Original Article

Preoperative blood testing for glioblastoma, brain metastases, and primary central nervous system lymphoma differentiation

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Background: Differentiating glioblastoma (GBM), brain metastases, and primary central nervous system lymphoma (PCNSL) in clinical practice is difficult. This study aimed to evaluate the diagnostic value of routine blood biomarkers in patients with GBM, brain metastases, and PCNSL and find a preoperative differential diagnostic tool for these tumors.

Methods: The perioperative medical records of 70 GBM, 41 PCNSL, and 81 brain metastases patients and their preoperative blood test results were compared and analyzed, and a diagnostic model to differentiate among them established.

Results: Patient age, plateletcrit, international normalized ratio (INR), and thrombin time (TT) were independently associated with differential diagnosis by multinomial logistic regression. Compared with GBM patients, brain metastases patients were significantly older (OR =1.055, 95% CI: 1.016–1.094, P=0.005) and had lower plateletcrit levels (OR =0.008, 95% CI: 0.004–0.017, P=0.027). In addition, patients with GBM had lower INR and higher TT than patients with the other two tumor types. A diagnostic model including these parameters, had an accuracy of 88.2% and 76.1% for brain metastases and GBM, respectively.

Conclusions: Preoperative plateletcrit, INR, and TT may be used as inexpensive blood diagnostic biomarkers for differentiating brain metastases from other intracranial malignant tumors.

Keywords: Brain metastases; glioblastoma (GBM); primary central nervous system lymphoma (PCNSL)

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Introduction

Glioma, brain metastases (BM), and primary central nervous system lymphoma (PCNSL) are common solid tumors located in the supratentorial brain parenchyma. Considering the pathological type, glioblastoma (GBM) and BM from lung adenocarcinoma are the most frequent types of glioma and BM (1,2). Their clinical presentation is similar to that of PCNSL, including headache, nausea, and vomiting caused by intracranial hypertension (2). In clinical practice, the presence of a mass in the brain makes it easy to diagnose a BM in patients who previously had a malignant tumor elsewhere in the body. However, in patients first identified by their brain lesion symptoms and without other malignant tumor pathography, a diagnosis of BM is very difficult, especially in case of solitary brain metastases (sBM). Besides, the significance of conventional neuroimaging techniques like CT and MRI is also limited because the three types of cancer all have signs of mass effect and

edema. Thus, it is difficult to achieve a differential diagnosis among GBM, PCNSL and BM only considering symptoms or with common radiology methods.

Further, the treatment after definitive histological diagnosis of these three types of tumors is remarkably different. GBM and PCNSL's treatment is more concerned with the control of intracranial tumors, while BM's usually requires dealing with lung lesions (2-4). In addition, the preoperative management also differs. GBM and metastatic brain tumors can be treated with a combination of dexamethasone and mannitol in patients with significant discomfort due to intracranial hypertension. However, PCNSL cannot be treated by this therapy regimen to avoid the disappearance of PCNSL tumor lesions in MRI (4). Therefore, an accurate diagnosis is crucial for the appropriate selection of preoperative treatment and surgery strategy.

Advanced neuroimaging techniques such as diffusion tensor imaging, multivoxel proton magnetic resonance spectroscopic imaging, and dynamic susceptibility contrast–perfusion weighted imaging have been used to identify brain lesions such as those in GBM, BM, and PCNSL (5-7). However, these advanced methods are neither specific for definitive diagnosis nor cost-effective for clinical practice.

However, changes in the levels of white blood cells, neutrophils, lymphocytes, monocytes, platelets, C-reactive protein, albumin, international normalized ratio (INR), thrombin time (TT), and some other parameters are frequently used to characterize the inflammatory response and coagulatory function in patients (8-10). Obtaining these blood test parameters is simple, low-cost, and widely applied preoperatively. Recent studies have reported that blood biomarkers such as red blood cell width, neutrophil/lymphocyte ratio (NLR), derived NLR, platelet/lymphocyte ratio, and lymphocyte/monocyte ratio have been identified as useful biomarkers in cancer diagnosis and prognosis prediction (8,11-13). However, their clinical value for the differential diagnosis of GBM, BM, and PCNSL is unclear.

