] It remains so far unclear whether these cases are coincidental or could be related to breast implants.

We report 3 cases of Epstein-Barr virus (EBV)$^{+}$ diffuse large B-cell lymphomas (DLBCLs) occurring in contact with breast implants. These cases were also characterized by various degrees of invasion of the periprosthetic capsule but no tumor mass, which make them distinct from classical primary breast DLBCLs.[8,9] To our knowledge, no series of DLBCL adjacent to breast implants has been documented so far. This study was approved by the institutional review board of the Institut Paoli-Calmettes, and all patients gave their informed consent.

In the 3 patients (aged 61 to 72 years), the diagnosis was allowed by excision of the periprosthetic capsule due to esthetical issues in cases 1 and 3 or incidental positron emission tomography (PET) scanner during breast cancer surveillance in case 2 (Table 1). In all cases, the lymphoma tumor was strictly confined to the capsule surrounding breast implants (macrotextured type from Allergan), and the PET computed tomography finding was negative otherwise. The bone marrow biopsy result was also negative. No seroma had been observed prior to capsulectomy in any case, which prevented any fluid aspiration and cytologic analysis. None of the patients had any known immunodeficiency or pharmacologic immunosuppression.

Formalin-fixed and paraffin-embedded capsulectomy samples from the 3 cases were extensively characterized using histological, phenotypical, cytogenetic, and molecular analyses, including targeted next-generation sequencing (tNGS) and array comparative genomic hybridization (aCGH), as described in supplemental Materials and methods (available on the *Blood* Web site). Clinicopathological and biological features of the 3 cases are detailed in Table 1 and supplemental Tables 1 to 4 and illustrated in Figure 1 and supplemental Figure 1.

The 3 cases shared common pathological features consisting of sheets, clusters, and ribbons of large pleomorphic CD30^{+} EBV-infected B-cells, with EBER expression in virtually all lymphoma cells. The latency profile was type III (LMP1^{+}/EBNA-2^{+}) in 2 cases, whereas the remaining case was negative for both LMP1 and EBNA2. Postresection plasma EBV levels were positive in the 2 analyzed cases, with a decrease over time (supplemental Table 1). Lymphoma cells were observed on the luminal side of the capsule or suspended in a fibrinoid material with constant thickening and invasion of the capsule. This invasion formed cell

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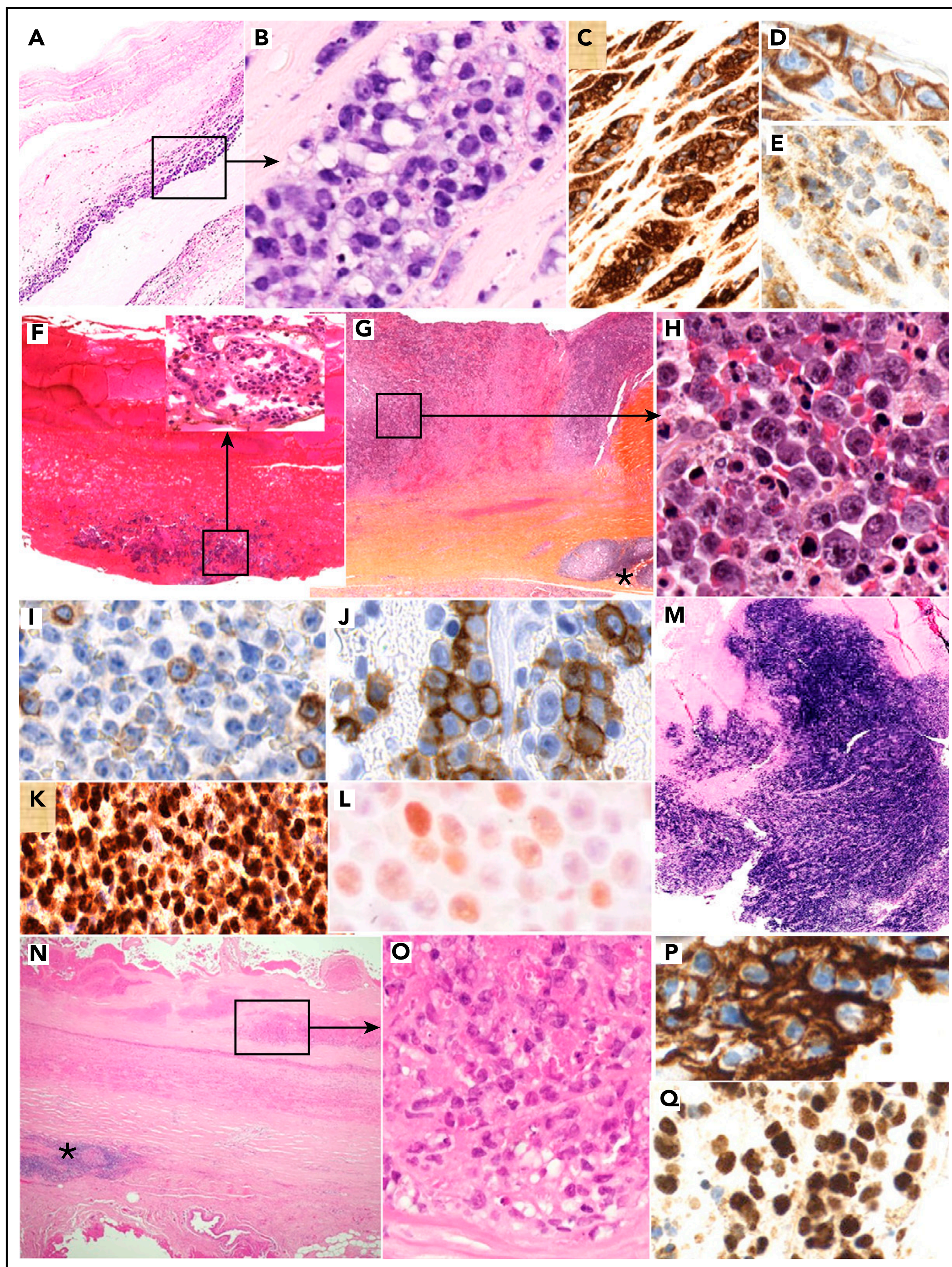

