

# Plasmablastic lymphoma with unfavorable chromosomal abnormalities related to plasma cell myeloma: A borderline case between plasmablastic lymphoma and plasmablastic plasma cell myeloma

**Keywords:** plasmablastic lymphoma, plasmablastic plasma cell myeloma, t(4;14), 1q gain, add(3q27)

## CASE REPORT

Plasmablastic lymphoma (PBL) is an aggressive subtype of DLBCL, first reported in HIV-infected patients<sup>1</sup> and subsequently recognized in the WHO 2008 classification.<sup>2</sup> PBL often arises in the oral cavity, but other sites include the nasal cavity, GI tract, skin, bone, and lungs.<sup>3-5</sup> PBL mainly affects those with immunodeficiency,<sup>3-5</sup> but can affect some immunocompetent individuals.<sup>6</sup> Histologically, PBL presents as dense proliferation of immature cells like Burkitt's lymphoma.<sup>2,5,7</sup> The immunophenotype of PBL, however, resembles myeloma cells: CD38<sup>+</sup>, CD138<sup>+</sup>, cyIg<sup>+</sup>, MUM1<sup>+</sup>, CD45<sup>-</sup>, CD20<sup>-</sup>, and smIg<sup>-</sup>.<sup>3-5</sup> EBV is mostly positive.<sup>3-5,7</sup>

A 53-year-old HIV-negative and immunocompetent woman was admitted because of chest pain and dyspnea. CT scanning revealed a large tumor in the right chest wall (Figure 1A), pleural effusion, para-aortic lymph node swelling, and a tumor in the sacral bone (Figure 1B and 1C, respectively). Laboratory findings are shown in Table 1. Serum IgG was 7,633 mg/dL, and revealed to be IgG- $\lambda$  monoclonal protein. Many atypical plasma cell-like cells with CD38<sup>+</sup>, CD56<sup>+</sup>, CD138<sup>+</sup>, cyIgG<sup>+</sup>, and cy $\lambda$ <sup>+</sup> phenotype were observed in the pleural effusion (Figure 2). The karyotype was abnormal, with a complex involving chromosomes 1 and 3 (Table 1).<sup>8-10</sup> Furthermore, FISH analysis demonstrated t(4;14).<sup>11</sup> The chest tumor histologically exhibited dense proliferation of large immature cells (Figure 3A, B), and these cells were positive for CD138 and  $\lambda$  light chain (Figure 3C and 3D, respectively). A tentative diagnosis of multiple myeloma was made.

She refused treatment with conventional anti-cancer agents. We therefore treated her with novel agents for myeloma, which were available in 2015 without any obvious response. Then, we performed radiotherapy for the chest tumor and other tumoral lesions. However, she died four months after admission. Histopathological re-examination of the chest tumor revealed it to be PBL. Immunostaining for *myc* was strongly positive as reported in PBL,<sup>4,5</sup> and FISH split signal analyses for *c-myc*, but not for *Bcl-2* or *Bcl-6*, yielded split signals and amplification of this gene (Figure 3F). Serum virus genomes for EBV and HHV-8 were not detected by PCR.

This patient appeared to have a borderline feature

between plasmablastic plasma cell myeloma (PBPCM)<sup>12</sup> because the tumor-involvement site was atypical for PBL<sup>3-5</sup> and this patient carried multiple chromosomal abnormalities related with aggressive multiple myeloma.<sup>8-11</sup> The genetic background of PBL has not yet fully understood<sup>5</sup>; therefore, accumulation of PBL cases and further molecular studies are required regarding clinical features and molecular profiles of PBPCM.

## CONFLICT OF INTEREST

The authors disclose that we have no conflicts of interest with any individuals or companies.