The aim of this study was to evaluate the diagnostic significance of routine blood biomarkers in patients with GBM, sBM, and PCNSL, and its potential as a promising preoperative differential diagnostic tool. We present the following article in accordance with the STARD reporting checklist (available at https://tcr.amegroups.com/article/view/10.21037/tcr-21-1957/rc).

Methods

Patients

A total of 323 patients, including 92 with GBM, 185 with sBM, and 46 with PCNSL who underwent surgery at the Department of Neurosurgery at the Chinese National Cancer Center between November 2018 and March 2020 were selected and retrospectively analyzed. Patients included in the study had to meet the following criteria: (I) GBM, sBM, and PCNSL verified by pathological diagnosis; (II) no prior medical history and treatment with radiotherapy or chemotherapy; (III) no peripheral hematological or infectious diseases, pyrexia, serious vital organ dysfunction, autoimmune or inflammatory disease, or medication use related to an inflammatory condition; (IV) complete information of preoperative blood test; (V) solitary tumor on MRI/CT scan; and (VI) informed consent for treatment. The study was conducted in accordance with the Declaration of Helsinki (as revised in 2013). This study was approved by the Ethics Committee of Cancer Hospital, Chinese Academy of Medical Sciences (No. NCC2014G-12) and requirement of individual consent for this retrospective analysis was waived.

Data collection and study design

A database was created for the 323 patients mentioned above. Pertinent preoperative information, including demographic data, surgical pathologic findings, preoperative routine blood test outcomes, coagulation function test outcomes, and biochemistry test results were entered into the database. There are 70 parameters were included: White blood cell, Neutrophil rate, Neutrophil value, Monocyte rate, Monocyte value, Lymphocyte rate, Lymphocyte value, Eosinophils rate, Eosinophils value, Basophilic rate, Basophilic value, Blood platelet, Red blood cell, Hemoglobin, Hematocrit value, Mean corpuscular erythrocyte volume, Hemoglobin red blood cell, Hemoglobin concentration red blood cell, Red blood cell width distribution, Red blood cell width variation, Mean platelet volume, Large scale platelet rate, Platelet width distribution, Plateletcrit, Granulofilocyte, Alanine aminotransferase, Aspartate aminotransferase, Lactate dehydrogenase (LDH), γ-glutamyl transpeptidase, Alkaline phosphatase, Hydroxybutyrate-dehydrogenase, Creatine Kinase, Triglyceride, High density lipoprotein cholesterol, Low density lipoprotein Cholesterol, β2-macroglobulin, Immunoglobulin A, Immunoglobulin G, Immunoglobulin M, Total protein, Albumin, Globulin, Albumin/Globulin ratio, Prealbumin, Lipoprotein a, Superoxide dismutase, Homocysteine, C-reactive protein, α1-globulin, α2-globulin, β1-globulin, β2-globulin, γ-globulin, Adenosine deaminase, Apolipoprotein B, Apolipoprotein A1, Prothrombin time,

Prothrombin time activity, INR, TT, D-Dimer, Fibrin degradation product (FDP), Fibrinogen, Activated partial thromboplastin time, Antithrombin III, NLR, Platelet/Lymphocyte ratio, Lymphocyte/Monocyte ratio patient sex and patient age. Patients not meeting the inclusion criteria were excluded from the study. The enrolled patients were classified into three different tumor groups: GBM, PCNSL, and sBM, according to their pathological diagnosis, and preoperative clinical blood test parameters, including blood routine test, biochemical examination and coagulation action test, compared between groups. To make full use of the data, we trisected the INR and TT into three levels. The INR classification was summarized as level 0 (≤0.91), level 1 (0.92–0.98) and level 2 (≥0.99). The TT classification was summarized as level 0 (≤17 s), level 1 (17.10–18.90 s), and level 2 (≥19 s).

