Clinics in Surgery

Research Article
Published: 23 Mar, 2022

Plasma Cell Tumor in Central Nervous System: A Report of 39 Cases from a Single Center

Huan Li, Da Li, Liang Wang, Li-Wei Zhang, Jun-Ting Zhang, Xiu-Jian Ma and Zhen Wu**

Department of Neurosurgery, Beijing Tiantan Hospital, Capital Medical University, China

Abstract

Objectives: This study aims to report the clinical characteristics and outcomes for the patients with Central Nervous System (CNS) solid Plasma Cell Tumor (PCT), including Solitary Plasmacytoma (SPC) and Multiple Myeloma (MM) with a solid mass.

Methods and Materials: Patients' medical records, surgical reports, and follow-up materials were respectively reviewed. Statistical analysis was used to compare the differences between patients with SPC (n=22) and patients with MM (n=17).

Results: The median age was 55.0 years with a male proportion of 48.7%. Tumors located in the skull base, non-skull base and spinal were observed in 24 (61.5%) cases, 8 (20.5%) cases, and 7 (18.0%) cases, respectively. The median diameter was 5.0 cm. Overall, Gross Total Resection (GTR), radiotherapy and chemotherapy were respectively achieved in 13 (33.3%) cases, 15 (44.1%) cases and 16 (47.1%) cases. Follow-up materials were available in 34 (87.2%) patients. When the study ended 21 (61.8%) patients suffered disease progression with a 3-year Progression-Free Survival (PFS) of 38.7%; 11 (32.4%) patients died with a 3-year Overall Survival (OS) of 71.5%. Regarding the differences, SPC affected the skull base more frequently than MM (p=0.006); while patients with MM had a higher frequency (p=0.017) in chemotherapy but the 3-year OS was poorer than SPC.

Conclusion: Solid PCT in CNS was a highly heterogeneous disease with a wide spectrum of outcomes. Normalized examinations should be performed prior to the diagnosis of CNS SPC to rule out MM. The treatments for patients with SPC and MM should be differed and further tailored.

Keywords: Central nervous system; Solitary plasmacytoma; Multiple myeloma; Clinical characteristics

Abbreviations

PCT: Plasma Cell Tumor; MM: Multiple Myeloma; SPC: Solitary Plasmacytoma; OS: Overall Survival; GTR: Gross Total Resection; NGTR: Non-Gross Total Resection; IHC: Immunohistochemical; MRI: Magnetic Resonance Image; CT: Computed Tomography

Introduction

According to 2016 WHO classification, Solitary Plasmacytoma (SPC) is regarded as one of the plasma cell tumors, and is subdivided into SPC of bone (SPB), and extraosseous (or extramedullary) SPC (EPM) [1]. The definition of this tumor is the verification of a solitary lesion with the absence of the systematic involvements that include hypercalcemia, renal insufficiency, anemia, or multiple bone lesions; otherwise, Multiple Myeloma (MM) should be diagnosed [2]. There were several studies that focused on intracranial metastases from MM [3-5], and the rate was reported to be 0.7% [6]. For these MM patients with intracranial metastases, the management was a great challenge, and the outcome was extremely dismal (median overall survival 6.7 months) [7,8]. Our previous research exclusively described the clinical characteristics of primary intracranial SPC. We found that the majority of primary intracranial SPCs were located in the skull base, and with the use of radiotherapy, patients with this disease could achieve a favorable OS [7]. However, the understanding of the solid PCT (Plasma Cell Tumor) in CNS, which might present as SPC or MM with a solid mass, is still insufficient. In this study, we retrospectively reviewed patients with the solid PCT, which initially presented as a solid tumor in CNS (spine and cranial space) and subsequently was surgically removed. The clinical features and outcomes for patients with SPC and MM were analyzed and subsequently compared.

OPEN ACCESS

Correspondence:
Zhen Wu, Department of Neurosurgery, Beijing Tiantan Hospital, Capital Medical University, Xilu 119, Nanxihuan, Fengtai District, Beijing, PR China, Tel: +86 10 67098431; Fax: +86 10 67051337;
E-mail: wz_ttyy@163.com
Xiu-Jian Ma, Department of Neurosurgery, Beijing Tiantan Hospital, Capital Medical University, Xilu 119, Nanxihuan, Fengtai District, Beijing, PR China, Tel: +86 10 67098431; Fax: +86 10 67051337;
E-mail: NIL

Received Date: *27 Jan 2022*
Accepted Date: *09 Mar 2022*
Published Date: *23 Mar 2022*

Citation:
Li H, Li D, Wang L, Zhang L-W, Zhang J-T, Ma X-J, et al. Plasma Cell Tumor in Central Nervous System: A Report of 39 Cases from a Single Center. Clin Surg. 2022; 7: 3460.