Figure 1. Histophenotypical features of BI-associated DLBCLs. In case 1, the capsule was infiltrated by cell aggregates within fibrin deposits (A, hematoxylin & eosin [H&E] stain ×25), and neoplastic cells disclosed pleomorphic irregular nuclei, with slightly lytic features and apoptotic bodies (B, H&E stain ×400); they expressed CD20 (C, immunohistochemistry [IHC] stain ×200), CD30 (D, IHC stain ×400), and LMP1 (E). In case 2, the breast tumor was composed of dense cell aggregates within abundant fibrinous deposits (F, H&E stain ×25) but also showed massive capsule invasion (G, H&E stain ×25). Hyperplasic lymphoid follicles were present in the external part of the capsule (G, *). Tumor cells displayed plasmablastic features (H, H&E stain ×600). CD79a was positive in a minority of lymphoma cells (I, IHC stain ×400), whereas CD30 was positive (J, IHC stain ×400) and the Ki-67 proliferative index was ~100% (K, IHC stain ×200). P-STAT3 was also positive (L, IHC stain ×600). In situ hybridization showed that virtually all neoplastic cells were EBV infected (M, EBER stain ×25). In case 3, cell aggregates were mostly located at the surface of the capsule within fibrinous deposits (N, H&E stain ×25). Hyperplasic lymphoid follicles were present in the deep capsule (N, *). Atypical large cells were altered by early necrosis (O, H&E stain ×400); they displayed CD20 (P, IHC stain ×400) and EBNA2 positivity (Q, IHC stain ×400).

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Table 1. Clinical, pathological, and molecular features of breast implant–associated DLBCLs