Statistical analysis

Statistical analysis was performed using SPSS (version 23.0, SPSS Inc.). The Kolmogorov-Smirnov test was used to determine the normal distribution of the variables. None of the data in our study were normally distributed so they are presented as median with interquartile range (IQR). For nonparametric data, the Kruskal-Wallis test was used for comparisons among the three tumor groups. The chi-square test was used to assess categorical variables. A filtration multinomial logistic regression model was used to identify efficient predictors from numerous parameters. Parameters extracted by the above test were input into a multinomial logistic regression to find the correlation between them and the three tumors. Statistical significance was set at P<0.05.

Results

Baseline parameters and potential diagnostic biomarkers

All 323 surgical patients were included in the study. Among these, 131 were eventually excluded due to incomplete baseline data and multiple intracranial lesions. Accordingly, 192 patients were enrolled in our cohort, including 70 patients with GBM, 41 patients with PCNSL, and 81 patients with sBM.

We collected 70 parameters from routine preoperative blood examination and demographic characteristics, of which 23 were found to have significant differences among GBM, sBM, and PCNSL. These parameters are listed in *Tables 1*,*2*. The median age (IQR) for patients with GBM, PCNSL, and sBM was 53 years [41–64], 59.5 years [48–64] and 59.5 years [52–67], respectively, and significantly different (P=0.015) among groups, as were white blood cells and neutrophil values or biochemical parameters such as lactate dehydrogenase (LDH) and β2-macroglobulin (β2-MG) (*Table 1*).

Calculated laboratory parameters such as NLR (P=0.048) and coagulation function parameters such as fibrin degradation product (FDP) (P=0.015), TT (P<0.001), and INR (P<0.001) significantly differed among the three brain tumors (*Tables 1*,*2*).

Diagnostic biomarker filtration

To find a more efficient method, we used a multinomial logistic regression model as a filtration tool to choose the most important diagnostic predictors among the 23 parameters, finding that the model's diagnostic accuracy negatively correlated with the cut-off value. When the cut-off value decreased, the predicted parameter and accuracy increased. As shown in *Figure 1*, for >8 parameters the accuracy does not increase much, and the cut-off value is <0.48. Therefore, we chose eight parameters as predictive factors in the multinomial logistic regression, namely, patient age, PCT, LDH, β2-MG, α2-globulin (α2-G), INR, TT, and FDP. All these parameters differed between GBM, PCNSL, and sBM (*Figure 2*).

Multinomial logistic regression analysis of diagnostic factors

Age, PCT, LDH, β2-MG, α2-G, INR, TT, and FDP were subjected to multinomial logistic regression analysis to identify useful diagnostic factors for differentiating GBM, PCNSL, and sBM. In the multinomial logistic regression, we set the GBM as the reference object. As shown in *Table 3*, we found that patient age, PCT, INR, and TT were significantly associated with a differential diagnosis of the three brain tumors. For differentiating among GBM, PCNSL, and sBM, we determined that patient age was independently associated with sBM (OR =1.055, 95% CI: 1.016–1.094, P=0.005), whereas PCT was independently negatively associated with sBM (OR =0.008, 95% CI: 0.004–0.017, P=0.027). Furthermore, while classifying INR and TT, we found that INR had an independently positive correlation with PCNSL and sBM when compared with GBM; however, TT was negatively correlated with PCNSL and sBM. Compared with patients with level 2 (≥0.99) INR,

Table 1 Univariate analysis of blood and clinical parameters among glioblastoma, PCNSL and solitary brain metastases