## ACKNOWLEDGMENT

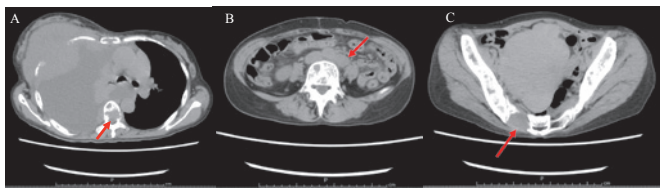
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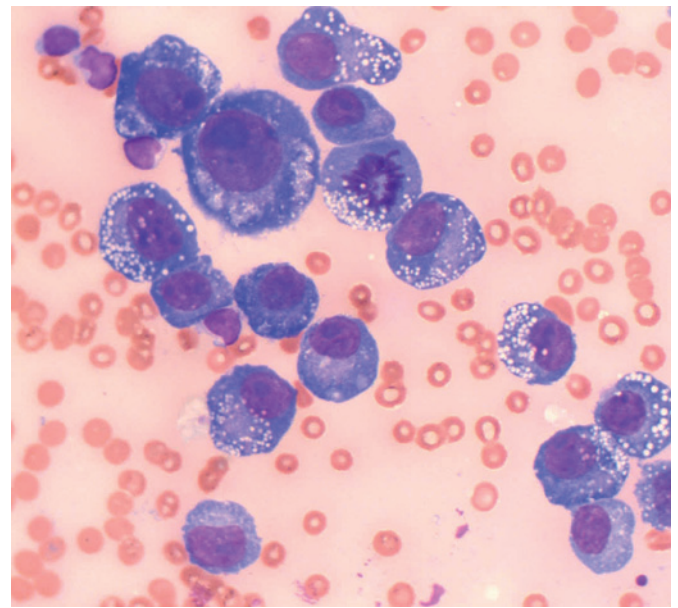
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**Fig. 1.** Whole body CT scanning on admission. **A:** A bulky mass involving the right chest wall. Rib bones were destroyed and abundant pleural effusion was observed. A lytic bone lesion was seen in the sixth thoracic vertebra (arrow). **B:** CT imaging at the level of L4. Para-aortic lymph nodes were swollen (arrow). **C:** Imaging at the sacral bone level. A lytic bone lesion was seen.