Case	Clinical presentation and staging	Treatment and follow-up	Pathological features	Phenotypical features	EBV status	Cell of origin	Clonality	Cytogenetic and molecular features
1	72-y-old female, no symptoms. Removal of silicone macrotextured implant (Allergan) for esthetical issues 8 y after left breast adenocarcinoma ECOG = 0, normal PET scan, normal LDH; stage I, aaIPI = 0	"Watch and wait" Complete remission 19 mo from surgery	Left capsulectomy showing patchy infiltrate of large pleomorphic cells invading the capsule with fibrinous deposits and necrotic areas Inflammatory background of plasma cells and neutrophils	Positive markers: CD45, CD19 (w), CD20, CD22 (w) CD79a, PAX5, CD30, MUM1, CD43, CD138(w), BCL2, MYC (40%), Ki67 (~100%) P-STAT3: negative; CD56 and HHV8: negative	Tumor*: $LMP1^+$ $EBNA2^+$ $EBER^+$ Plasma: 3183 U/mL†	ABC according to IHC (unclassified according to RT-MLPA)	Major monoclonal Ig rearrangement and minor TCR rearrangement (1-2% T cells‡)	FISH: no rearrangement of *BCL2*, *BCL6*, *MYC*. aCGH: no detectable aberration tNGS (30% tumor cells‡): damaging somatic mutations of *IRF4* (p.L24F; VAF 10.4%), ARID1A (p.H684Y; VAF 3.37%), *TET2* (p.R1465§; VAF 4.5%)
2	61-y-old female, no symptoms. Incidental detection of PET fixation around silicone macrotextured implants (Allergan) 13 y after right breast adenocarcinoma ECOG = 0, normal PET scan, normal LDH; stage I, aaIPI = 0	Watch and wait Complete remission 21 mo from surgery	Right capsulectomy showing a plurinodular infiltrate of large cells with plasmablastic features invading the capsule with fibrinous deposits Inflammatory background of plasma cells and reactive lymphoid follicles	Positive markers: CD45, CD79a (w/F), CD4 (w/F), CD30 (F), MUM1, CD10 (F), Bcl6 (F), κ, MYC (70%), PD1 (20%), EMA (F), Ki67(~100%) P-STAT3: positive; CD56, CD138 and HHV8: negative	Tumor*: LMP1- EBNA2- $EBER^+$; plasma: 1990 U/mL†	ABC according to RT-MLPA (unclassified according to IHC)	Major monoclonal IG rearrangement and minor TCR rearrangement (10% T-cells‡)	FISH: *IGH-MYC* translocation, no rearrangement of *BCL2* or *BCL6*. aCGH: X monosomy, 7q deletion, 13q deletion involving *RB1*) and 14q deletion (involving *IGH*) tNGS (90% tumor cells‡): damaging somatic mutations of *STAT3* (pG1618R; VAF 48%), *SOCS1* (p.Y203N; VAF 46%), FOXO1 (pS205R; VAF 45%), *CCND2* (pV284G, VAF 43%)

aaIPI, age-adjusted International Prognostic Index; CHOP, cyclophosphamide, doxorubicin, vincristine, and prednisone; EBER, EBV-encoded small RNA: F, focal; FISH, fluorescence in situ hybridization; Ig, immunoglobulin; IHC, immunohistochemistry; LDH, lactate dehydrogenase; ND, not done; RT-MLPA; reverse transcriptase multiplex ligation-dependent probe amplification; TCR, T-cell receptor; VAF, variant allele frequency; w, weak.

*Positivity for EBER restricted to virtually all large ($CD30^+$) lymphoma cells, with negativity of reactive T cells.

†Highest detected value among different postresection time points (detailed in supplemental Results).

‡Percentage of cells in the macrodissected area used for DNA extraction.

§Stop codon.

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Table 1. (continued)

Case	Clinical presentation and staging	Treatment and follow-up	Pathological features	Phenotypical features	EBV status	Cell of origin	Clonality	Cytogenetic and molecular features
3	69-y-old female, no symptoms. Removal of silicone macrotextured implant (Allergan) for esthetical issues 9 y after cosmetic breast augmentation ECOG = 0, normal PET scan, normal LDH; stage I, aaIPI = 0	Chemotherapy (3 R-CHOP cycles) with intrathecal prophylaxis Complete remission 20 mo from end of treatment	Right capsulectomy showing patchy infiltrate of large pleomorphic cells invading the capsule with fibrinous deposits and necrotic areas Inflammatory background of plasma cells and reactive lymphoid follicles	Positive markers: CD45, CD19, CD20, CD22, CD79a, CD30, MUM1, Bcl2, Λ light chain, Ki67 (80%) P-STAT3: negative; CD56, CD138 and HHV8: negative	Tumor§: LMP1^{+} EBNA2^{+} EBER^{+}; plasma: ND	ABC according to IHC	Major monoclonal Ig rearrangement and minor TCR rearrangement (1-2% T-cells‡)	FISH: no rearrangement of BCL2, BCL6, MYC. aCGH: no detectable aberration tNGS (20% tumor cells‡): damaging somatic mutations of ARID5B (p.P79T, VAF 12%), EXT2 (p.S270L, VAF 10%), CREBBP (p.M721I, VAF 8.5%), GNA13 (p.P6L, VAF 5.1%)