Methods and Materials

Our study enrolled patients who were pathologically diagnosed with SPC and MM at our center from January 2008 to January 2017. Solid PCT defined in this study excludes patients only with Cerebrospinal Fluid (CSF) spread or diffuse leptomeningeal involvement, which is one of the common presentations of the advanced phase of systematic MM [9]. In this study, all of the patients accepted surgical treatment because of radiologically visible solid tumor (tumor diameter [defined below] >2 cm) in cranial space or spine. Their medical records, surgical reports, and radiological data were respectively extracted. This study was approved by the Research Ethics Committee of Beijing Tiantan Hospital. Patients were followed up *via* clinic visits, phone calls or e-mails. Tumor diameter represented the longest size measured on MRI (Magnetic Resonance Image) scans or CT (Computed Tomography) scans if MRI was not available. If the tumor was multiple, only the diameter of the one that we planned to remove was used. Tumor location was classified into three subgroups: skull base, non-skull base, and spine. Gross Total Resection (GTR) was recorded when there was no visible remnant on follow-up MRI, which was usually performed 3 months after the surgery; otherwise, the surgical extent was defined as Non-Gross Total Resection (NGTR). Two neuropathologists independently reviewed the specimens both pathologically and immunohistochemically (CD138, CD79a, and CD38). Before the final diagnosis of SPC, the patients would experience examinations, for example, bone marrow biopsy, blood cell account and whole-body bone scan, etc., to rule out MM. Tumor progression referred to a 2 mm increase in diameter or new lesions in other sites. For SPC, progression was recorded if there was any evidence suggesting that SPC developed into MM. Progression-Free Survival (PFS) was the duration between the diagnosis and tumor progression; Overall Survival (OS) was the duration between the diagnosis and patients' death. Since none of the numeric variables (age, symptom duration, tumor diameter, follow-up duration) was consistent with normal distribution, this study used the median (IQR, Interquartile Range); for the categorical variables, proportions were used. When comparing differences, two-sample Wilcoxon rank-sum (Mann-Whitney) test, Chi-Square test and univariate analysis in the Cox Regression Model were employed. Statistically, the significant level was set at $p<0.05$. The statistical analysis was conducted in STATA 15.0 (StataCorp, Lakeway Drive College Station, Texas).

Results

Demographic features

This study ultimately enrolled 39 patients, and SPC and MM were observed in 22 (56.4%) cases and 17 (43.6%) cases, respectively. Notably, none of the 17 patients with MM had a history of MM presentations previously, but all were diagnosed within the perioperative period. The individual information for the 39 patients was exhibited in Table 1. Overall, the median age at diagnosis was 55.0 (IQR 47.0-62.0) years old (Table 2). Male gender accounted for 47.7% (n=19). Neurological deficits (n=25, 78.1%), especially Cranial Nerve (CN) VI (n=11, 34.4%), represented the most common presentations for cranial lesions. Considering spinal lesions, paresthesia (n=6, 85.7%) and muscle weakness (4, 57.1%) were the most common symptoms. Median symptom duration before surgery was 2 (IQR 1-6) months.

Radiological characteristics

The tumors tended to invade skull base (n=24, 61.5%) the most, followed by non-skull base (n=8, 20.5%) and spine (n=7, 18.0%). Tumors in the thoracic spine were found in 4 cases; tumors in the cervical spine, lumbar spine, and sacral spine were found in each 1 case. The median diameter was 5.0 (IQR 3.7-5.7) cm. The radiological features of SPC were well depicted in our previous studies. Only 2 cases were diagnosed with solid PCTs preoperatively. The common misdiagnoses contained chordoma (15 cases), meningioma 14 cases), and schwannoma (3 cases), etc.

Treatments

The initial surgical treatments for the 39 patients were all performed in our institute. GTR was achieved in 13 (33.3%) cases. Postoperatively, CN deficits, intracranial infections, and muscle weakness were found in 3 cases, 2 cases and 1 case, respectively, without any severe surgical complication. After the diagnosis of solid PCT, only 2 patients met the diagnostic criteria of MM; but further workups identified another 16 MM patient. Postoperatively, 15 (44.1%) cases accepted various forms of radiotherapy, including fractioned routine radiotherapy (n=13, 86.6%), gamma-knife (n=1, 6.7%) and cyber radiation (n=1, 6.7%), with a median dose of 45.0 Gray (available in 9 cases). Chemotherapy was applied in 16 (47.1%) cases. Thalidomide-based regimens (4 cases) and/or bortezomib-based (3 cases) regimens represented the most common strategies.

Follow-up and outcomes

After a median follow-up of 41.7 (IQR 20.7-65.2) months, 34 (87.2%) patients were available. When the study ended, 21 (61.8%) patients had disease progression, 12 (57.1%) of whom suffered from local tumor recurrence *In situ*. The 3-year Progression-Free Survival (PFS) was 38.7% with a median PFS of 26.5 (IQR 12.0-48.8) months. After identification of tumor progression, 5 (23.8%) patients declined any modalities of treatments. For the remaining 16 patients, salvage interventions included surgery alone (n=2), chemotherapy alone (n=4), radiotherapy alone (n=3), surgery plus chemotherapy and/or radiotherapy (n=4), and chemotherapy plus radiotherapy with/or without high-dose chemotherapy (n=3). At the end of follow-up, eleven (32.4%) patients died of disease progression with a 3-year Overall Survival (OS) of 71.5%.