Variable	GBM	PCSNL	Solitary brain metastasis	P*
Age (years) {median [IQR]}	53.00 [41, 64]	59.50 [48, 64]	59.50 [52, 67]	0.015
White blood cell (10^9/L) {median [IQR]}	7.36 [5.90, 9.42]	6.66 [5.47, 7.88]	7.73 [6.14, 10.14]	0.016
Neutrophil value (10^9/L) {median [IQR]}	4.61 [3.44, 7.18]	4.17 [3.30, 5.52]	5.13 [4.05, 7.09]	0.01
Monocyte rate (%) {median [IQR]}	6.20 [4.40, 7.70]	6.60 [5.48, 8.67]	5.55 [4.18, 7.40]	0.044
Basophilic value (10^9/L) {median [IQR]}	0.02 [0.01, 0.03]	0.03 [0.02, 0.04]	0.03 [0.02, 0.05]	0.006
Blood platelet (10^9/L) {median [IQR]}	236.50 [195.25, 274.00]	215.50 [185.75, 255.00]	250.50 [201.75, 315.25]	0.02
Mean platelet volume (fL) {median [IQR]}	10.60 [9.97, 11.50]	10.45 [9.90, 11.40]	10.20 [9.50, 10.72]	0.024
Large scale platelet rate (%) {median [IQR]}	29.30 [24.20, 36.50]	28.25 [23.95, 35.90]	26.25 [20.50, 31.00]	0.02
PCT (%) {median [IQR]}	0.25 [0.12, 0.55]	0.22 [0.12, 0.37]	0.25 [0.10, 0.47]	0.028
LDH (U/L) {median [IQR]}	157.50 [142.75, 180.50]	174.00 [155.00, 203.75]	170.00 [148.00, 199.25]	0.017
HBDH (U/L) {median [IQR]}	130.00 [116.00, 148.75]	141.00 [126.25, 169.75]	133.00 [115.50, 152.00]	0.031
CK (U/L) {median [IQR]}	51.50 [38.00, 70.25]	51.00 [36.25, 81.75]	42.00 [31.75, 52.25]	0.011
β2-MG (mg/L) {median [IQR]}	1.60 [1.30, 1.90]	1.80 [1.52, 2.40]	1.70 [1.50, 2.10]	0.005
G (g/L) {median [IQR]}	25.25 [22.58, 27.58]	26.85 [25.15, 30.87]	25.95 [23.65, 28.25]	0.025
α1-G (%) {median [IQR]}	3.90 [3.50, 4.30]	3.80 [3.50, 4.30]	4.10 [3.70, 4.60]	0.02
α2-G (%) {median [IQR]}	9.70 [8.28, 10.33]	9.45 [8.83, 10.23]	10.00 [9.40, 11.30]	0.002
β1-G (%) {median [IQR]}	5.90 [5.57, 6.40]	5.75 [5.32, 6.00]	5.75 [5.40, 6.10]	0.046
γ-G (%) {median [IQR]}	15.75 [13.67, 16.92]	16.95 [16.30, 19.48]	15.85 [13.78, 17.85]	0.001
D-D (mg/L) {median [IQR]}	0.32 [0.23, 0.54]	0.60 [0.30, 0.94]	0.35 [0.21, 0.63]	0.015
FDP (μg/mL) {median [IQR]}	3.02 [2.38, 3.34]	3.07 [2.56, 3.46]	3.16 [2.80, 3.86]	0.015
NLR {median [IQR]}	2.52 [1.73, 5.20]	2.30 [1.68, 3.30]	2.84 [2.13, 4.64]	0.048

*, all P values are reported as Kruskal-Wallis test between glioblastoma, brain metastases and primary central nervous lymphoma. And P<0.05 was considered statistically significant. IQR, interquartile range; PCT, plateletcrit; LDH, lactate dehydrogenase; HBDH, hydroxybutyrate-dehydrogenase; CK, Creatine Kinase; β2-MG, β2-macroglobulin; G, globulin; α1-G, α1-globulin; α2-G, α2-globulin; β1-G, β1-globulin; γ-G, γ-globulin; D-D, D-Dimer; FDP, fibrin degradation product; NLR, neutrophil/lymphocyte ratio; GBM, glioblastoma; PCNSL, primary central nervous lymphoma.

