Supplemental Material

Genomic sequencing

DNA was extracted using the Qiagen DNA FFPET kit (Qiagen, Valencia, CA). Library preparation and whole-exome sequencing (WES) was performed using Illumina NovaSeq 6000 for cases 1-5. A targeted panel containing genes frequently mutated in lymphoma was performed for case 6.

The raw sequencing reads were evaluated using FastQC (v0.11). After trimming adapter sequences using Trimmomatic (v0.36), the reads were aligned to the human reference genome hg38 using Burrows-Wheeler Aligner (v0.7). The aligned reads were duplicate marked and realigned locally using Picard (v2.9) and Genome Analysis Toolkit (v4.2). The variants were called by using two variant callers, VarScan2 (v2.4) and Genome Analysis Toolkit (v4.2). The annotation was applied to the variants using Annovar (http://annovar.openbioinformatics.org). A Bayesian logistic regression model based FFPE artifact detector, Strand Orientation Bias Detector (v1.0.4), was added to estimate the likelihood that variants were introduced by formalin.

Variants were included if the variants 1) were supported by at least four alternative alleles and had both forward and reverse reads with minimum variant allele frequency of 5%; 2) changed protein sequences in exon or splicing sites. Variants were filtered out if they 1) existed in gnomAD SNP databases with population frequency more than 1%; 2) were in a region of segmental duplication; 3) were highly recurrent in normal in-house samples and cross samples; 4) were not expressed in an in-house B-cells expression database. Variants that were called by variant callers and passed the SOB score 0.5 were identified as high confidence.

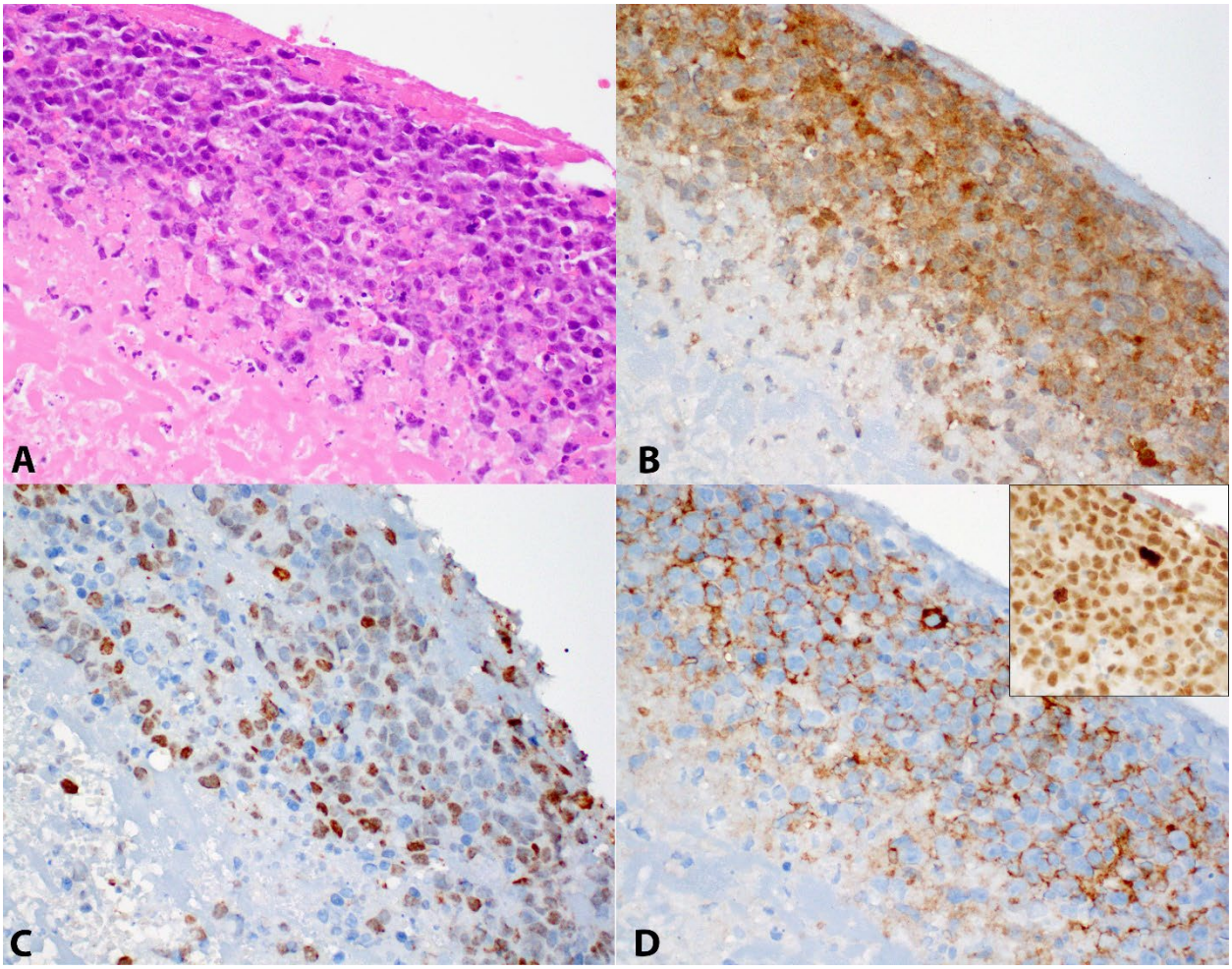
Supplemental Table 1. Immunohistochemistry stains