Differences between SPC and MM

Further analysis showed SPC (n=18, 81.8%) affected the skull base more frequently than MM (n=6, 35.3%; p=0.006). With regards to therapy, patients with MM (n=10, 71.4%) had a higher frequency (p=0.017) in chemotherapy treatment than SPC (n=6, 30%). The 3-year PFS of SPC (49.4%) appeared longer than that of MM (22.2%), but the difference was not significant (Table 2 and Figure 1A; p=0.094). The 3-year OS of MM (55.1%) was significantly (p=0.044) poorer than that of SPC (81.2%; Figure 1B).

Discussion

The majority of cases with CNS plasma cell tumor were reported by hematologists or oncologists [3,4,10,11], where this disease could exhibit as localized lesions in very late phase, SPC or CNS myelomatosis [12]. In these studies, CNS tumors were metastasized from systematic MM that had been treated by advanced forms of chemotherapy, and were considered as terminal events for the affected patients [13]. Consequently, their outcomes were dismal (median overall survival 6.7 months) [7,8]. On the other hand, there were also patients without any prior interventions who presented to neurosurgeons because of solid masses in CNS, later confirmed as SPC or MM with a solid mass. Reports on patients with solid PCT were limited.

Table 1: The individual clinical features, treatments and outcomes of the 39 cases.

Case	Sex/age	Presentations, duration (mos)	Location/size (cm)	Pre./postop. Diagnosis	Initial treatments	Progression (PFS)/salvage treatments	Death (OS, mo)
1	F/57 yr	Headache/0.5	NSB (temporal)/4.2	Meningioma/MM	NGTR	*In situ* (2.1)/surgery	DOD (6)
2	F/28 yr	CN VIII, IX, XII/23	SB (clivus)/4.0	Chordoma/SPC	NGTR		
3†	M/59 yr	CN VI, 15	SB (clivus)/3.4	Chordoma/SPC	NGTR+SC	*In situ* (45)/GTR+RT	Alive (128.1)
4†	F/45 yr	Headache and CN II, 16	SB (orbitotemporal)/6.9	Meningioma/SPC	NGTR	*In situ* (3) + MM (120)/RT	Alive (125.6)
5	F/63 yr	CN VIII, IX, XII/0.8	SB (clivus)/4.5	Chordoma/MM	GTR+RT+SC	*In situ* (6)/surgery	DOD (20)
6†	M/35 yr	CN VIII/IX, ataxia, 23	SB (petrous apex)/3.3	Schwannoma/SPC	NGTR+RT (45 Gy)	MM (100)/RT	Alive (121.8)
7	M/62 yr	Back pain/1	SP (T12-L1)/5.4	Meningioma/SPC	NGTR	*In situ* (45)/surgery +RT+CMT (T)	DOD (108)
8†	M/42 yr	CN V, VI, VII, VIII, IX, X/21	SB (clivus)/4.8	Chordoma/SPC	NGTR+RT (50 Gy) +SC (T+other agents)	no	Alive (117.6)
9	F/47 yr	CN VI/4	SB (petroclivus)/3.4	schwannoma/MM	NGTR		
10	M/60 yr	Headache/9	NSB (parietal)/7.3	Meningioma/MM	GTR+RT+SC	*In situ* (12)/RT	DOD (55.3)
11†	F/56 yr	Dizziness and CN II/14	SB (sellar)/4.3	Pituitary/SPC	NGTR	*In situ* (58)/none	DOD (60.2)
12	F/47 yr	CN VIII, face numbness/9	SB (sellar, parasellar, jugular foramen)/5.3	Meningioma/MM	NGTR+RT+SC	Systemic spread (2)	DOD (4)
13	M/26 yr	Headache, CN VI, IX, X, XII/14	NSB (multiple [frontoparietal and petroclivus])/4.4	MM/MM	GTR+RT+SC (T)	Ex situ (5.8)	Alive (100.6)
14†	M/54 yr	CN VIII/10	SB (clivus)/4.6	Chordoma/SPC	NGTR+RT	no	Alive (96.7)
15†	F/58 yr	CN II, III, VI/20	SB (MCB)/3.8	Meningioma/SPC	NGTR	no	DOD (41.1)
16	M/66 yr	Muscle weakness/1	SP (S1-2)/3	Chordoma/MM	NGTR+RT	*In situ* (37.9)/none	DOD (37.9)
17	F/50 yr	Hand numbness, weakness/3	SP (C5-6)/2.7	Schwannoma/SPC	GTR	no	Alive (68.4)
18†	F/47 yr	CN VI/4	SB (clivus)/3.1	Chordoma/SPC	GTR+RT (45 Gy)+SC	*In situ* (7) +MM (7)/SC	DOD (28.2)
19	M/56 yr	Back pain/3	SP (T5)/3.0	Meningioma/SPC	NGTR+RT	*In situ* (26.8)/surgery+CMT (B)	Alive (65.2)
20	M/62 yr	Chest numbness, pain, ataxia/9	SP (T4-5)/5.0	Meningioma/MM	NGTR	*In situ* (26.2)/RT+SC (L+B)	DOD (35.2)
21	F/23 yr	Back pain, numbness, weakness/3	SP (T4-10)/16.6	Lymphoma/MM	NGTR+SC+HDCMT	Ex situ (43.3)/RT+SC (HDCMT)	Alive (59.4)
22†	M/68 yr	None/19	NSB (frontal)/2.0	Eosinophilic/SPC	GTR	no	Alive (57.8)
23	M/58 yr	CN II/6	NSB (temporal)/3.8	Meningioma/MM	GTR+RT+SC	no	Alive (48.9)
24	M/59 yr	Dizziness/1	NSB (frontotemporal)/5.4	Meningioma/MM	GTR+RT+SC (T)	no	Alive (55.6)
25†	M/64 yr	CN VI/13	SB (clivus)/3.8	Chordoma/SPC	NGTR	*In situ* (14)/RT+SC	Alive (52)
26	M/48 yr	limb numbness, weakness, gatism/1.3	SP (multiple [T6-11])/7.0	MM/MM	NGTR		
27	M/59 yr	CN II, VI/3	SB (clivus)/4.3	Chordoma/SPC	NGTR		
28†	F/47 yr	CN II/14	SB (clivus)/4.0	Chordoma/SPC	NGTR	*In situ* (10) +MM(10)/ NGTR+RT+S(T)	Alive (42.4)
29	M/52 yr	Headache, CN VI, VIII/6	SB (clivus)/5.2	Meningioma/MM	NGTR		
30†	F/73 yr	Dizziness, CN VI/6	SB (clivus)/4.0	Chordoma/SPC	NGTR+SC (B+T+L)	no	Alive (35.5)
31†	F/55 yr	None/11	SB (parasellar)/5.3	Meningioma/SPC	GTR+RT	MM (23)/SC (T)	Alive (35.4)
32†	M/50 yr	CN VI/14	SB (clivus)/5.8	Chordoma/SPC	NGTR+RT (42 Gy)	no	Alive (33.3)
33†	F/54 yr	Headache, aphasia, CN IX, X/14	SB (clivus)/5.4	Chordoma/SPC	NGTR+RT (40Gy) +SC	MM (17)/SC	DOD (20.7)
34†	F/57 yr	Headache, aphasia, CNIX, X/14	SB (temporal)/4.2	Meningioma/SPC	GTR	no	Alive (27.4)
35†	F/59 yr	CN III, VII/9	SB (PCB)/3.4	squamous carcinoma/ SPC	GTR+SC	no	Alive (20.2)
36	F/55 yr	CN VIII, IX, XII/5	SB (occipital condyle)/2.2	schwannoma/MM	GTR+SC (B+DXM)	no	Alive (17.5)
37	F/66 yr	None/5	NSB (frontoparietal)/4.5	Chordoma/MM	GTR+SC (B)	no	Alive (16.6)
38	M/53 yr	None/2	NSB (temporoparietal)/5.0	Meningioma/MM	GTR+SC	no	Alive (16.4)
39	F/63 yr	CN II, VI/1	SB (clivus)/2.4	Chordoma/MM	NGTR	*In situ* (5.9)/SC (B+DXM)	Alive (15.9)

