Annals of Diagnostic Pathology 27 (2017) 1–6

Contents lists available at ScienceDirect

Annals of Diagnostic Pathology

Original Contributions

Solitary plasmacytoma associated with Epstein-Barr virus: a clinicopathologic, cytogenetic study and literature review

Jiaqi Yan, MD, Jianchao Wang, MD, Wenyan Zhang, MD, PhD, Min Chen, MD, Jie Chen, BSc, Weiping Liu, MD *

Department of Pathology, West China Hospital, Sichuan University, No. 37 Guo Xue Xiang, Chengdu, Sichuan 610041, China

ARTICLE INFO

Keywords:
Solitary plasmacytoma
Epstein-Barr virus
Cytogenetic analysis

ABSTRACT

Solitary plasmacytoma (SP) is an uncommon, indolent tumor of plasma cell neoplasms that presents as a mass lesion in extramedullary sites. Evidence of Epstein-Barr virus (EBV) infection is frequently associated with various lymphatic and hematopoietic malignancies but is relatively rare in SP. Moreover, it is essential to distinguish EBV-positive plasmacytoma from plasmablastic lymphoma. In this study, we found 4 EBV-encoded RNA (EBER)–positive patients among 46 consecutive immunocompetent patients of SP and compared the clinicopathologic features of these patients with those of the EBER-negative cohort. In the 4 EBER-positive patients, the common presenting feature was a local mass lesion without symptoms of chronic active EBV infection. Upon histologic examination, neoplastic cells demonstrated well-differentiated morphology in the absence of plasmablastic lymphoma components. Fluorescence in situ hybridization analysis showed that all cases were negative for del13q14, t(11;14)(q13;32) and MYC rearrangement but that 1 case had cytogenetic aberrations involving del17p13. Follow-up data revealed that EBER-positive patients had benign prognoses without aggressive clinical course and that there was no significant difference in the overall survival time between the 2 groups, but EBER-positive patients were more likely to have disease progression (relapse/progression to multiple myeloma) compared with EBER-negative patients. More case studies are needed to better understand the impact of EBV on disease pathogenesis and development in immunocompetent patients of SP.

1. Introduction

Plasmacytoma is a malignant tumor that consists of a monoclonal proliferation of plasma cells that are derived from mature, terminally differentiated B cells. It presents either as a single mass lesion originating in the bones or extramedullary tissues without bone marrow involvement (solitary plasmacytoma [SP]) or as multiple lesions localized in bone marrow (multiple myeloma [MM]). Solitary plasmacytoma is an uncommon type which accounts for 5% to 10% of all plasma cell malignancies [1-3]. The osseous sites of SP primarily involve the vertebrae, whereas the nonosseous sites of SP mainly involve the upper respiratory tract, especially the nasal cavity and paranasal sinuses. Histologically, SP is composed of monomorphic, well-differentiated, or atypical neoplastic plasma cells that are indistinguishable from plasmablastic lymphoma (PBL). The PBL is a high-grade malignant B-cell neoplasm that frequently develops in immunodeficient patients. Epstein-Barr virus (EBV) infection occurs in 60% to 75% of PBL patients, but SP is rarely associated with EBV infection. Immunodeficient patients, such as those with an HIV infection and those undergoing immunosuppressive drug therapies or transplantation, have a slightly increased risk of developing EBV-associated plasmacytomas. Based on a review of the literature, only 14 cases of EBV-encoded RNA (EBER)+ SPs in immunocompetent patients have been reported to date [4-11]. In this study, we investigated 46 SPs in immunocompetent patients and found 4 new cases of tumors associated with EBV. We described the 4 EBER+ patients and compared the clinicopathologic, immunophenotypic, and cytogenetic characteristics of the tumors between the EBER+ patients and the EBER− patients. In addition, it is important to pay attention when making the differential diagnosis of PBL and EBER-positive SP.

2. Materials and methods

Forty-six cases of SPs were collected from the Department of Pathology, West China Hospital of Sichuan University, between June 2008 and September 2015. A histologic diagnosis of each tumor was made according to the criteria set by the World Health Organization classification for tumors of hematopoietic and lymphoid tissues (2008) [12]. The diagnostic criteria used were as follows [13]: (1) cases diagnosed as plasma cell neoplasm by biopsy; (2) bone marrow biopsy with less than 5% clonal plasma cells; (3) a normal skeletal survey and no lesions in the spine as detected using magnetic resonance imaging; (4) little or no serum/urine M band on a gel electrophoresis separation of proteins (level of >20 g/L indicates MM); (5) no anemia, hypercalcemia, or renal involvement was attributed to the plasma cell dyscrasia; and

* Corresponding author. Tel.: +86 28 85422699, +86 18980601641 (mobile); fax: +86 28 85422699.
E-mail address: liuweiping2001@vip.sina.com (W. Liu).

http://dx.doi.org/10.1016/j.anndiagpath.2016.09.002
1092-9134/

(6) no previous immunosuppressive therapy, organ transplantation, or history or evidence of HIV infection. The medical records for the patients were available from the hospital information system and telephone follow-ups.