Table 2 Univariable test for classification of INR and TT

	Range	GBM	PCNSL	Solitary Brain Metastasis	χ^2	P*
INR						
Level 0	≤0.91	33 (47.1%)	11 (26.8%)	18 (22.2%)		
Level 1	0.92–0.98	29 (41.4%)	12 (29.3%)	22 (27.2%)		
Level 2	≥0.99	8 (11.4%)	18 (43.9%)	41 (50.6%)	27.97	<0.001
TT (s)						
Level 0	≤17 s	10 (14.3%)	10 (24.4%)	45 (55.6%)		
Level 1	17.10–18.90 s	15 (21.4%)	20 (48.8%)	27 (33.3%)		
Level 2	≥19 s	45 (64.3%)	11 (26.8%)	9 (11.1%)	58.43	<0.001

*, all P values are reported as χ^2 comparisons between glioblastoma, brain metastases and primary central nervous lymphoma. And P<0.05 was considered statistically significant. INR, international normalized ratio; TT, thrombin time; GBM, glioblastoma; PCNSL, primary central nervous lymphoma.

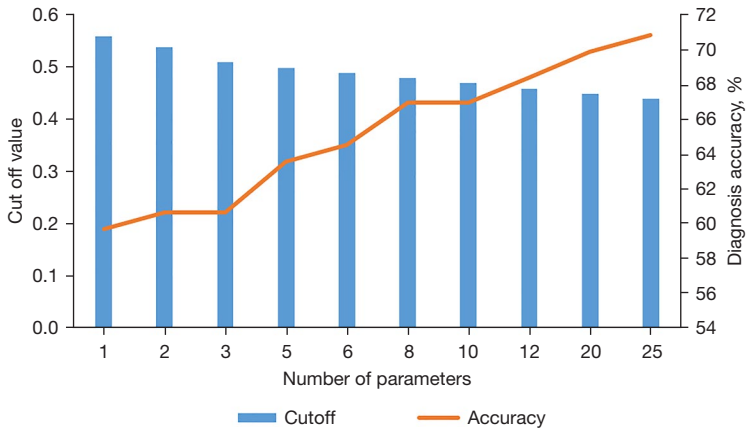

Figure 1 Diagnosis accuracy increase trend begins to slow down when the number of parameters is more than 8 and cut off value is below 0.48. The horizontal axis represents the number of parameters used in the filtration multinomial logistic regression model. The left vertical axis represents calculated cut off value and the right vertical axis represents the diagnosis accuracy.

