Annals of Hematology (2019) 98:2617–2619
https://doi.org/10.1007/s00277-019-03807-7

LETTER TO THE EDITOR

Primary intraocular natural killer-cell lymphoma successfully treated using a multidisciplinary strategy

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Received: 10 September 2019 / Accepted: 26 September 2019 / Published online: 21 October 2019

Dear Editor,

We here report an extremely rare case of primary intraocular natural killer (NK)-cell lymphoma that was successfully treated with a multidisciplinary strategy. A 70-year-old female was referred to our hospital with a complaint of blurred vision. Her medical history included hypertension, brain infarction, and surgically resected thyroid cancer. Severe vitreous opacity was observed in the right eye (Fig. 1a) and right visual acuity was reduced to 20/200. There was no tumor in the orbit (Fig. 1b). Aspiration of right vitreous fluid revealed infiltration of large abnormal lymphoid cells with oval or convoluted nuclei (Fig. 1c), which were positive for CD2, CD7, CD56, and HLA-DR, and negative for CD3, CD4, CD8, CD5, CD16, CD20, and CD57, with concomitant infiltration of normal T cells and a small fraction of CD20-positive B cells (Fig. 1d). Light chain restriction or polymerase chain reaction analysis for detection of rearrangement of the immunoglobulin heavy chain gene was negative in aspirated floating cells. The interleukin (IL)-10/IL-6 ratio in intraocular was 0.013. A blood test showed slight elevation of soluble IL-2 receptor to 797 U/mL (normal range 122–496 U/mL). Bone marrow aspiration and cerebrospinal fluid revealed no infiltration of abnormal cells. Magnetic resonance imaging and positron emission tomography with 2-deoxy-2-[F18]fluoro-D-glucose integrated with computed tomography showed no involvement of lymphoma. Accordingly, the patient was diagnosed with primary intraocular NK-cell lymphoma of the right eye. She received weekly intraocular administration of methotrexate (MTX) four times and was then treated with focal irradiation of 50 Gy. Her visual acuity was largely improved after radiotherapy. Subsequently, she received two courses of modified SMILE chemotherapy, consisting of MTX (1 g/m^2), ifosfamide (1200 mg/m^2 for 3 days), dexamethasone (40 mg for 3 days), etoposide (80 mg/m^2 for 3 days), and L-asparaginase (4800 U/m^2 for 7 days). She attained complete response (CR) and has maintained a relapse-free status for 40 months since achievement of CR.

Primary intraocular lymphoma (PIOL) originating from NK cells is extremely rare, with only three previous cases reported [1–3]. Diagnosis of PIOL requires caution and is frequently based only on cytologic and immunophenotypic assessments because it is difficult to obtain a sufficient number of tumor cells. In our case, cells of the second most frequent fraction in aspirated floating cells were considered to be identical to cytologically abnormal neoplastic NK cells. Additionally, the treatment strategy in our case needed to satisfy at least three requirements: efficacy for intraocular lesions and in the central nervous system because PIOL is classified as a disease subtype of primary central system lymphoma [4]; agents that are not influenced by multidrug resistant (MDR) because NK-cell tumors frequently overexpress MDR genes [5]; and treatment that can improve visual function as quickly as possible. We used a sequential multidisciplinary therapeutic strategy with intraocular administration of MTX, localized irradiation, and systemic SMILE chemotherapy [6–9]. This approach eventually resulted in a favorable outcome.