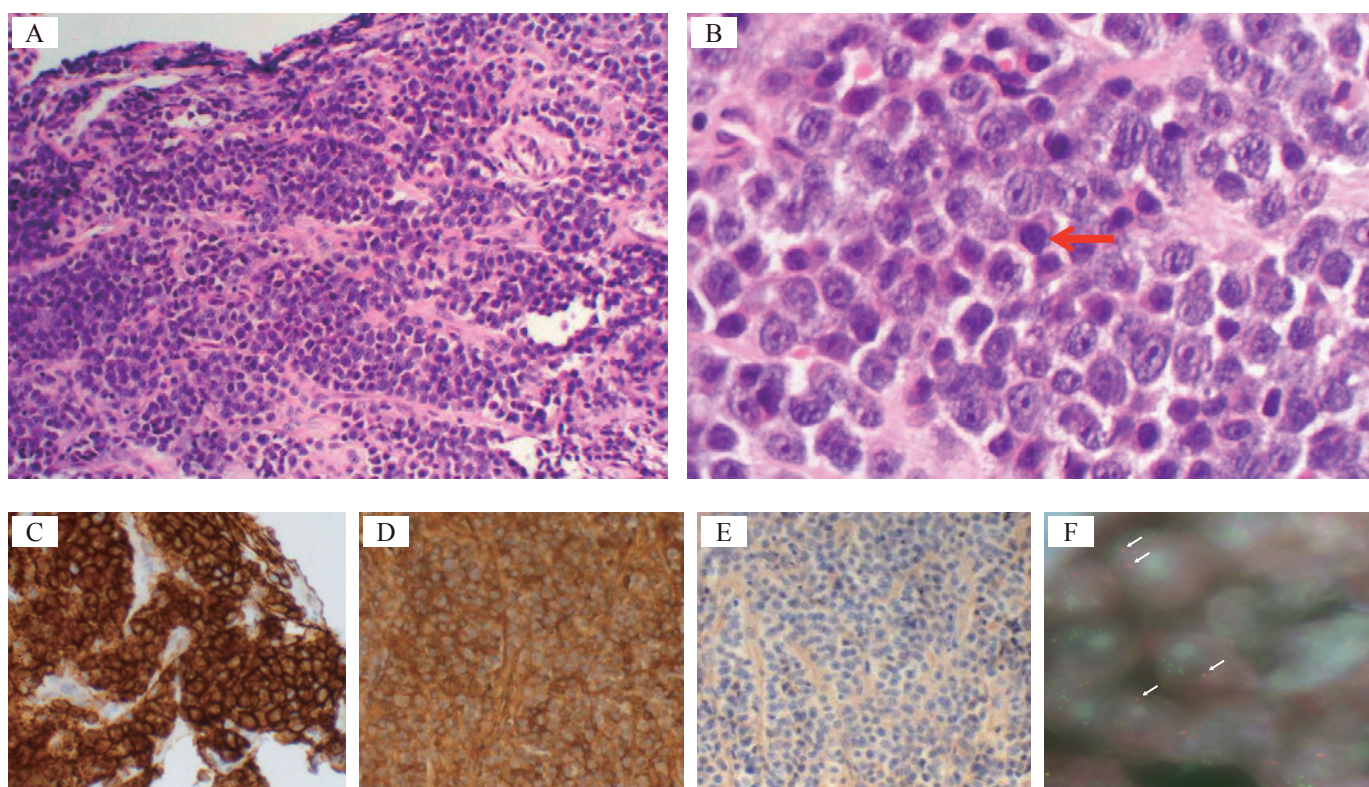


**Fig. 2.** A smear preparation of abnormal plasma cells in the pleural effusion. Many atypical and large plasma cell-like cells with cytoplasmic vacuoles were observed.

**Table 1.** Laboratory findings on admission (July 2015) and chromosomal analysis

| Hematology |                         | Chemistry   |           | chromosomal analysis                  |
|------------|-------------------------|-------------|-----------|---------------------------------------|
| WBC        | 1.04×10 <sup>9</sup> /L | TP          | 13.2g/dL  | (pleural effusion)                    |
| Neu        | 57.1%                   | Alb         | 2.7g/dL   | 46, XX,add3(p11), +add3(q27),         |
| Eos        | 0.0%                    | AST         | 29IU/L    | -8, -13, del(13;14)(q10;q10),         |
| Bas        | 0.0%                    | ALT         | 14IU/L    | der19t(1;19)(q21;q13.3),              |
| Mon        | 7.3%                    | T-Bil       | 0.8mg/dL  | add20(q13.3), ?add22(p11.2), +2mar[1] |
| Lym        | 32.3%                   | LDH         | 633IU/L   | /47, idem, +11[3]                     |
| atyp. Lym  | 2.3%                    | UA          | 14.5mg/dL | /47, idem, add1(q21), +11[4]          |
| Plasma     | 1.0%                    | BUN         | 26.1mg/dL | /45-47, XX, +add3(q27),               |
| RBC        | 338×10 <sup>6</sup> /L  | Cr          | 0.93mg/dL | -8, -13, der(13;14)(q10;q10),         |
| Hb         | 10.5g/dL                | Na          | 131mEq/L  | der19t(1;19)(q21;q13.3),              |
| Ht         | 31.3%                   | K           | 4.6mEq/L  | add20(q13.3), ?add22(p11.2),          |
| MCV        | 92.6fl                  | Cl          | 102mEq/L  | +1-3mar[cp3]                          |
| Plt        | 269×10 <sup>3</sup> /L  | Ca          | 11.7mg/dL | (observed in 11/11 cells analyzed)    |
|            |                         | P           | 4.7mg/dL  | t(4;14) not be confirmed              |
| Serology   |                         | CRP         | 1.41mg/dL | FISH (pleural effusion):              |
| IgM        | 24.0mg/dL               |             |           | t(4;14) (952/1000 cells analyzed)     |
| IgG        | 7,633mg/dL              | Coagulation |           |                                       |
| IgA        | 36.0mg/dL               | PT          | 13.8S     |                                       |
| β2MG       | 11.3mg/dL               | PT-INR      | 1.16      | SerumEBV&HHV-8 by PCR: negative       |
|            |                         | APTT        | 27.2S     |                                       |

Abbreviations: atyp.lym: atypical lymphocytes, β2MG: beta 2 microglobulin (normal range: below 200 μg/L)  
 FISH: fluorescence in situ hybridization.EBV: Epstein-Barr virus, HHV-8: human herpesvirus 8.