aaIPI, age-adjusted International Prognostic Index; CHOP, cyclophosphamide, doxorubicin, vincristine, and prednisone; EBER, EBV-encoded small RNA: F, focal; FISH, fluorescence in situ hybridization; Ig, immunoglobulin; IHC, immunohistochemistry; LDH, lactate dehydrogenase; ND, not done; RT-MLPA; reverse transcriptase multiplex ligation-dependent probe amplification; TCR, T-cell receptor; VAF, variant allele frequency; w, weak.

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aggregates or sheets within the capsule but without tumor beyond it or lymph node involvement. Plasmablastic differentiation was observed in 1 case, whereas cytological features in the 2 remaining cases were mostly immunoblastic, though uneasy to classify, especially within fibrin deposits (Figure 1). The latter pattern was somewhat reminiscent of BI-ALCL.[1,2] Variable amounts of inflammatory cells were present in all cases. They all harbored a major B-cell clone and were of non–germinal center cell of origin. These features could meet the criteria for either DLBCL associated with chronic inflammation (DLBCL-CI), or fibrin-associated DLBCL (FA-DLBCL).[1] DLBCL-CI, which are characterized as EBV-associated DLBCLs occurring in the context of chronic inflammation and developing in cavities or enclosed spaces, sometimes adjacent to a foreign body, have been initially described in the pleural cavity as pyothorax-associated lymphomas.[1] They have been more recently described in bones, joints, or periarticular soft tissues in association with metallic implants.[10,11] Our series suggests that breast implants could be added to the list of foreign bodies that could favor the onset of DLBCL occurring in the context of chronic inflammation.

Although prototypic DLBCL-CI like pyothorax-associated lymphomas were initially reported to present as aggressive mass-forming tumors,[12] there is accumulating evidence that DLBCL-CI can exhibit variable presentation and clinical course.[1,13,14] Such particular variants include EBV+ DLBCLs arising within cardiac myxoma, which are regarded as DLBCL-CI with indolent behavior.[15] Our 3 patients could represent such indolent DLBCL-CI, since the lesions were non–mass forming and strictly localized to the peri-implant capsule.

The clinical presentation of the 3 patients without tumor mass and the localization of lymphoma cells within fibrin deposits are also evocative of FA-DLBCL, another subset of EBV+ DLBCL. FA-DLBCL is a rare lymphoma presenting without clinical mass and consisting of aggregates of large EBV+ B cells within fibrin layers.[13,14,16] As a matter of fact, the diagnosis was incidental in the 3 patients, who had neither clinical nor biological symptoms.

However, our 3 cases displayed various degrees of capsule infiltration, a feature more suggestive of DLBCL-CI.[1] In addition, case 2 contained a MYC-immunoglobulin H (IGH) translocation, which is in accordance with the known occurrence of MYC alterations in DLBCL-CI, whereas they have not been so far reported in FA-DLBCL.[17] In contrast, aCGH analysis in the 2 remaining cases did not detect any abnormality. Thus, it appears that our series displayed intermediate features between FA-DLBCL and DLBCL-CI, which fits with the emerging concept that FA-DLBCL could be regarded as an incidental form of DLBCL-CI.[1]

Despite the T-cell origin and EBV negativity of BI-ALCL, which are major differences with BI-DLBCL, it has to be stressed that the differential diagnosis between the 2 entities may be a pitfall. The neoplastic infiltrate of the current 3 cases indeed exhibited both "fibrin-associated" and "infiltrative" patterns, which could mimic BI-ALCL.[2,3] Of note, patient 2 from the current series was initially suspected to present BI-ALCL in view of the clinical presentation together with a preliminary phenotype showing CD20 negativity associated with CD30, EMA, and CD4 positivity. The correct diagnosis could be eventually assessed owing to the demonstration of CD79a positivity and κ light-chain restriction (Table 1). Expression of T-cell markers, like CD4 and CD43 in 2 of our cases, is a well-known phenomenon in some EBV-associated DLBCLs such as DLBCL-CI and plasmablastic lymphomas, which can cause problems in lineage assignment.[1]

