Clinical Case Report

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Central nervous system leukemia in a patient with concurrent nasopharyngeal carcinoma and acute myeloid leukaemia

A case report

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Abstract

Rationale: Concurrent case of nasopharyngeal carcinoma (NPC) and acute myeloid leukemia (AML) has not been reported. Here, we report a case of NPC, who was concurrently suffered from AML one mother after the NPC diagnosis.

Patient concerns: The patient was a 45-year-old male who presented with a mass on his right side neck.

Diagnoses: The patient was diagnosed with Epstein–Barr virus negative type-2 non-keratinizing carcinoma with clivus involvement and unilateral metastasis to the cervical lymph node.

Interventions: He was treated with one cycle of cisplatin and 69.76 Gy of concurrent external-beam radiation.

Outcomes: Three months after completion of chemo-radiotherapy, the patient was diagnosed as acute myeloid leukemia, which achieved complete remission after one course induction chemotherapy. Two months later, however, the patient was diagnosed as central nervous system leukemia. He ultimately died of relapsed leukemia. The overall survival of the patient was 10 months.

Lessons: The co-occurrence of NPC and AML is rare and prognosis is poor. Radiotherapy in NPC can disrupt the blood-brain barrier, which may contribute to the pathogenesis of central nervous system leukemia. Early alert and prevention of central nervous system leukemia following radiotherapy in NPC patient is recommended.

Abbreviations: AML = acute myeloid leukaemia, CGH = comparative genomic hybridisation, CR = complete remission, EBER = EBV-encoded RNAs, EBV = Epstein–Barr virus, MRI = magnetic resonance imaging, NPC = nasopharyngeal carcinoma, WBC = white blood cells, WHO = World Health Organization.

Keywords: acute myeloid leukaemia, blood–brain barrier, central nervous system leukemia, nasopharyngeal carcinoma

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Authors' contributions: J-QL, W-YM, S-BW, Y-JL, and W-LX were involved in patient care. J-QL, W-LX, S-XY, and JJ were involved in manuscript preparation and revisions. All authors have read and approved the final manuscript.

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1. Introduction

Nasopharyngeal carcinoma (NPC) is a squamous cell carcinoma that occurs in the epithelium of nasopharyngeal mucosa with clinical manifestation of nasal obstruction, cervical lymph node enlargement, epistaxis, and headache. NPC has a distinctive geographical distribution and is most commonly reported in Southeast Asia, North Africa, the Middle East, Alaska, and South China.[1,2] Epstein–Barr virus (EBV) plays an important role in NPC pathogenesis, and approximately 90% of NPC patients are EBV-encoded RNAs (EBERs) positive. EBV is also an important pathogenic factor in lymphocytic neoplasms such as non-Hodgkin lymphoma, Hodgkin lymphoma, and acute lymphoblastic leukemia, and number cases of the concurrent NPC and lymphocytic neoplasms have been reported.[3,4] However, concurrent case of NPC and acute myeloid leukemia (AML) has not been reported. Here, we report a case of NPC, who was concurrently suffered from AML one mother after the NPC diagnosis.

2. Case presentation

A 45-year-old, previously healthy man, presented with a mass on the right side of his neck without fever, throat pain, bleeding, or other discomfort. Physical examination identified a 2×2 cm enlarged lymph node on the right side of his neck. Magnetic resonance imaging (MRI) of the head and neck area showed a