**Fig. 3.** Histopathological examination of a biopsy sample from the right chest wall tumor. **A:** Many immature cells were monotonously proliferating (H. E. staining,  $\times 100$ ). **B:** Some of these abnormal cells exhibited differentiation toward plasma cells (arrow) (H. E. staining,  $\times 400$ ). These cells were positive for CD138 (**C**) and  $\lambda$  (**D**) but not  $\kappa$  (**E**) light chains ( $\times 100$ ). (**F**) FISH split analysis for *c-myc* on the chest wall tumor. Split *c-myc* signals (red) (arrows) and 4 to 6 signals for the genomic locus of *c-myc* (green) in each cell were seen, indicating amplification of this gene.

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**Yumi Aoyama,<sup>1)</sup> Hiroko Tsunemine,<sup>1)</sup> Taiichi Kodaka,<sup>1)</sup>  
Nao Oda,<sup>2)</sup> Hirofumi Matsuoka,<sup>2)</sup> Tomoo Itoh,<sup>3)</sup>  
Takayuki Takahashi<sup>1)</sup>**

<sup>1)</sup>Departments of Hematology, Shinko Hospital, <sup>2)</sup>Respiratory Medicine, Shinko Hospital, <sup>3)</sup>Department of Diagnostic Pathology, Kobe University Graduate School of Medicine, Kobe, Japan.

**Corresponding author:** Takayuki Takahashi,  
Department of Hematology, Shinko Hospital, 4-47,  
Wakihama-cho, 1-chome, Chuo-ku, Kobe 651-0072,  
Japan.

E-mail: [takahashi.takayuki@shinkohp.or.jp](mailto:takahashi.takayuki@shinkohp.or.jp)

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Takata K

## EXPERT'S COMMENTS

Although plasmablastic lymphoma (PBL) is a non-Hodgkin lymphoma with a B-cell phenotype that was originally reported to occur at the intra-oral site in patients with human immunodeficiency virus (HIV) infection, extra-oral PBL is common, and 50% of cases are associated with Epstein-Barr virus (EBV).<sup>1</sup> PBL is now known as an aggressive B-cell lymphoma without expression of CD20. As for the differential diagnosis of HIV (-) EBV (-) PBL, plasma cell myeloma with blastic morphology (PCM-B) and HHV8 (-) primary effusion lymphoma should be considered. Both PBL and PCM-B morphologically consist of large-sized plasmablastic cells, and immunophenotypically express both CD138 and MUM-1, and lack both PAX-5 and CD20, causing the diagnostic dilemma. The points for their distinction are as follows:

- (1) Anatomically involved sites and clinical presentation: The head and neck area is the most frequently involved site in PBL. Lymphadenopathy is sometimes accompanied. On the other hand, PCM-B presents with bone marrow disease and lymphadenopathy is less frequent.<sup>2</sup> Bone marrow involvement was not detected in this case.
- (2) Genetic alteration: *MYC* alterations are frequently found (approximately 50%) in PBL, whereas they are found in only 15% of PCM-B cases. Moreover, half of all PBL cases exhibit *PRDM1* somatic mutations.<sup>3</sup> Translocation of *FGFR3* and *IGH* for t(4;14)(p16;q32) was reported to show poor prognosis in PCM.<sup>4</sup> This case had both genetic alterations of *MYC* and *FGFR3*.
- (3) Immunophenotype: Most immunocompetent cases of EBV (-) PBL exhibit BCL2 (+) and p53 (+), although the frequency of expression in PCM-B is not known.<sup>5</sup> When tumor cells expressed IgM, the diagnosis of PBL was likely. A recent report demonstrated the marked difference in CD117(c-kit) expression between PBL and PBM (PBL: 0/10 vs PBM: 6/9). It may be useful to try c-kit immunostaining.<sup>6</sup>

There are overlapping features in PBL and PCM-B, and grey zone cases are sometimes encountered. Integration of clinical, pathological, and molecular information is indispensable for the diagnosis. PBL was favored as the diagnosis of this interesting case.

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**Katsuyoshi Takata**

Department of Pathology,

Okayama University

E-mail: katsuyoshi.t@h5.dion.ne.jp