Furthermore, our 3 cases harbored not only major clonal rearrangements of immunoglobulin genes but also minor rearrangements of T-cell receptor genes consisting of multiple small-sized peaks. Since the reactive T-cell infiltrate in each case was minimal (Table 1), this pattern could be due to either pseudoclonality or an oligoclonal/restricted T-cell response. Interestingly, this peculiar clonality profile has been already reported in other EBV-associated DLBCLs, likely reflecting clonal expansion of cytotoxic lymphocytes.[13,18,19]

As expected, tNGS analysis of our series could detect mutations in various genes known to be recurrently mutated in DLBCL, such as *CREBBP*, *GNA13*, *TET2*, and *IRF4*. Case 2 also carried *STAT3* and *SOCS1* mutations, which are common in BI-ALCL but also occur in DLBCL.[20-22] Thus, case 2 raises the possibility that the JAK-STAT pathway could favor B-cell lymphomagenesis in the context of BI. Environmental factors in the enclosed space formed by the peri-implant cavity might be also involved, like the IL-6 and IL-10 cytokines, which are suspected to favor DLBCL-CI.[23,24]

It is noteworthy that our patients had all macrotextured implants, which are considered as a risk factor for BI-ALCL and are currently subject to widespread limitation.[2,3,25] Thus, BI-related lymphomas are probably doomed to become extremely rare, though they will likely persist in the next few years. This implies that pathologists must stay aware of the diversity of these tumors.

An indolent clinical course was observed in our series, all patients being in complete remission after an average follow-up of 20 months, although 2 of our 3 patients received no treatment after surgery. Although this apparently indolent behavior has to be confirmed by a longer follow-up, it suggests that a "watch and wait" management of BI-DLBCL could be considered after complete tumor resection when there is no evidence of dissemination. Nonetheless, our small series makes it difficult to draw definitive conclusions, and additional cases are needed to complete the understanding of this rare, previously unrecognized subset of BI-related lymphomas.

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Authorship

Contribution: L.M., D.B., A.W., P.G., and L.X. performed pathological analyses, interpreted molecular data, and wrote the paper; C.L. and J.-M.P. were involved in pathological analysis; V.C., J.-M.S., R.B., and M.B. handled the clinical management of patients; I.B.-R. performed PET investigations; and J.A., A.G., P.R., P.-J.V., F.J., E.B., and C.R. performed molecular analyses.

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Footnotes

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REFERENCES

1. *WHO Classification of tumours of Haematopoietic and Lymphoid Tissues*. Revised 4th Edition. Lyon: International Agency for Research on Cancer; 2017.

2. Laurent C, Delas A, Gaulard P, et al. Breast implant-associated anaplastic large cell lymphoma: two distinct clinicopathological variants with different outcomes. *Ann Oncol*. 2016;27(2):306-314.

3. Laurent C, Haioun C, Brousset P, Gaulard P. New insights into breast implant-associated anaplastic large cell lymphoma. *Curr Opin Oncol*. 2018;30(5):292-300.

4. Said JW, Tasaka T, Takeuchi S, et al. Primary effusion lymphoma in women: report of two cases of Kaposi's sarcoma herpes virus-associated effusion-based lymphoma in human immunodeficiency virus-negative women. *Blood*. 1996;88(8):3124-3128.

5. Smith BK, Gray SS. Large B-cell lymphoma occurring in a breast implant capsule. *Plast Reconstr Surg*. 2014;134(4):670e-671e.

6. Messer A, Jenkinson H, Wang W, Duvic M. New B-cell lymphomas in the setting of a previous rare breast implant-associated B-cell lymphoma. *Plast Reconstr Surg Glob Open*. 2016;4(11):e1148.

7. Chen V, Hoang D, Clancy S. Breast implant-associated bilateral B-cell lymphoma. *Aesthet Surg J*. 2020;40(2):NP52-NP58.

8. Aviv A, Tadmor T, Polliack A. Primary diffuse large B-cell lymphoma of the breast: looking at pathogenesis, clinical issues and therapeutic options. *Ann Oncol*. 2013;24(9):2236-2244.