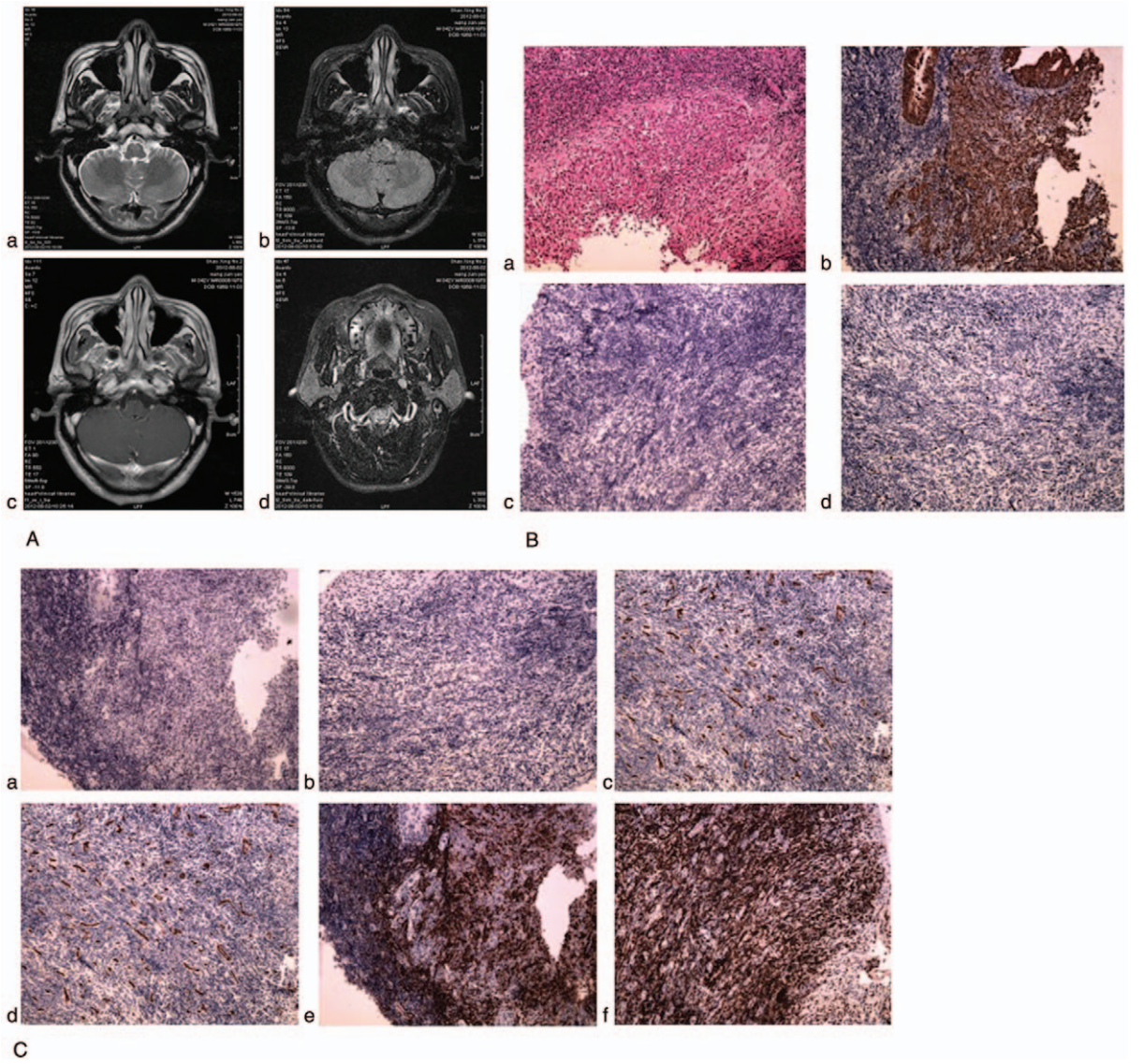

Figure 1. Characterization of the nasopharyngeal mass. (A). A nasopharyngeal mass was identified by MRI scanning. Axial T1-weighted (a), axial T2-weighted (b), and axial contrast-enhanced, T1-weighted (c) MR images show the left nasopharyngeal mass with clivus involvement (arrows). An axial T2-weighted MR image (d) shows the unilateral retropharyngeal lymph node (arrow). (B). Histology of the nasopharyngeal mass and immunohistochemical staining for the specific biomarker of nasopharyngeal carcinoma. (a). Hematoxylin-eosin staining, which showed the redundant lymphocytes infiltrating the non-keratinizing carcinoma cells. (b) Positive staining of CK by immunohistochemistry. (c). Negative staining of EBER by immunohistochemistry, and (d). Negative staining of Ki-67 by immunohistochemistry. Magnification: 200×. (C). Immunohistochemical staining for the specific biomarkers of nasopharyngeal granulocyte sarcoma with negative staining of the biomarkers: (a) MPO, (b) Tdt, (c) CD3, (d) CD34, (e) CD20, and (f) CD43. ^^Magnification: 200×. EBER = EBV-encoded RNAs, MPO = myeloperoxidase, MRI = magnetic resonance imaging.

large, soft-tissue mass in the left nasopharynx of the patient (Fig. 1A). A biopsy of the mass in the left nasopharyngeal recess was taken under nasopharyngoscopy. Immunohistochemical examination of the biopsy showed a nonkeratinizing carcinoma (Fig. 1B and C), and the patient was diagnosed as EBV negative type-2 non-keratinizing carcinoma, according to the World Health Organization (WHO) criteria, with clivus involvement and unilateral metastasis in the cervical lymph node (stage III; T3, N1, M0). The patient's blood test was normal (5×10^9/L white blood cells with normal differential count, 140 g/L hemoglobin, and 177×10^9/L Platelet), and he was treated with 1 cycle of cisplatin with concurrent external-beam radiation to 69.76 Gy, and the patient had grade 3 neutropenia following the therapy.