Antibody/Probe	**Clone**	**Company**
PTEN	SP218	Ventana
CA9	D47G3	Cell Signaling
pSTAT3	D3A7	Cell signaling
pAKT-T308	Thr308	Sigma Aldrich
LMP1	CS.1-4	Dako
EBNA2	PE2	Abcam
MYC	Y89	Epitomics
PD-L1	E1L3N	Cell Signaling Technology
EBER		ACD Bio

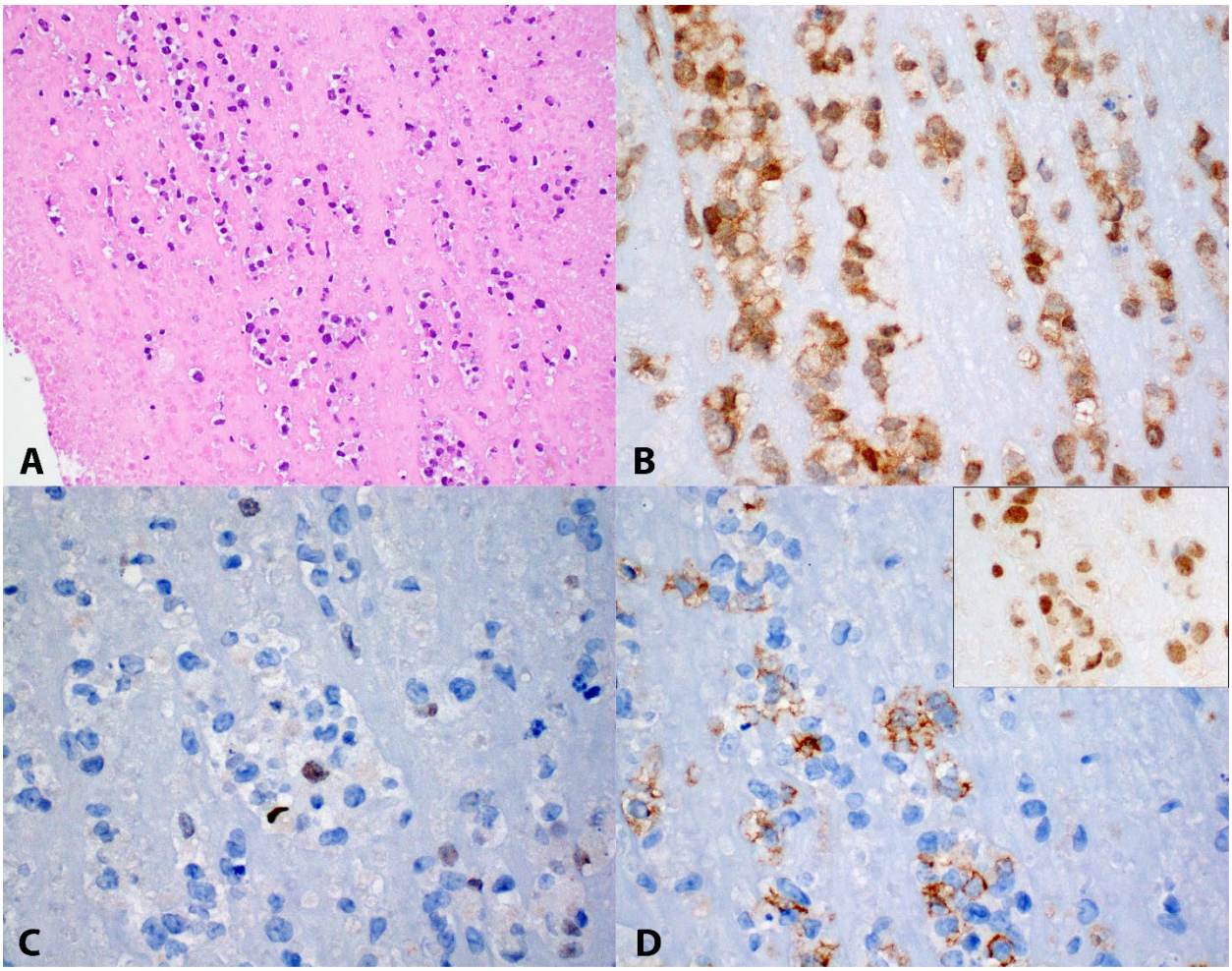
Supplemental Table 2. Additional immunostains performed on fibrin-associated large B-cell lymphoma.