B: Bortezomib; CN: Cranial Nerve; DXM: Dexamethasone; GTR: Gross Total Resection; HDCMT: High-Dose Chemotherapy; L: Lenalidomide; MCB: Middle Cranial Base; MM: Multiple Myeloma; NGTR: Non-Gross Total Resection; PCB: Posterior Cranial Base; RT: Radiotherapy; SC: Systemic Chemotherapy; T: Thalidomide

† Cases had been reported by our team members previously

Table 2: Summary of clinical characteristics of 39 patients with solid PCT.

Variable	Overall		ISPC		MM		p
	AN	Value	AN	Value	AN	Value	
Median age: yrs (IQR)	39	55.0 (47.0-62.0)	22	55.5 (47.0-59.0)	17	55.0 (48.0-62.0)	0.499‡
Male (%)	39	19 (48.7)	22	10 (45.5)	17	9 (52.9)	0.643
Diameter: cm (IQR)†	39	5.0 (3.7-5.7)	22	5.0 (3.7-5.8))	17	4.5 (3.8-5.3)	0.547‡
Tumor location	39		22		17		0.006§*
Skull base		24 (61.5)		18 (81.8)		6 (35.3)	
Non-skull base		8 (20.5)		1 (4.6)		7 (41.2)	
Spine		7 (18.0)		3 (13.4)		4 (23.5)	
Surgery (%)	39		22		17		0.110§
Non-gross total resection		26 (66.7)		17 (77.3)		9 (52.9)	
Gross total resection		13 (33.3)		5 (22.7)		8 (47.1)	
Radiotherapy (%)	39		20		14		0.563§
No		19 (55.9)		12 (60.0)		7 (50.0)	
Yes		15 (44.1)		8 (40.0)		7 (50.0)	
Chemotherapy (%)	39		20		14		0.017§*
No		18 (52.9)		14 (70.0)		4 (28.6)	
Yes		16 (47.1)		6 (30.0)		10 (71.4)	
Median follow-up: mos (IQR)	34	41.7 (20.7-65.2)	20	54.9 (34.3-102.3)	14	27 (16.4-55.3)	0.761‡
Progression (%)	34	21 (61.8)	20	12 (60.0)	14	9 (64.3)	0.800§
3-yr PFS (%)		38.7		49.4		22.2	0.094¶
Death (%)	34	11 (32.4)	20	5 (25.0)	14	6 (42.9)	0.273§
3-yr OS (%)		71.5		81.2		55.1	0.044¶*

AN: Available Number; IQR: Interquartile Range
† Tumor diameter referred to the largest length
‡ Two-sample Wilcoxon rank-sum (Mann-Whitney) test
§ Chi-Square test
¶ Univariate analysis in Cox Regression Model
*p<0.05

Table 3: Summaries of publications with CNS-involved PCT (n>10 cases).