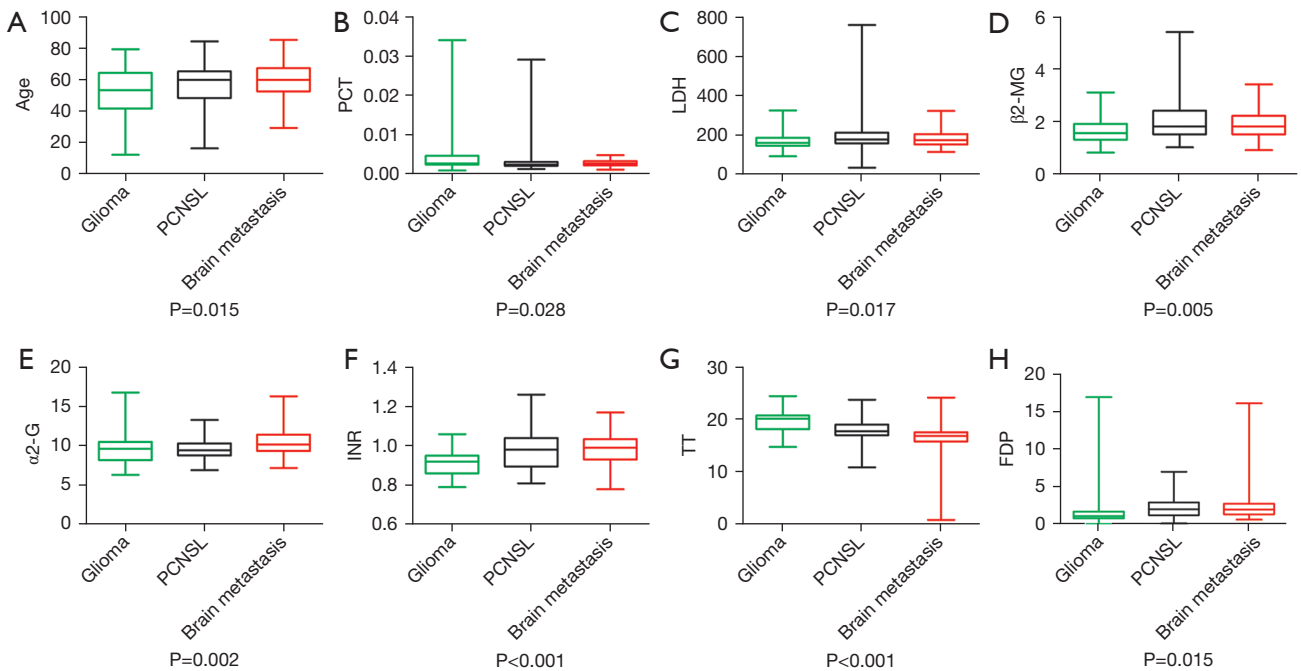

Figure 2 Comparison of different parameters between glioblastoma (GBM), primary central nervous system lymphoma (PCNSL) and solitary brain metastases (sBM): (A) patient age; (B) plateletcrit (PCT); (C) lactate dehydrogenase (LDH); (D) β2-macroglobulin (β2-MG); (E) α2- globulin (α2-G); (F) international normalized ratio (INR); (G) thrombin time (TT) and (H) fibrin degradation product (FDP).

level 0 (OR =0.11, 95% CI: 0.029–0.413, P=0.001) and level 1 (OR =0.119, 95% CI: 0.032–0.442, P=0.001) patients were more likely to be diagnosed with GBM than sBM. In contrast, compared with patients with level 2 (≥19 s) TT, level 0 (OR =16.31, 95% CI: 5.188–51.26, P<0.001) and level 1 (OR =6.455, 95% CI: 2.07–20.13, P=0.001) patients were more prone to be diagnosed as sBM than GBM. The same trend was observed when comparing PCNSL with GBM; patients with INR level 0 (OR =0.166, 95% CI: 0.044–0.619, P=0.007) and level 1 (OR =0.181, 95% CI: 0.047–0.694, P=0.013) were more prone to develop GBM than patients with INR level 2. Patients with TT level 1 (OR

Table 3 Result of multinomial logistic regression analysis

Variable	PCNSL					sBM				
	95% CI					95% CI				
	b	OR	Lower	Upper	P	b	OR	Lower	Upper	P
Intercept	–2.300					–3.544				
LDH	0.009	1.009	0.998	1.021	0.099	0.005	1.005	0.994	1.016	0.374
β2-MG	0.357	1.429	0.540	3.787	0.472	–0.552	0.576	0.206	1.607	0.292
α2-G	–0.147	0.863	0.647	1.152	0.317	0.154	1.166	0.900	1.510	0.245
FDP	0.029	1.029	0.843	1.256	0.776	0.045	1.046	0.827	1.325	0.706
Age	0.032	1.033	0.996	1.071	0.083	0.053	1.055	1.016	1.094	0.005*
PCT	–3.318	0.013	0.009	19.16	0.397	–200.3	0.008	0.004	0.017	0.027*
INR										
Level 0	–1.798	0.166	0.044	0.619	0.007*	–2.206	0.110	0.029	0.413	0.001*
Level 1	–1.710	0.181	0.047	0.694	0.013*	–2.132	0.119	0.032	0.442	0.001*
Level 2			Reference					Reference		
TT										
Level 0	1.075	2.931	0.883	9.732	0.079	2.792	16.31	5.188	51.26	<0.001*
Level 1	1.271	3.566	1.231	10.331	0.019*	1.865	6.455	2.070	20.13	0.001*
Level 2			Reference					Reference		