9. Yhim H-Y, Kim JS, Kang HJ, et al. Matched-pair analysis comparing the outcomes of primary breast and nodal diffuse large B-cell lymphoma in patients treated with rituximab plus chemotherapy. *Int J Cancer*. 2012;131(1):235-243.

10. Rajeev A, Ralte A, Choudhry N, Jabbar F, Banaszkiewicz P. Diffuse B cell non-Hodgkin's lymphoma presenting atypically as periprosthetic joint infection in a total hip replacement. *Case Rep Orthop*. 2017;2017:7195016. 10.1155/2017/7195016

11. Sanchez-Gonzalez B, Garcia M, Montserrat F, et al. Diffuse large B-cell lymphoma associated with chronic inflammation in metallic implant. *J Clin Oncol*. 2013;31(10):e148-e151.

12. Narimatsu H, Ota Y, Kami M, et al. Clinicopathological features of pyothorax-associated lymphoma; a retrospective survey involving 98 patients. *Ann Oncol*. 2007;18(1):122-128.

13. Loong F, Chan ACL, Ho BCS, et al. Diffuse large B-cell lymphoma associated with chronic inflammation as an incidental finding and new clinical scenarios. *Mod Pathol*. 2010;23(4):493-501.

14. Boroumand N, Ly TL, Sonstein J, Medeiros LJ. Microscopic diffuse large B-cell lymphoma (DLBCL) occurring in pseudocysts: do these tumors belong to the category of DLBCL associated with chronic inflammation? *Am J Surg Pathol*. 2012;36(7):1074-1080.

15. Yan J, Luo D, Zhang F, et al. Diffuse large B cell lymphoma associated with chronic inflammation arising within atrial myxoma: aggressive histological features but indolent clinical behaviour. *Histopathology*. 2017;71(6):951-959.

16. Kameda K, Shono T, Takagishi S, et al. Epstein-Barr virus-positive diffuse large B-cell primary central nervous system lymphoma associated with organized chronic subdural hematoma: a case report and review of the literature. *Pathol Int*. 2015;65(3):138-143.

17. Boyer DF, McKelvie PA, de Leval L, et al. Fibrin-associated EBV-positive large B-cell lymphoma: an indolent neoplasm with features distinct from diffuse large B-cell lymphoma associated with chronic inflammation. *Am J Surg Pathol*. 2017;41(3):299-312.

18. Petitjean B, Jardin F, Joly B, et al. Pyothorax-associated lymphoma: a peculiar clinicopathologic entity derived from B cells at late stage of differentiation and with occasional aberrant dual B- and T-cell phenotype. *Am J Surg Pathol*. 2002;26(6):724-732.

19. Dojcinov SD, Venkataraman G, Pittaluga S, et al. Age-related EBV-associated lymphoproliferative disorders in the Western population: a spectrum of reactive lymphoid hyperplasia and lymphoma. *Blood*. 2011;117(18):4726-4735.

20. Ohgami RS, Ma L, Monabati A, Zehnder JL, Arber DA. STAT3 mutations are present in aggressive B-cell lymphomas including a subset of diffuse large B-cell lymphomas with CD30 expression. *Haematologica*. 2014;99(7):e105-e107.

21. Zhou XA, Louissaint A Jr., Wenzel A, et al. Genomic analyses identify recurrent alterations in immune evasion genes in diffuse large B-cell lymphoma, leg type. *J Invest Dermatol*. 2018;138(11):2365-2376.

22. Laurent C, Nicolae A, Laurent C, et al. Gene alterations in epigenetic modifiers and JAK-STAT signaling are frequent in breast implant-associated ALCL. *Blood*. 2020;135(5):360-370.

23. Kanno H, Naka N, Yasunaga Y, et al. Production of the immunosuppressive cytokine interleukin-10 by Epstein-Barr-virus-expressing pyothorax-associated lymphoma: possible role in the development of overt lymphoma in immunocompetent hosts. *Am J Pathol*. 1997;150(1):349-357.

24. Tosato G, Tanner J, Jones KD, Revel M, Pike SE. Identification of interleukin-6 as an autocrine growth factor for Epstein-Barr virus-immortalized B cells. *J Virol*. 1990;64(6):3033-3041.

25. Calobrace MB, Schwartz MR, Zeidler KR, Pittman TA, Cohen R, Stevens WG. Long-term safety of textured and smooth breast implants. *Aesthet Surg J*. 2017;38(1):38-48.

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