Author	Number of cases	Treatment Strategies	OS after CNS involvement
Fassas et al. [16]	25 (CNS-involved MM)	44% RT: 72% CMT: 32% HDCMT: 44% SCT: 92% ITCMT	3 mos (median)
Ozashin et al. [29] †	11 (skull SPC)	83.0% RT alone: 13.2% RT plus CMT: 3.1% surgery alone	NA (10-yr OS 54% for whole cohort)
Gozzetti et al. [27] †	50 (intracranial MM)	50% RT: 92% CMT: 24% HDCMT: 24% SCT: 10% ITCMT	6 mos (median)
Chen et al. [3]	37 (CNS-involved MM)	78% RT: 100% CMT: 5% SCT: 81% ITCMT	4.6 mos (median)
Abdallah et al. [25]	35 (CNS-involved MM)	17.1% RT: 80% CMT: 54.3% SCT and 88.6% ITCMT	4 mos (median)
Jurczyszyn et al. [8] †	172 (CNS-involved MM)	36% RT: 76% CMT: 32% IT	6.7 mos (median)
Paludo et al. [6]	29 (CNS-involved MM)	76% RT: 62% CMT: 24% SCT: 24% ITCMT	3.4 mos (median)
Goyal et al. [26]	143 (CNS plasmacytomas)	NA	91.9 mos (median)
Thumallapally et al. [30] †	49 (CNS SPC)	30.6% RT alone: 32.7% surgery alone: both 34.7%: neither 2.0%	92.6% for RT alone: 52.9% surgery alone: and 67.8% surgery plus RT (5-yr OS)
Varga et al. [23]	13 (CNS-involved MM)	15.4% RT: 76.9 CMT: 38.5 HDCMT: 30.8% SCT: 46.2% ITCMT	3 mos (median)
Dias et al. [14]	20 (CNS-involved MM)	62.5% RT: 70% CMT: 10% HDCMT: 40% SCT: 10% ITCMT	40.3 mos (median)
Nandeesh et al. [28]	18 (cranial plasmacytomas)	NA	NA

NA: Not Available; IT: Intrathecal CMT; SCT: Stem Cell Transplantation
† Multicenter-based data
Note: Cases from Fassas (1990-2003) might party overly with cases from Abdallah (1996-2012) because these two reports were from same center

Clinical features and diagnosis

The median age for patients with solid PCT was 55 years old, and this figure was correspondent to that of the previous studies [14-16]. It was believed that SPC and MM were different phases in the development course of plasma cell tumors [17,18]. It would take 2 to 4 years for SPC to develop into MM [19]. However, the indifference in age between patients with SPC and patients with MM (Table 2) in part challenged the statement that CNS MM only develops from SPC. Similar to primary intracranial SPC [7], a slight female predominance was observed in this study. Primary intracranial SPC tended to invade

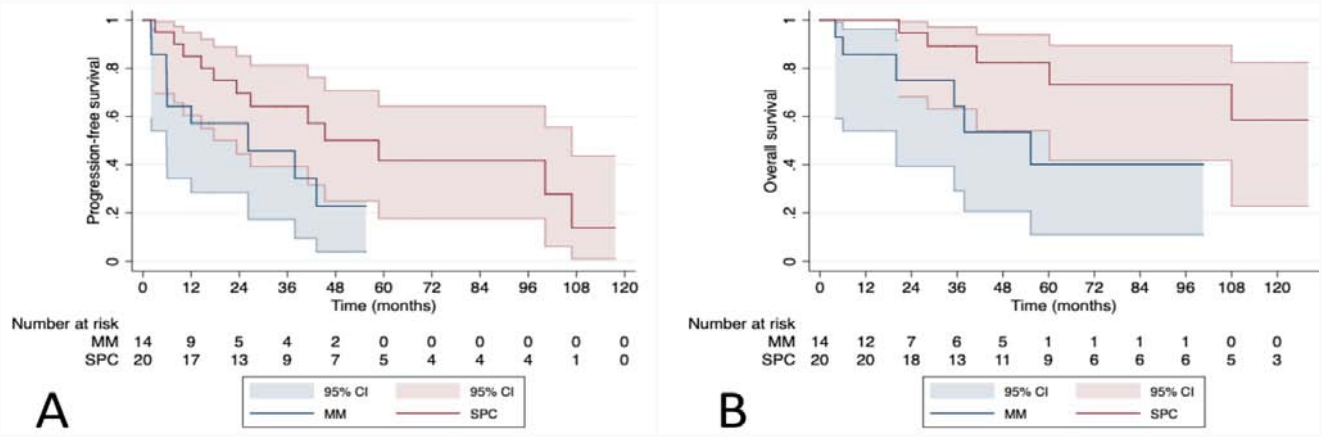

Figure 1: Kaplan-Meier survival curves. **A** showed the 3-year PFS of patients with SPC appeared longer than that of MM: but the difference was not significant; **B** indicated that the 3-year OS of MM was significantly poorer than that of SPC.