	LMP1	EBNA2	EBER-ISH	MYC	PD-L1
Case 1	+	+	+	15%	+
Case 2	+	+	+	15%	+
Case 3	ND	ND	+	ND	ND
Case 4	ND	ND	+	50%	ND
Case 5	ND	ND	+	40%	ND
Case 6	-	-	-	<10%	-

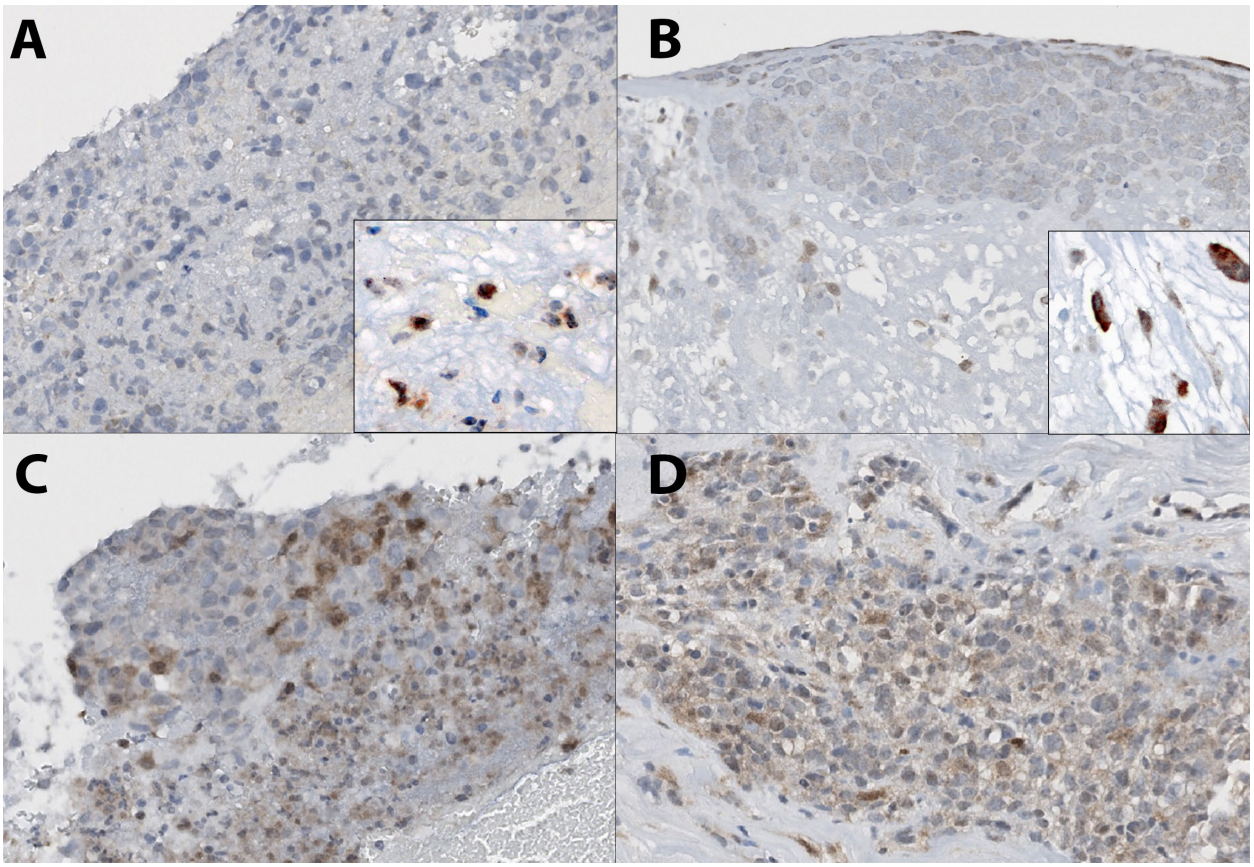
ND=not done.



