



Medulloblastoma and ABO-Rh Blood Group: Evidence of an Association between the Distribution of Blood Group Antigens and Medulloblastoma

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Abstract

Objective Medulloblastoma is the most common central nervous system embryonal tumor and the most common malignant brain tumor of childhood. This study aims to find out the incidence of the ABO-Rh blood group in medulloblastoma patients of northern India to assess the utility of the blood group as a preclinical non-modifiable risk factor.

Materials and Methods The study cohort consisted of 87 pediatric patients (age up to 18 years) who were diagnosed after histopathological examination with medulloblastoma at a university hospital in Lucknow between 2014 and 2019. Hundred random pediatric individuals from the same population who were admitted to the same hospital between 2014 and 2019 for non-tumor cases were selected as the control group. Data concerning characteristics including age, sex, ABO blood group, and Rh factor were collected from hospital records. The distribution of ABO-Rh blood groups in the study population was compared with the general population using the χ^2 test. Statistical analysis of the ABO-Rh blood groups in the study population was done using the IBM SPSS statistics version 24.0.

Results Data analysis revealed that blood group A was significantly associated with medulloblastoma cases (odds ratio [OR] = 2.93; 95% confidence interval [CI]: 1.35–6.34). We find that the classical subtype was prevalent with the blood group A (43.8%), while the desmoplastic subtype was associated with the blood group O (38.5%).

Conclusion Blood group A has a higher risk for the development of medulloblastoma while blood group O has the least risk. These findings suggest that blood group antigen should be considered as a non-modifiable preclinical risk factor for developing medulloblastoma.

Keywords

- ▶ medulloblastoma
- ▶ ABO-Rh
- ▶ blood groups antigens

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Introduction

Cancer is one of the most important causes of death worldwide and its management is the principal cause for concern. Many factors have been evaluated in the pathogenesis of cancer and ABO blood group antigens expressed on red blood cells is one of them. Several studies have confirmed a link between the distribution of ABO blood group antigens and the risk of developing gastric, pancreatic, ovarian, breast, and nasopharyngeal cancer.¹⁻⁴ A few studies have been done correlating the ABO blood group antigen and intracranial neoplasm but with conflicting results. Allouh et al reported a higher incidence of glioblastoma in individuals with blood group A while Kumarguru et al reported no significant association between the central nervous system (CNS) neoplasm and the ABO blood group.^{5,6} Medulloblastoma is the most common malignant CNS embryonal tumor of childhood. No study determining the relation between the ABO blood group and medulloblastoma in the pediatric age group has been done in the past. In the present study, we aimed to investigate the relationship between the distributions of ABO-Rh blood group antigens in pediatric medulloblastoma patients of northern India to assess the utility of the blood groups as a non-modifiable preclinical risk factor.

Materials and Methods

The study cohort consisted of 87 pediatric patients (age up to 18 years) who were diagnosed with medulloblastoma at a university hospital in Lucknow between 2014 and 2019. Diagnostic criteria include histopathological confirmation after surgery or biopsy from the tumor tissue. Age, sex, ABO blood group, and Rh factor of included patients were collected from hospital records. Hundred random pediatric individuals from the same population who were admitted to

the same hospital between 2014 and 2019 for non-tumor cases were selected as the control group. Data concerning characteristics of the control groups including age, sex, ABO blood group, and Rh factor were collected from blood bank records from the same hospital.

Statistical Analysis

The statistical analysis was done using the IBM SPSS statistics version 24.0. Categorical variables were compared using the χ^2 test. Continuous variables were compared using the independent sample *t*-test. Odds ratios (OR) and corresponding 95% confidence interval (CI) were calculated. For the blood groups, OR was calculated using logistic regression. Blood group O was taken as the reference group and other groups were compared with the reference group.

Results

This study was designed with the aim to find out an association of the blood group of the north Indian population with the medulloblastoma. Here, our investigation suggests that out of 87 patients, predominantly, males were affected more than the females with an M:F ratio of 2.2:1 (►Table 1). A summary of the characteristics of medulloblastoma patients and control populations is provided in ►Table 1. The cases and control group in terms of age and sex distribution were comparable and had a similar distribution in this study ($p > 0.05$, ►Table 1).

Medulloblastoma Patients versus Controls

Our data suggest that the distribution of the blood groups in patients for O, B, AB, and A were 34, 36, 8, and 22%, respectively, in the control group while these were 21.8, 26.4, 10.3, and 41.4%, respectively, in the medulloblastoma

Table 1 Characteristics of pediatric medulloblastoma patients and control group and its correlation with blood groups.