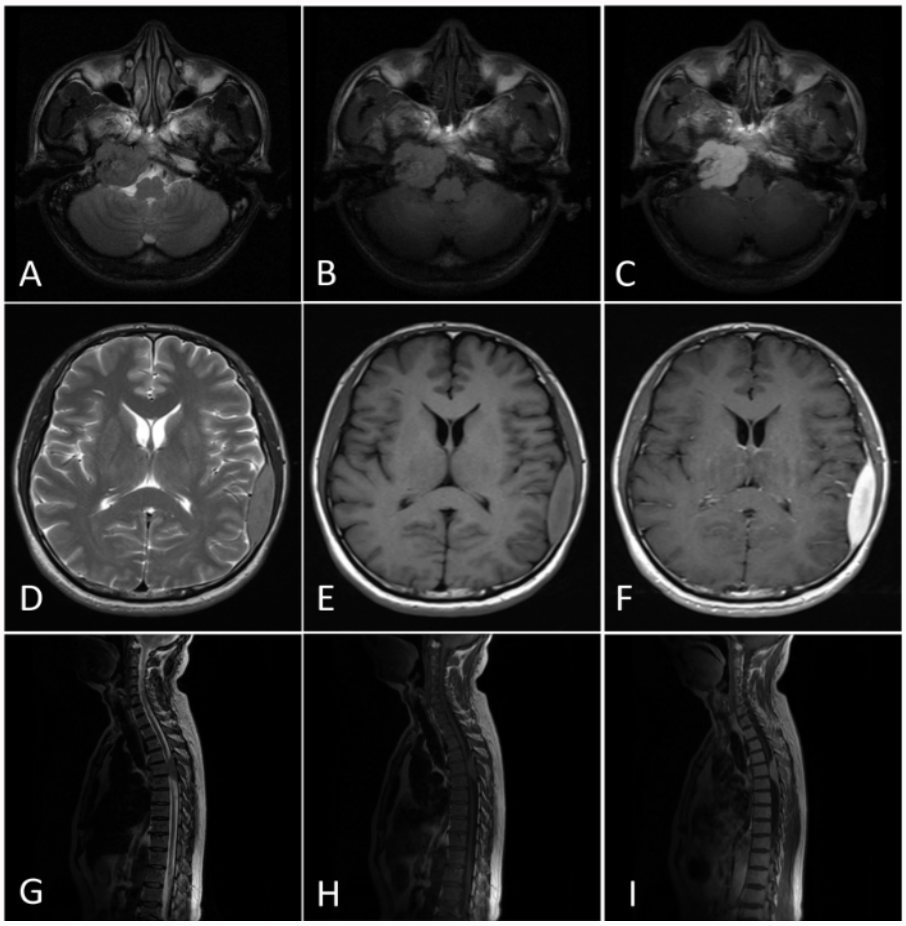

Figure 2: MRI scans for three illustrative cases. **A-C** showed a mass in the posterior fossa (axial; T2WI: T2WI and contrast enhancement series for A: B and C: respectively). **D-F** unveiled a lesion in left temporoparietal region (axial; T2WI: T2WI and contrast enhancement series for D: E and F: respectively). **G-I** revealed a mass inside the thoracic spine canal (sagittal; T2WI: T2WI and contrast enhancement series for G: H and I: respectively).

the skull base the most, followed by the spine and intracranial non-skull base space; while MM preferred to affect intracranial non-skull base space the most, followed by skull base and spine (Table 2). The spine was the most common site for MM to metastasize to CNS [20]. The tumor was radiologically characterized by homogeneous enhancement on MRI and osteolytic appearance on CT [7,21]. Either the low incidence or nonspecific radiological features contributed to a high rate of misdiagnoses. Apart from the morphological observation in the pathological examination, the expression of CD138 and CD79A was indispensable in the accurate diagnosis of solid PCT [7,21]. In our study, nearly half of the patients were finally confirmed to be MM after the thorough tests. Therefore, the diagnosis of the SPC should be carefully made in clinical practice; otherwise, the therapeutically aggressive treatments for MM would be delayed.