Three months after the completion of chemoradiotherapy, the patient was readmitted to the hospital with cough and a petechial rash on his legs. Laboratory examination showed that white blood cells (WBCs) count was 28.5×10^9 cells/L, platelets were 23×10^9 cells/L, and hemoglobin (Hb) levels were 79 g/L. The differential count of WBC showed 10% monoblasts and 50% promonocytes, whereas a bone marrow examination revealed 57% monoblasts and promonocytes combined (Fig. 2A and B). Flow cytometry analysis indicated that 65.53% of leukocytes was positive for CD117, HLA-DR, CD34, CD33, CD13, CD56, and CD65s, whereas CD7 was rarely positive (Fig. 2C). Chromosome analysis of the bone marrow revealed a normal karyotype. However, gene mutation spectrum analysis showed a c-kit mutation and a core-binding factor beta-myosin heavy chain 11

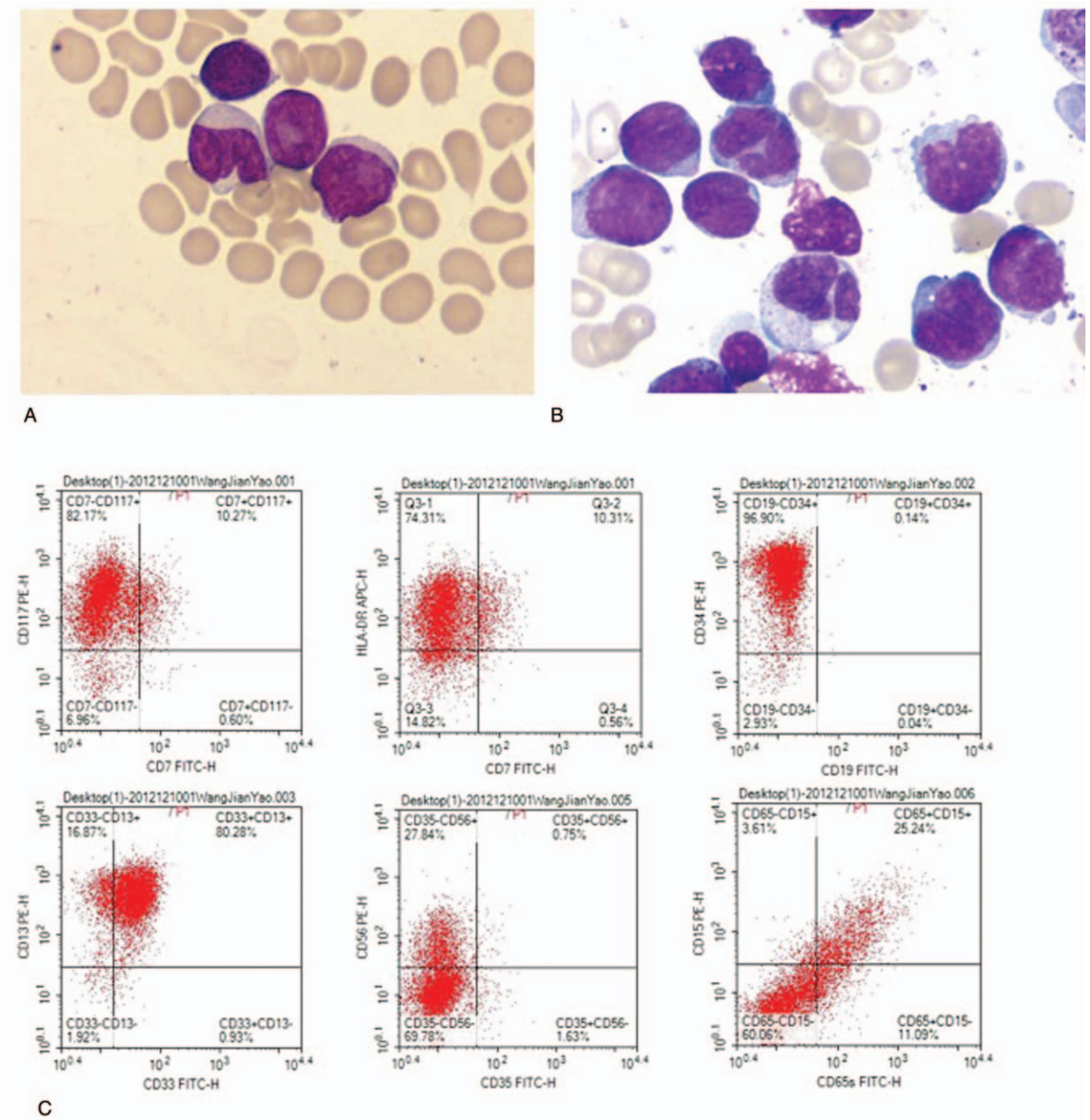

Figure 2. Analysis of peripheral blood and bone marrow cells. Microphotograph images (magnification:1000×; Wright–Giemsa stain) showed an increase of monoblasts and promonocytes in the patient's peripheral blood (A) and bone marrow (B). (C) Analysis of bone marrow cells by flow cytometry with the following cell surface markers: CD7/CD177, CD7/HLA-DR, CD19/CD34, CD33/CD13, CD35/CD56, CD65s/CD15. Leukemia cells positively expressed CD117, HLA-DR, CD34, CD33, CD13, CD56, and CD65s.