*, all P values are reported as multinomial logistic regression model involved glioblastoma, solitary brain metastases and primary central nervous lymphoma and P<0.05 was considered statistically significant. b was reported as regression coefficient in multinomial logistic regression analysis. PCT, plateletcrit; LDH, lactate dehydrogenase; β2-MG, β2-macroglobulin; α2-G, α2-globulin; FDP, fibrin degradation product; INR, international normalized ratio; TT, thrombin time; PCNSL, primary central nervous lymphoma; sBM, solitary brain metastases.

=3.566, 95% CI: 1.231–10.331, P=0.019) were more prone to PCNSL than patients with TT level 2.

Preoperative diagnostic model efficacy

The formula for the diagnostic model was as follows: PrY1 = In (PCNSL/GBM) = intercept + $\sum_{k=1}^{n} b_k x_k$, PrY2= In (sBM/GBM) = intercept + $\sum_{k=1}^{n} b_k x_k$, PrY3=0 (reference). Where "intercept" represents the constant of the regression model, "b0…bn" the regression model coefficients and x1…xn predictor variables. All of these parameters are listed in *Table 3*. We input the eight parameters into this formula to calculate the PrY1, PrY2, and PrY3 values. Then, we used the formula: P1=exp (PrY1)/[exp (PrY1) exp (PrY2) exp (PrY3)], P2=exp (PrY2)/[exp (PrY1) exp (PrY2) exp (PrY3)], P3= exp (PrY3)/[exp (PrY1) exp (PrY2) exp (PrY3)] to calculate the possibility of PCNSL (P1), sBM (P2), and GBM (P3). The diagnostic model chose the maximum value as a result.

The diagnostic accuracy rate for this multinomial regression model is shown in *Table 4*. The diagnosis accuracy was best in sBM (correct percentage =88.2%), for GBM it was 76%, and for PCNSL only 22%.

Discussion

Since GBMs, sBM, and PCNSLs tend to have similar clinical symptoms and radiological characteristics (2,14,15), their differential diagnosis remains a clinical challenge. In the present study, we identified 23 parameters significantly different between GBM, sBM, and PCNSL. However, 23 prediction parameters were inconvenient for differential diagnosis, and a more efficient and laconic method should be adopted. Among those, we chose age, PCT, LDH, β2-M, α2-G, INR, TT, and FDP to build the diagnosis model. Among these eight indicators, PCT, INR, and TT might be used as biomarkers to independently differentiate GBM,

Table 4 The correct rate of multinomial logistic regression diagnosis model for diagnosis

Tumor diagnosis	Predicted			Correct rate
	GBM	PCNSL	Solitary brain metastasis	
GBM	51	6	10	76.1%
PCNSL	14	9	18	22.0%
Brain metastasis	7	2	67	88.2%

GBM, glioblastoma; PCNSL, primary central nervous lymphoma.

PCNSL, and sBM.