Treatments

To better understand current studies related to this disease, publications that reported patients (n>10) with plasma cell tumor in CNS were summarized in Table 3 [3,6,8,14,16,22-30]. As Table 3 showed, the majority of previous studies focused on CNS-involved MM, which occurred after several lines of treatment for primary MM. The presence of CNS-involved MM represented the terminal events for those patients with a median OS of 3 to 6.7 months [3,6,8,,16,23,25,27]. In this scenario, aggressive treatment strategies, including High-Dose CMT (HDCMT), Stem Cell Transplantation (SCT) and Intrathecal CMT (ITCMT), were used in addition to systemic CMT and RT. From a neurosurgeon's respective, some patients could present with a radiographically visible mass, but without PCT-related history, which later led to the diagnosis of SPC or MM. Our study exclusively reported these populations and revealed that 3-year OS surpassed 50% for MM, two thirds for the entire cohort, and three quarters for SPC. There were two similar studies in CNS SPC (Table 3), whose cohort sizes (n=143 [26] and n=49 [30]) were larger than ours. However, both of them were from multicenter and described CNS PCT under the context of PCT in whole body, resulting in limited description in CNS PCT. Thus, our studies represented the largest cohort size that reported patients with CNS solid PCT from a single center. Patients with solid PCT were referred to neurosurgeons because of visible masses in CNS. Regarding the treatment strategies, surgery should be the cornerstone for this disease. An accurate diagnosis would not be made until the tumor was resected and further examined in pathological and IHC approaches [31]. For SPC that was adjacent to vital neurovascular structures, to avoid severe surgical complications after aggressive surgery, biopsy was recommended in that SPC was sensitive to radiotherapy [7,32-34]. Either for patients with SPC or MM, GTR for the visible mass should be recommended if accessible [24]. There were also data supporting that that the solid mass of MM in CNS responded to radiotherapy [35,36]. Therefore, postoperative radiotherapy was worth using for CNS MM considering its aggressive biology. While the use of chemotherapy for patients with SPC was controversial [19,37], it was indisputable that patients with MM should be administrated with chemotherapy [12]. Traditional systemic chemotherapy agents, including melphalan, vincristine, and doxorubicin, had limited ability to penetrate the Blood-Brain Barrier (BBB) [12]. The emerging novel agents (lenalidomide and marizomib) seemed promising in recent years [7]. Although high-dose chemotherapy combined with stem-cell rescue had been proven effective in MM [10], its role in CNS solid PCT remained uncertain.

Limitations

This study was designed in a retrospective manner. Thus, intrinsic biases existed. The median follow-up of 41.7 months was relatively short. Thus, we failed to prove that the PFS between SPC and MM was significantly different, but a tendency that the PFS of SPC was longer than that of MM was observed (Figure 1A). We did not test risk factors for PFS and OS because of the limited cohort size (39 cases), which might lead to a less convincing result. However, this study was still one of the largest cohorts that focused on solid PCT in CNS. Our research, from the neurosurgical perspective, was valuable in updating the understanding of this disease and catching more attentions on this field. We would also continue to follow those patients up and collect more patients to further understand SPC and MM.

Conclusion

Solid PCT in CNS was a highly heterogeneous disease with a wide spectrum of outcomes. Normalized examinations should be performed prior to the diagnosis of CNS SPC to rule out MM. The treatments for patients with SPC and MM should be differed and further tailored.

Acknowledgment

This work was supported in part by the National Natural Science Foundation of China (Grant No. 81672506 to Z.W). Meanwhile, we appreciated professor Guilin Li and professor Jiang Du, both from the Department of Pathology, Beijing Neurosurgical Institute/Beijing Tiantan Hospital, who offered considerable histopathological and IHC assistance.

References

1. Swerdlow SH, Campo E, Pileri SA. The 2016 revision of the World Health Organization classification of lymphoid neoplasms. Blood. 2016;127:2375-90.
2. Rajkumar SV, Dimopoulos MA, Palumbo A. International Myeloma Working Group updated criteria for the diagnosis of multiple myeloma. Lancet Oncol. 2014;15:e538-548.
3. Chen CI, Masih-Khan E, Jiang H. Central nervous system involvement with multiple myeloma: Long term survival can be achieved with radiation, intrathecal chemotherapy, and immunomodulatory agents. Br J Haematol. 2013;162:483-8.
4. Azoulay D, Lavie D, Horowitz N. Bortezomib-induced peripheral neuropathy is related to altered levels of brain-derived neurotrophic factor in the peripheral blood of patients with multiple myeloma. Br J Haematol. 2014;164:454-6.
5. Schluterman KO, Fassas AB, Van Hemert RL, Harik SI. Multiple myeloma invasion of the central nervous system. Arch Neurol. 2004;61:1423-9.
6. Paludo J, Painuly U, Kumar S. Myelomatous involvement of the central nervous system. Clin Lymphoma Myeloma Leuk. 2016;16:644-54.
7. Ma XJ, Li D, Wang L. Clinical features, radiological profiles, and surgical outcomes of primary intracranial solitary plasmacytomas: A report of 17 cases and a pooled analysis of individual patient data. J Neuro-Oncol. 2019;142:273-4.
8. Jurczyszyn A, Grzasko N, Gozzetti A. Central nervous system involvement by multiple myeloma: A multi-institutional retrospective study of 172 patients in daily clinical practice. Am J Hematol. 2016;91:575-80.
9. Haegelen C, Riffaud L, Bernard M, Carsin-Nicol B, Morandi X. Dural plasmacytoma revealing multiple myeloma. Case report. J Neurosurg. 2006;104:608-10.
10. Child JA, Morgan GJ, Davies FE. High-dose chemotherapy with hematopoietic stem-cell rescue for multiple myeloma. N Engl J Med. 2003;348:7-16.
11. Marchesi F, Masi S, Summa V. Flow cytometry characterization in central nervous system and pleural effusion multiple myeloma infiltration: An Italian national cancer institute experience. Br J Haematol. 2016;172:980-2.
12. Nieuwenhuizen L, Biesma DH. Central nervous system myelomatosis: Review of the literature. Eur J Haematol. 2010;80:1-9.
13. Gangatharan SA, Carney DA, Prince HM. Emergence of central nervous system myeloma in the era of novel agents. Hematol Oncol. 2012;30:170-4.
14. Dias A, Higashi F, Peres ALM. Multiple myeloma and central nervous system involvement: Experience of a Brazilian center. Rev Bras Hematol Hemoter. 2018;40:30-6.
15. Chang WJ, Kim SJ, Kim K. Central nervous system multiple myeloma: A

different cytogenetic profile? Br J Haematol. 2014;164:745-8.