(CBFβ-MYH11) fusion gene; thus, the patient was diagnosed as CBFβ-MYH11. The patient was treated with idarubicin and cytarabine (ara-C) (idarubicin 8 mg/m^2 body area/d for 3 days plus ara-C 100 mg/m^2 body area/d for 7 days) as induction chemotherapy. The patient achieved complete remission (CR) after one course of therapy as evidenced by bone marrow examination. Unfortunately, 2 months later, the patient complained headache and was diagnosed as central nervous system leukemia even though he was still in bone marrow CR following completion of second course of chemotherapy. His intracranial pressure was 190 mm H_2O. Cerebrospinal fluid examination showed 18 cells/dL WBCs and 0.21 g/L total protein, and leukemia cells was found in his cerebrospinal fluid by flow cytometry analysis. Although he achieved CR again after intrathecal chemotherapy with ara-C 50 mg 2 times per week and medium-dose (MD)-ara-C (2 g/m^2 q12h d1–3) chemotherapy, ultimately, he died of relapsed leukemia. The overall survival of the patient was 10 months.

3. Discussion

The coexistence of NPC and AML in a patient is rare, regardless it simultaneously or sequentially occurs. In some cases, myeloid sarcoma has been shown to mimic NPC;[5] thus, when the patient of this case report was initially diagnosed as AML, we conducted immunohistochemical examination using acute leukemia cell-specific antibodies to confirm the NPC diagnosis and to exclude myeloid sarcoma by demonstrating that the mass in the

nasopharynx was negative for the leukemia cell markers including CD34, HLA-DR, myeloperoxidase, CD3, CD19, Tdt, CD20, and CD43.

While pathogenesis of EBV-negative NPC is not well understood, genomic abnormalities may contribute to the development of EBV-negative NPC. In this content, gains of chromosomes 1q, 3q, 8q, and 12, and losses of 3p, 9p, 11q, and 14q, in NPC have been identified by the comparative genomic hybridization (CGH) studies.[6–9] In addition, CGH analysis in NPC also detected frequent amplifications of several oncogene loci, including MYCL1 at 1p34.3 (66.7%), TERC at 3q26.3 (46.7%), ESR at 6q25.1 (46.7%), and PIK3CA at 3q26.3 (40%).[10] Cytogenetic analysis in NPC further showed many structural and numerical alterations in chromosomes 1p, 3p, 3q, 5q, 9p, 12, 11q, 13q, 14q, 16q, and X.[11–16] Among these alterations, deletion of 3p and gain of 3q were the most frequent events.[17,18] Moreover, c-kit overexpression and intron mutation were found in NPC cell lines.[19] These genetic mutations and alterations may also contribute to the pathogenesis of acute leukemia. However, none of aforementioned genetic changes was identified in the patient of current case report, who had concurrent NPC and AML.

Prognosis of NPC is fairly good with 75 to 80% of 5-year overall survival rate[20–23] and the survival rate of EBV-negative NPC patients may be superior to that of EBV-positive NPC patients.[23,24] The survival rate of NPC patients who concurrently suffered from a second neoplasm is poor, usually it is less than 1 year in most patients.[25,26] AML patients with a CBFβ-MYH11 fusion have been shown to have a favorable prognosis. Overall survival of the patient in this case report however was only 10 months although the patient achieved CR after the first course of chemotherapy.

Radiotherapy is often the first choice for NPC treatment, and concurrent cisplatin-based chemoradiotherapy is used in up to 70% of stage III to IV patients.[27,28] However, it has been reported that radiotherapy may destroy the blood-brain barrier in NPC patients.[29–31] Qin et al[32] reported in a retrospective study that irradiation with a 2-Gy-fraction dose resulted in maximal opening of the blood-brain barrier for over half a year. Moreover, Chan et al[31] observed blood–brain-barrier disruption by MRI in 89% of radiotherapy-treated, NPC patients, even 2 to 10 years after radiotherapy. Consistent with these reports, disruption of the blood–brain barrier might occur following radiotherapy in this patient, which resulted in shorter overall survival due to the development of central nervous system leukemia in this patient.

4. Conclusion

In conclusion, the co-occurrence of NPC and AML is rare. The patient in this case study was diagnosed with NPC followed by AML, and he had a poor prognosis. This case report suggests that central nervous system leukemia is a serious complication resulting from radiotherapy-induced blood-brain barrier destruction in NPC patients. Thus, early alert and prevention of central nervous system leukemia in NPC may extend patient's overall survival rate.

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