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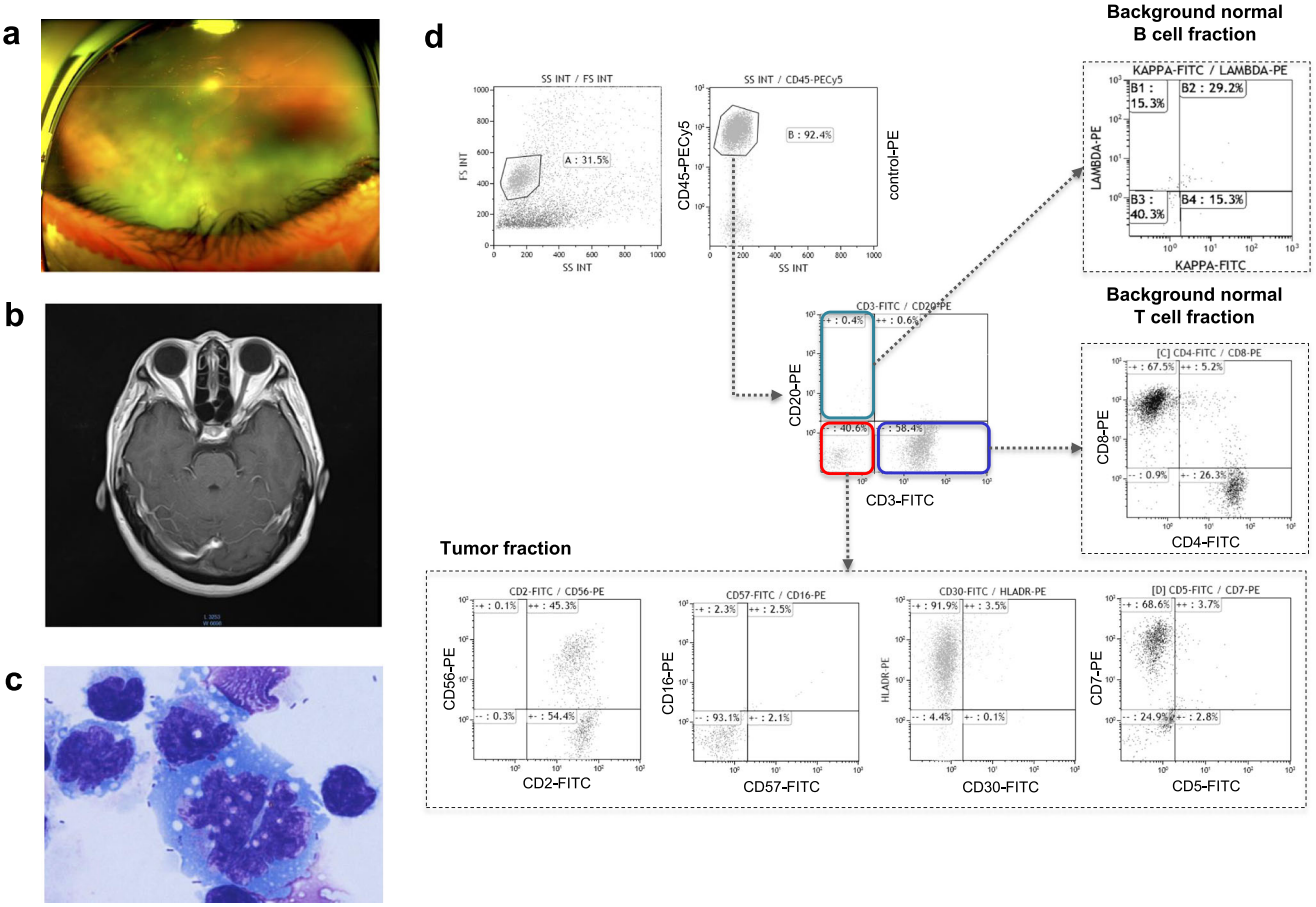

Fig. 1 **a** Gross appearance of the right eye on panoramic ophthalmoscopy. Severe vitreous opacity was found at the time of diagnosis. **b** Gadolinium-enhanced T1-weighted magnetic resonance imaging around the eyes and brain. **c** Cytologic appearance of abnormal lymphoid cells in vitreous fluid. Cells were subjected to cytospin and Wright-Giemsa staining. Large abnormal lymphoid cells were observed with oval or convoluted nuclei with prominent nucleoli. **d** Flow cytometric analysis of cells aspirated from vitreous fluid. CD3-negative and CD20-negative cells (red square) were positive for CD2, CD7, CD45, CD56, and HLA-DR, indicating the presence of NK lymphoma cells. CD3-positive and CD20-negative cells (blue square) were positive for CD4 or CD8, indicating the presence of non-clonal T cells. CD3-negative and CD20-positive cells (green square) were negative for light chain restriction, indicating the presence of non-clonal B cells

Compliance with ethical standards

Conflicts of interest The authors declare that they have no conflict of interest.

Ethical approval All procedures performed in this report were in accordance with ethical standards of our institute and with the 1964 Helsinki declaration and its later amendments.

Informed consent Informed consent was obtained from the patient described.

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