Platelets play an important role in the physiology of primary hemostasis and in the pathophysiological activity of arterial thrombosis. PCT is calculated by mean platelet volume and platelet count, which describes the platelet mass in a unit of volume, such as hematocrit for erythrocytes (16,17). In previous studies, PCT was used to identify the disease stage of autoimmune gastritis, coronary artery disease, diabetes mellitus, and pulmonary tuberculosis (18,19). Recently, some studies have reported the association between PCT and tumors. Higher PCT levels were found in papillary thyroid carcinoma patients than in healthy controls and multinodular goiters (20). In addition, high PCT levels have been associated with a poor prognosis of pancreatic adenocarcinoma and non-small cell lung cancer (21,22). However, studies focusing on the diagnostic significance of PCT are limited. In our study, PCT was independently and negatively associated with sBM. sBM patients were more prone to having lower PCT levels than GBM patients. Platelets also play a crucial role in the pathophysiology of inflammation, especially in vascular inflammation (23-25). PCT as an inflammatory biomarker also differ between GBM and sBM. Although the mechanism for lower PCT levels in sBM remains unknown, PCT may be a valuable parameter to distinguish sBM from GBM. Cancer cells can activate the hemostatic system through the expression of procoagulant proteins, exposure of procoagulant lipids, inflammatory cytokine release, and adhesion to host vascular cells, thus increasing the risk of both thrombosis and hemorrhage (26,27). Tissue factor (TF) is the most typical cancer procoagulant, which leads to excessive coagulation triggering with the consequent thrombi formation and results in a reduction of prothrombin time (PT) and INR. TF expression has been reported to be particularly high in GBM (28,29). Our results showing that GBM patients had a lower INR level than PCNSL and sBM patients agreed with this phenomenon. In addition, prolonged PT and INR have been significantly associated with adverse prognosis in lung cancer patients (30). Thus, INR may have diagnostic and prognostic value in patients with malignancy, even though the mechanisms are still not completely understood and require further investigation.

In contrast, we found that patients with sBM were more likely to have a lower TT level. Heparinase can degrade heparin and heparin sulfates in the extracellular matrix, thus promoting tumor invasion and reducing the content of internal heparin (26). TT is a common hemostatic parameter used to describe fibrinolytic function and significantly interferes with the serum heparin level. Compared with GBM, sBM have a stronger capacity for invasion and metastasis. Heparinase in sBM may be more active or abundant than in GBMs, which prolongs TT in sBM.

Our diagnostic model utilized eight blood parameters to discriminate between GBM, PCNSL, and sBM, and had an accuracy of 76.1% and 88.2% in GBM and sBM, respectively, suggesting its usefulness in identifying GBM and sBM. It has been reported that the accuracy of advanced neuroimaging techniques for differentiating GBM, BM, and PCNSL ranges from 80% to 90% (15,31). Our diagnostic model presents a diagnostic accuracy comparable to that, but at a lower cost. Nevertheless, the present model was less precise in diagnosing PCNSL, with a diagnostic accuracy of 22%. The low number of PCNSL patients enrolled in this study may be a potential reason for this issue.

There are some limitations to our study. First, this research is the result of a nonrandomized retrospective study in a single center, having the typical limitations of such a study design. Second, the sample size of PCNSL patients was insufficient. Third, the major type of sBM enrolled in our study was lung cancer. Although the most common primary tumor associated with sBM, other types

of cancer need to be further studied.

Conclusions

Despite these limitations, our results provide valuable insights for neurosurgeons differentiating GBM, PCNSL, and sBM before surgery. Our findings showed that PCT, INR, and TT significantly differed between the GBM, PCNSL, and sBM patients in our study. In multinomial logistic regression analysis, PCT and TT were independently and negatively associated with sBM than with GBM, and INR was a positive predictor for diagnosis of sBM rather than GBM. Therefore, preoperative PCT, INR, and TT are useful supplementary methods for differentiating patients with sBM from other intracranial malignant tumors.

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Footnote

Reporting Checklist: The authors have completed the STARD reporting checklist. Available at https://tcr.amegroups.com/article/view/10.21037/tcr-21-1957/rc

Data Sharing Statement: Available at https://tcr.amegroups.com/article/view/10.21037/tcr-21-1957/dss

Conflicts of Interest: All authors have completed the ICMJE uniform disclosure form (available at https://tcr.amegroups.com/article/view/10.21037/tcr-21-1957/coif). The authors have no conflicts of interest to declare.

Ethical Statement: The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. The study was conducted in accordance with the Declaration of Helsinki (as revised in 2013). This study was approved by the Ethics Committee of Cancer Hospital, Chinese Academy of Medical Sciences (No. NCC2014G-12) and individual consent for this retrospective analysis was waived.

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