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LETTER TO THE EDITOR

# Diffuse large B cell lymphoma with chromosomal translocation t(14;19)(q32;q13) occurring in IgG4-related disease

Yuka Kawaji[1,2] · Hiroaki Nagata[2] · Ayako Muramatsu[2] · Kodai Kuriyama[2] · Muneo Ohshiro[2] · Yoshiko Hirakawa[2] · Toshiki Iwai[2] · Tsutomu Kobayashi[1] · Hitoji Uchiyama[2] · Yoji Urata[3] · Junya Kuroda[1]

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Dear Editor,

We report a rare case of diffuse large B cell lymphoma (DLBCL) that likely developed from nodal involvement of IgG4-related disease (IgG4-RD). A 70-year-old Japanese female presented to a primary hospital complaining of asthmatic symptoms. Serological tests identified abnormalities of elevated polyclonal IgG of 7035 mg/dL, IgG4 of 2550 mg/dL, and soluble interleukin-2 receptor (sIL-2R) of 2140 U/mL. A $^{18}$F-FDG-PET/CT scan identified lymphadenopathies with mild FDG uptake in the neck, mediastinum, and abdomen. A biopsy specimen of the right supraclavicular fossa lymph node disclosed massive follicular hyperplasia with prominent plasma cell infiltration around follicles and marginal sinuses (Fig. 1a–c). In addition, a small number of plasma cells that were strongly positive for IgG4 had infiltrated into follicles (Fig. 1d). Neither immunohistochemical staining (Fig. 1e, f) nor flow cytometric analysis (Supplemental Fig. 1a) showed light chain restriction in lymphoid cells of the biopsied specimen. Chromosomal analysis by Giemsa-banding showed a normal karyotype. These findings led to a diagnosis of IgG4-related lymphadenopathy.

After four years of watch and waiting, the patient showed general malaise with non-infectious pyrexia, mild dyspnea, body weight loss of 10 kg, and systemic lymphadenopathies of the neck, supraclavicular fossa, axillary fossa, and inguinal region. Serological data revealed increases of IgG to 2263 mg/dL, IgG4 to 1010 mg/dL, and sIL-2R to 7730 U/mL. $^{18}$F-FDG-PET/CT showed FDG-avid systemic lymphadenopathy and bilateral pleural effusion. Histopathological assessment of the biopsied right axial lymph node identified diffuse infiltration of abnormal large lymphoid cells (Fig. 1g, h) that were positive for CD20 (Fig. 1i) and MUM-1, but negative for CD3, CD5, CD10, BCL-6, and BCL-2, leading to diagnosis of DLBCL. Importantly, most lymphoma cells were IgG4-positive (Fig. 1j). Flow cytometric analysis (Supplemental Fig. 1b) identified kappa light chain restriction and Southern blot analysis (Supplemental Fig. 1c) confirmed Ig heavy chain (IgH) rearrangement. A Giemsa-banding study showed a complex abnormality: 47, XX, −1, add(1)(p11), −2, add(2)(p11.2), add(4)(q31), +add(5)(q31), del(5)(q?), add(6)(p21), del(6)(q?), add(7)(p11.2), t(14;19)(q32;q13.1), add(18)(q21), −21, −22, −22, +mar1, +mar2, +mar3, +mar4, +mar5 [5/9], and 46, XX [4/9]. Six courses of R-CHOP chemotherapy induced only partial response. Complete response was achieved with salvage R-DeVIC chemotherapy (rituximab, carboplatin, etoposide, ifosfamide, dexamethasone) and currently has been maintained for one year.

Recent studies have shown an increased risk of malignancy, including malignant lymphoma, in IgG4-RD [1–8]; however, the process of malignant transformation is still poorly understood. The lymphoma cells in our case harbored the reciprocal chromosomal translocation t(14;19)(q32;q13.1) for rearrangements of IgH and *BCL3* genes, of which the protein is a member of the IκB family and regulates the nuclear factor (NF)-κB family. DLBCL with *BCL3* rearrangement frequently has complex cytogenetic abnormalities [9]. In addition, *BCL3* rearrangement is more common in non-GC-

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✉ Junya Kuroda
junkuro@koto.kpu-m.ac.jp

[1] Department of Medicine, Division of Hematology and Oncology, Kyoto Prefectural University of Medicine, 465 Kajii-cho, Kamigyo-ku, Kyoto 602-8566, Japan

[2] Department of Hematology, Japanese Red Cross Kyoto Daiichi Hospital, 15-749 Honmachi, Higashiyama-ku, Kyoto 605-0981, Japan

[3] Department of Pathology, Japanese Red Cross Kyoto Daiichi Hospital, 15-749 Honmachi, Higashiyama-ku, Kyoto 605-0981, Japan