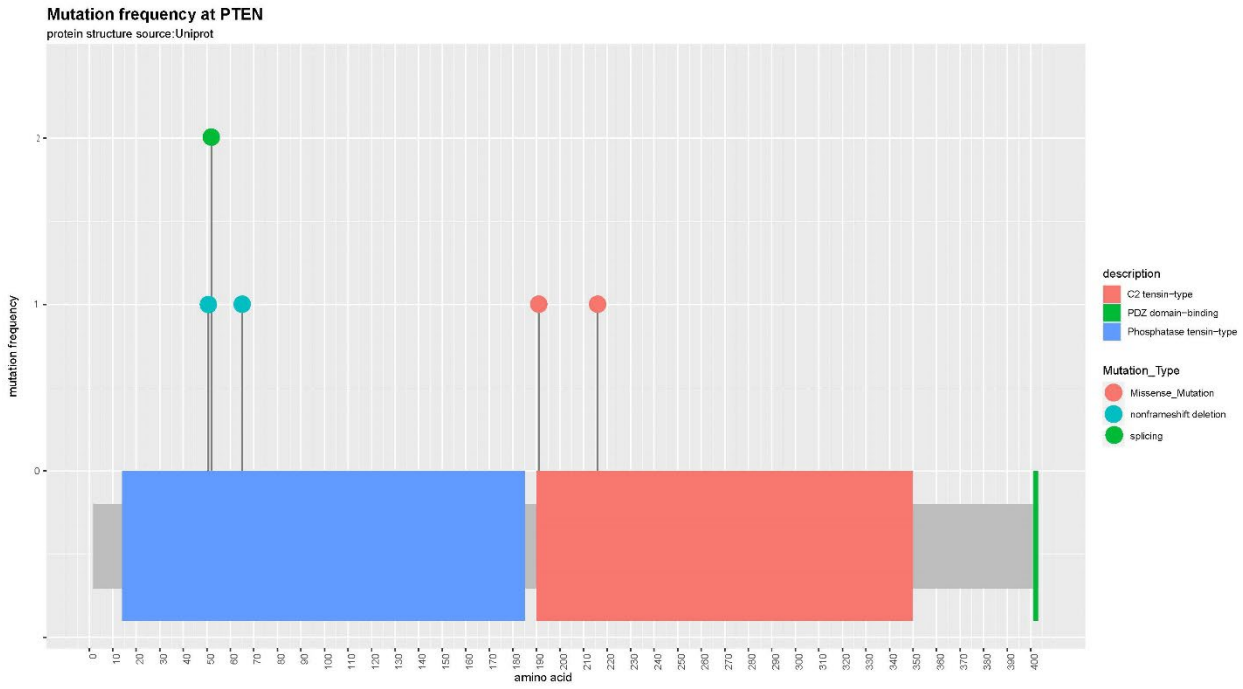
Supplemental Figure 1. Fibrin-associated large B-cell lymphoma (Case 4). A) H&E showing sheets of large atypical cells within a fibrinous background. B) The tumor cells show variable PTEN expression, C) are positive for pSTAT3, D) express CA9, and are positive for pAKT (inset).



Supplemental Figure 2. Fibrin associated large B-cell lymphoma (Case 5). A) H&E shows scattered nests of large, atypical cells in a dense fibrinous background that are positive for B) PTEN, C) negative for pSTAT3, D) express CA9, and are positive for pAKT (inset).



Supplemental Figure 3. Decreased expression of PTEN protein in cases of fibrin-associated large B-cell lymphoma. A) Case 2 with complete loss of PTEN expression. B) Case 6, C) Case 1 and D) Case 3 with variable decrease in expression of PTEN protein by immunohistochemistry. Insets in A and B show PTEN+ histiocytes from other fields of the same slide as an internal positive control.



Supplemental Figure 4. *PTEN* mutations identified in cases of fibrin-associated large B-cell lymphoma. Mutations related to non-frame shift deletions were seen in the phosphatase and C2 domain. Another case showed a stop gain mutation in the C2 domain. The other two cases showed a splice site mutation between exon 1 and exon 2.