16. Fassas AB, Ward S, Muwalla F. Myeloma of the central nervous system: strong association with unfavorable chromosomal abnormalities and other high-risk disease features. Leuk Lymphoma. 2004;45:291-300.

17. Eum JH, Jeibmann A, Wiesmann W, Paulus W, Ebel H. Multiple myeloma manifesting as an intraventricular brain tumor. J Neurosurg. 2009;110:737-9.

18. Holland J, Trenkner DA, Wasserman TH, Fineberg BP. Treatment results and conversion to myeloma. Cancer. 1992;69:1513-7.

19. Soutar R, Lucraft H, Jackson G. Guidelines on the diagnosis and management of solitary plasmacytoma of bone and solitary extramedullary plasmacytoma. Br J Haematol. 2004;124:717-26.

20. Brenner B, Carter A, Tatarsky I, Gruszkiewicz J, Peyser E. Incidence, prognostic significance and therapeutic modalities of central nervous system involvement in multiple myeloma. Acta Haematol. 1982;68:77-83.

21. Lee J, Kulubya E, Pressman BD. Sellar and clival plasmacytomas: Case series of 5 patients with systematic review of 65 published cases. Pituitary. 2017;20:381-92.

22. Bindal AK, Bindal RK, van Loveren H, Sawaya R. Management of intracranial plasmacytoma. J Neurosurg. 1995;83:218-21.

23. Varga G, Mikala G, Gopcsa L. Multiple myeloma of the central nervous system: 13 cases and review of the literature. J Oncol. 2018;2018:3970169.

24. Schwartz TH, Rhiew R, Isaacson SR, Orazi A, Bruce JN. Association between intracranial plasmacytoma and multiple myeloma: Clinicopathological outcome study. Neurosurgery. 2001;49:1039-44; discussion 1044-5.

25. Abdallah AO, Atrash S, Shahid Z. Patterns of central nervous system involvement in relapsed and refractory multiple myeloma. Clin Lymphoma Myeloma Leuk 2014;14:211-4.

26. Goyal G, Gonsalves WI, Go RS, Kumar S. Clinical features and outcomes of plasmacytoma in the United States: Analysis using the national cancer data base. Blood. 2016;128:3249.

27. Gozzetti A, Cerase A, Lotti F. Extramedullary intracranial localization of multiple myeloma and treatment with novel agents: A retrospective survey of 50 patients. Cancer. 2012;118:1574-84.

28. Nandeesh BN, Rao S, Sadashiva N. Clinicopathological study of extra-axial small round cell tumors of the cranium. Neurol India. 2020;68:1175-82.

29. Ozsahin M, Tsang RW, Poortmans P. Outcomes and patterns of failure in solitary plasmacytoma: A multicenter rare cancer network study of 258 patients. Int J Radiat Oncol Biol Phys. 2006;64:210-7.

30. Thumallapally N, Meshref A, Mousa M, Terjanian T. Solitary plasmacytoma: Population-based analysis of survival trends and effect of various treatment modalities in the USA. BMC Cancer. 2017;17:443.

31. Gagliardi F, Losa M, Boari N. Solitary clival plasmocytomas: Misleading clinical and radiological features of a rare pathology with a specific biological behaviour. Acta Neurochir (Wien). 2013;155:1849-56.

32. Na'ara S, Amit M, Gil Z, Billan S. Plasmacytoma of the skull base: A meta-analysis. J Neurol Surg B Skull Base. 2016;77:61-5.

33. Pritchard PB, Martinez RA, Hungerford GD, Powers JM, Perot PL, Jr. Dural plasmacytoma. Neurosurgery. 1983;12:576-9.

34. Wong ET, Lu XQ, Devulapalli J, Mahadevan A. Cyberknife radiosurgery for basal skull plasmacytoma. J Neuroimaging. 2006;16:361-3.

35. Annibali O, Nobile C, Greco R. The combination topotecan, temozolomide and dexamethasone associated with radiotherapy as treatment of central nervous system myeloma relapse. Int J Hematol. 2009;89:513-6.

36. Nahi H, Svedmyr E, Lerner R. Bendamustine in combination with high-dose radiotherapy and thalidomide is effective in treatment of multiple myeloma with central nervous system involvement. Eur J Haematol. 2014;92:454-5.

37. Aviles A, Huerta-Guzman J, Delgado S, Fernandez A, Diaz-Maqueo JC. Improved outcome in solitary bone plasmacytomata with combined therapy. Hematol Oncol. 1996;14:111-7.