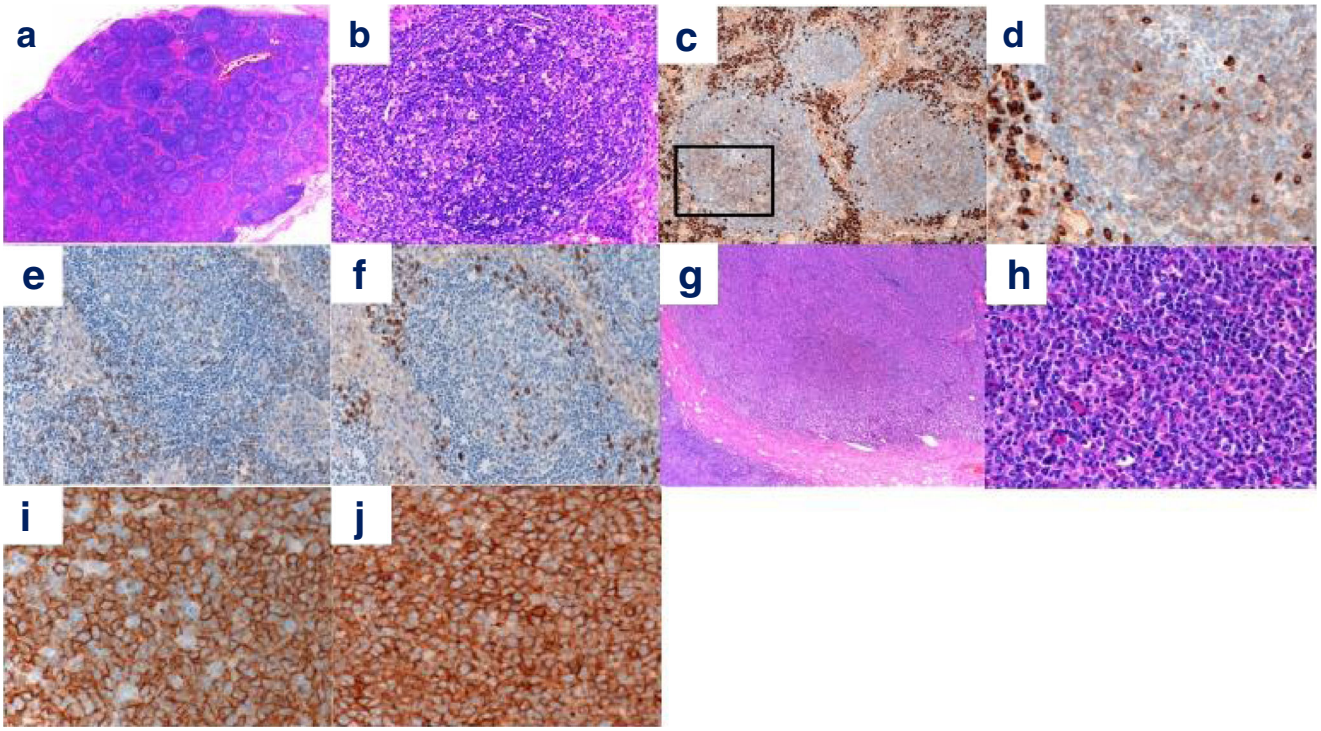


**Fig. 1** Histopathological and immunohistochemical (IHC) findings. Results are shown for biopsied specimens of the right supraclavicular fossa lymph node (**a**–**f**) and right axillary lymph node (**g**–**j**). (**a**) Low- and (**b**) high-power microscope views with hematoxylin and eosin (HE) staining of the right supraclavicular fossa lymph node. The structure of the lymph node was maintained, but there was slight fibrosis in sinusoids and follicles. (**c**) IgG4 immunostaining showed that plasma cells infiltrated around follicles and marginal sinuses were strongly positive for IgG4. (**d**) An enlarged view of the square in (**c**). A small number of IgG4-positive plasma cells were also found in follicles. No light chain restriction was observed in IHC for Ig-kappa chain (**e**) and Ig-lambda chain (**f**). (**g**) Low- and (**h**) high-power microscope views with HE staining of the right axillary lymph node. Diffuse infiltration of large abnormal lymphocytes was observed in the lymph node (**h**). The lymphoma cells were positive for CD20 (**i**) and IgG4 (**j**)

type DLBCL [10] and may be associated with a poor prognosis [9]. This uncommon translocation may have been related to emergence of lymphoma in our case. A future study with accumulation of similar events is needed to unveil the process of lymphoma development from IgG4-RD.

## Compliance with ethical standards

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

**Ethical approval** All procedures involving the patient were performed in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards. This article does not contain any work in animals.

**Informed consent** Informed consent was obtained from the patient for the procedures used in the study and for publication of the case report.

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