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The outcome of primary mediastinal B-cell lymphoma in a single center experience

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ABSTRACT

Introduction: Primary mediastinal B-cell lymphoma (PMBCL) is an aggressive distinct subtype of diffuse large B-cell lymphoma (DLBCL). There is no standard treatment for PMBCL and the value of mediastinal radiotherapy and autologous hematopoietic stem cell transplantation (AHSCT) remains to be elucidated. **Material and methods:** A retrospective analysis of 12 patients with PMBCL (8 male and 4 female) at median age of 36 years has been performed. Induction chemotherapy consisted of R-DA-EPOCH ($n = 7$), R-CHOP ($n = 4$) and R-CVP ($n = 1$). Second and third line treatments were administered in 6 and 2 patients, respectively. Nine patients were given involved field mediastinal radiotherapy. Finally, 8 patients were proceeded to AHSCT. **Results:** Four patients achieved CR and 4 PR after induction therapy with an overall response rate of 66%. In total, after completion all lines of the combined chemotherapy, the following disease responses have been observed: complete response (CR) in 4 patients, partial response (PR) in 6 and no response/disease progression (NR/PD) in 2. The overall response rate was 83%. Eight patients were proceeded to AHSCT (4 in CR and 4 in PR). The transplant-related mortality was 0% at day 100. Median follow-ups from diagnosis and from AHSCT were 39.5 months (range 8–106) and 32 months (range 3–95), respectively. All transplanted patients are alive with CR confirmed in PET scans. **Conclusions:** The vast majority of PMBCL patients are susceptible to immunochemotherapy with a high response rate achieved after R-DA-EPOCH/R-CHOP regimens. AHSCT seems to be an option for fit patients with disease chemosensitivity.

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Introduction

Primary mediastinal B-cell lymphoma (PMBCL) is an aggressive distinct subtype of diffuse large B-cell lymphoma (DLBCL) that arises in the thymus, and presents as a bulky mediastinal mass, often with pleural and pericardial effusions. The disease occasionally disseminates to extranodal sites including kidneys, brain, lungs or gastrointestinal organs. PMBCL affects females more frequently than men and median age at diagnosis is 30–40 years [1, 2]. A large proportion of patients have mutations in the B-cell lymphoma 6 gene (BCL6). PMBCL is also characterized by an amplification of the *REL* proto-oncogene and the *JAK2* tyrosine kinase gene which are normally observed in patients with Hodgkin's lymphoma, suggesting their common origin [3, 4]. An optimal chemotherapy schema as well as the role of radiotherapy in the management of PMBCL are to be elucidated. Cyclophosphamide, doxorubicin, vincristine, and prednisone (CHOP) regimen with or without radiotherapy was found to be effective in 50–60% of patients [5, 6]. The results of CHOP plus rituximab followed by radiotherapy were also found not to be fully satisfactory. In addition, the long-term side effects of mediastinal radiation especially in young adult patients might be devastating [7, 8]. A recently published study has suggested that more dose-intense regimen consisting of dose-adjusted etoposide, doxorubicin, cyclophosphamide with vincristine and prednisone plus rituximab (R-DA-EPOCH) without consolidation radiotherapy may improve outcome in patients with PMBCL [9].

Herein we report on the clinical outcome of our 12 patients with PMBCL treated in our center between 2005 and 2013.

Material and methods

Patients selection and characteristics

Between February 2005 and December 2013, twelve patients (8 male and 4 female) at median age at diagnosis of 36 years (range 22–58 years), with PMBCL were admitted to our institution. There were following complaints at admission: chest pain ($n = 7$), dyspnea ($n = 6$), fatigue ($n = 5$) and cough ($n = 8$). At diagnosis 3 patients demonstrated vena cava superior syndrome. Five patients presented with B symptoms. The disease stage was evaluated according to the Ann Arbor staging system and 8 patients had stage IV (pericardial and/or pleural effusion). The diagnostic work-up included a complete physical examination, routine hematology and biochemistry studies, chest X-ray, computed tomography of the neck, chest, abdomen, and pelvic and/or positron emission tomography (PET) scans and bone marrow biopsy. The final diagnosis was based on histological examination of the excised lymph node obtained during mediastinoscopy and performed by a local pathologist. Due to the fact that some patients were referred from other centers, not all data were available for all our patients. The clinical characteristics of study patients were presented in Table I.

Table I – Baseline patients characteristics

Parameter	$n = 12$ (%)
Gender male/female	8/4
Median age, year (range)	36 (22–58)
Bulky tumor ≥10 cm	5 (42)
Enlargement of subclavicular lymph nodes	4 (33)
Superior vena cava syndrome	3 (25)
Bone marrow involvement	0 (0)
B symptoms	5 (42)
Stage IV disease	8 (67)
Median hemoglobin concentration, g/dL (range)	12.5 (10–14.3)
Median WBC count, 10^9/L (range)	8.7 (5–11.2)
Median PLT count, 10^9/L (range)	354 (97–637)
Elevated LDH level	9 (75)
Elevated β_2 microglobulin	1 (8)

LDH: lactate dehydrogenase, WBC: white blood cells, PLT: platelets.

Treatment before AHSCT

Chemotherapy was not uniform in all studied patients and depended on the patient's overall condition (co-morbidities), year of diagnosis and physician's discretion. Induction therapy consisted of R-DA-EPOCH (rituximab, etoposide, prednisone, vincristine, cyclophosphamide, doxorubicin; $n = 7$), R-CHOP (rituximab, cyclophosphamide, doxorubicin, vincristine, prednisone; $n = 4$) and R-CVP (rituximab, cyclophosphamide, vincristine, prednisone; $n = 1$). Due to the insufficient response/early relapse after induction, 6 patients were given a second-line treatment consisting of R-ESHAP (rituximab, cisplatin, methylprednisolone, etoposide, cytarabine; $n = 4$) and R-CHOP ($n = 2$). Two patients received third-line schema: R-CHOP ($n = 1$) and IVAC (ifosfamide, etoposide, cytarabine; $n = 1$). In addition, 9 patients received involved field radiotherapy at a dose of 36 Grey (Gy). Finally, 8 patients were proceeded to AHSCT.

Response criteria

Complete remission (CR) was defined as a disappearance of all measurable lesions and symptoms for at least 4 weeks. Partial remission (PR) was defined as 50% reduction. Progressive disease (PD) was defined by any increase >25% in the sum of the diameter of any measurable lesions, or the appearance of a new lesion. CT was performed in all patients before treatment and after each line of therapy. The further evaluation using CT supported by PET was performed 3 and 6 months after AHSCT [10].

Transplant procedure

Mobilized peripheral blood was the source of stem cells for AHSCT in all transplanted patients. The regimen used for mobilization was IVE (ifosfamide, etoposide, epirubicine) in all 8 patients. The preparative regimens included CBV (cyclophosphamide, BCNU, etoposide; $n = 5$) and BEAM (BCNU, cytarabine, etoposide, melphalan; $n = 3$). Six patients required granulocyte colony stimulating factor (G-CSF) to expedite post-transplant regeneration.