Hematoxylin and eosin–stained sections of the tumors were used to assess their histopathologic features. We graded plasmacytomas according to the histologic grading criteria described by Bartl et al.[14]. The EnVision method was used for immunohistochemistry with the following antibodies: CD138 (MI15; GeneTech, San Francisco, CA), CD20 (L26; Dako, Glostrup, Denmark), CD79a (JCB117; Dako), PC (VS38C; Dako), Mum-1 (MUM1p; Dako), CD56 (123, C3; Zymed, South San Francisco, CA), CyclinD1 (SP4; Thermo, Waltham, MA), Ki-67 (MIB-1; Maixin, Shenzhen, China), κ and λ immunoglobulin light chains (polyclonal; NeoMarker, Fremont, CA). Diaminobenzidine was used as a substrate, and positive staining was dark brown.

In situ hybridization was performed using a digoxin-labeled oligonucleotide probe complementary to 2 EBV-encoded small RNAs, EBER-1 and EBER-2, (EBER1/2; Dako; No. Y520001). Rabbit antidigoxin antibody conjugated with horseradish peroxidase (Dako) was used to detect the probe. The dark-brown hybridizing signal was located in the cell nuclei. The number of positive cells was visually estimated at less than 1 (single), 1 to 25 (scatter), 25 to 100 (cluster), and more than 100 (diffuse) per medium-power field using a ×10 ocular lens and a ×20 objective. Cases in which the positive reaction presented as a cluster-type or diffuse-type were regarded as an EBV-positive lymphoma [15].

Fluorescence in situ hybridization (FISH) was performed using formalin-fixed, paraffin-embedded tissue sections. Four probes were used: the LSI c-Myc dual-color break-apart rearrangement probe, which hybridizes to band 8q24, and the presence of IGH translocations with CCND1 (11q13) was studied with the dual-color translocation probe LSI IGH/CCND1. The LSI Rb1 SpectrumOrange probe mapping at 13q14 was used to test for 13q deletions. The LSI TP53 SpectrumOrange probe mapping at 17p13 was used to test for 17p deletions (Abbott Diagnostics, Chicago, IL). All probes were used according to the manufacturer's recommendation. A total of 200 nonoverlapping nuclei were scored; the cutoff for del13q and del17p was conservatively set at 40%. The threshold of positivity was defined as greater than 15.5% for c-Myc, and the cutoff values for the translocation dual fusion probe IGH/CCND1 ranged from 10.8% to 20.1% [16].

Overall survival time was calculated from the date of diagnosis to the date of death or last follow-up. Survival data were assessed using the log-rank test. Fisher exact test was used for the determination of significant differences of clinical, immunophenotypic, and cytogenetic characteristics. A P value less than .05 was considered statistically significant. All statistical analyses were performed using SPSS software for Windows, version 22.0 (SPSS, Chicago, IL).

3. Results

3.1. Clinical features

A total of 46 cases were identified. None of the patients had been treated with immunosuppressive therapy, had undergone organ transplantation, or had a history or evidence of HIV infection. EBV-encoded RNA was positive in 4 patients (4/46; 8.7%). The clinical features of the EBER+ and EBER− patients are summarized in Tables 1 and 2. The EBER+ cohort had a median age of 44 years (range, 21-67 years) and consisted of 3 (75%) men and 1 (25%) woman. The average clinical history was 6.5 months. The sites of the neoplasms included the nasal cavity, skull, clavicle, and humerus. The clinical manifestations of patient 1 were closely related to the anatomic sites involved, and the symptoms were nasal obstruction, rhinorrhea, and epistaxis. Patient 2 presented with localized, painless masses. Patient 3 and patient 4 complained mainly of pain and enlarged masses. The sizes of their tumors ranged from 3.5 × 3 × 3 cm to 10 × 3 × 2 cm. Laboratory data and results of the auxiliary examination given at the time of diagnosis are summarized

Table 1
Clinical features of patients with EBV-positive SP

Patient	Age (y)/Sex	Tumor site	Size (cm)	Clinical history (mo)	Presentation	LDH (g/L)	β_2-microglobulin (mg/L)	Hb (g/L)	Serum Ca (mmol/L)	Serum Cr (μmol/L)	M-component serum urine	BM biopsy (PCs,%)	Bone destruction	Therapy	Outcome
1	27/M	Nasal cavity	3.5 × 3 × 3	12	Nasal obstruction, epistaxis	112	1.48	95	1.97	75.9	Neg	<1%	Yes	Resection + RT	ANED, 70 mo
2	67/M	Skull	4.5 × 4 × 4	9	Painless mass	158	1.65	132	2.19	84.0	Neg λ	1%	Yes	Resection + ADT	Progression to MM, DOD at 55 mo
3	38/M	Clavicle	4 × 4 × 3	2	Supraclavicular mass, pain	143	2.16	131	2.13	74.5	Neg	5%	No	Resection	AWD, 83 mo
4	50/F	Humerus	10 × 3 × 2	3	Mass in upper limb, pain	116	2.42	124	2.45	73.9	IgG, κ neg	<1%	Yes	Resection + RT	AWD, 21 mo

Abbreviations: ADT, doxorubicin, dexamethasone, thalidomide; ANED, alive with no evidence of disease; AWD, alive with relapsing disease; DOD, died of disease; F, female; FU, follow-up; M, male; RT, radiation therapy.