Variable	Cases N = 87	Control N = 100	p-Value	Odds ratio (95% confidence interval)
Blood group				
O	19 (21.8%)	34 (34.0%)	0.021	Ref.
B	23 (26.4%)	36 (36.0%)		1.14 (0.53–2.46)
AB	9 (10.3%)	8 (8%)		2.01 (0.67–6.08)
A	36 (41.4%)	22 (22%)		2.93 (1.35–6.34)
Rh factor				
Positive	84 (96.6%)	97 (97.0%)	0.862	0.87 (0.17–4.40)
Negative	3 (3.4%)	3 (3%)		
Sex				
Male	60 (69%)	69 (69%)	0.996	0.99 (0.54–1.86)
Female	27 (31%)	31 (31%)		
Age \pm SD in years	7.37 \pm 3.76	7.97 \pm 4.95	0.346	7.37 \pm 3.76

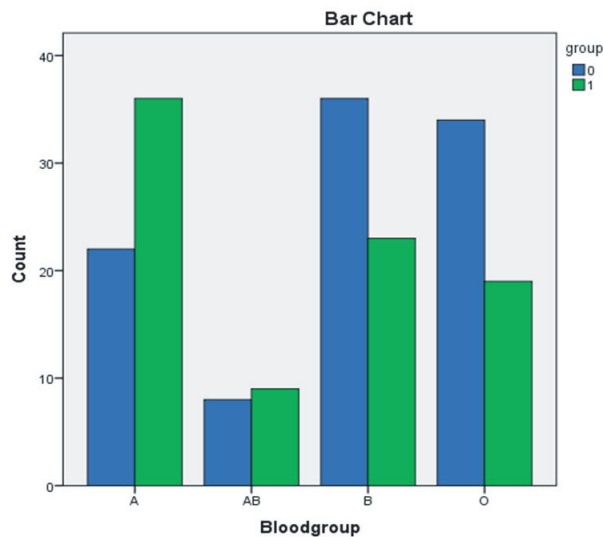


Fig. 1 Bar Graphical representation of results. Group 0: control, Group 1: cases.

patients (►Fig. 1 and ►Table 1). We observed that the distribution of blood groups between cases and control groups was significantly different ($p < 0.05$; ►Table 1). Further, we also observed that blood group A was significantly associated with medulloblastoma (OR = 2.93, 95% CI = 1.35–6.34; ►Table 1). In our investigation, we observed that the distribution of Rh⁺ blood group in cases and control groups were 96.6 and 97%, respectively, while it was 3.4 and 3% for Rh⁻ blood group. Analysis suggests that there was no significant difference in the distribution of Rh factor between case and control groups ($p = 0.862$, ►Table 1).

Medulloblastoma Patients Subtype Association with Blood Group

On the basis of the histopathological report of 87 patients, 73 patients were classified as Classical type, 13 as desmoplastic type, while one falls in a large cell type (►Table 2). The distribution of subtype of medulloblastoma was compared with the blood groups in the patients. We observed that classical type medulloblastoma distribution with blood groups A, B, AB, and O were 43.8, 26, 11, and 19.2%, respectively (►Table 2). Further, we observed that desmoplastic type distribution in patients with A, B, AB, and O blood groups were 23.1, 30.8, 7.7, and 38.5%, respectively (►Table 2). However, there was no significant association of the type of medulloblastoma with the specified blood group in patients ($p = 0.587$; ►Table 2). It was observed that the distribution of Rh⁺ blood groups with the classical, desmoplastic, and large cell subtype of medulloblastoma were 70, 13, and 1, respectively, while only classical subtype was observed in Rh⁻ group ($N = 3$). There was no significant association observed between Rh blood group and subtype of medulloblastoma ($p = 0.742$; ►Table 3).

Discussion

This is the first investigation of the association of the blood group and the medulloblastoma in the pediatric population in India. In our study, 60 patients were males and 27 females with a male to female ratio of 2.2:1. A similar preponderance of medulloblastoma cases was also observed in male patients by Muzumdar et al.⁷ In this study, the distribution of blood group in the control group was 34, 36, 8, and 22% for the O, B, AB, and A blood groups, respectively. A similar distribution with 37.12, 32.26, 7.74, and 22.8% for the O, B, AB, and A blood group was also observed in a pan India population

Table 2 Characteristics of medulloblastoma subtype and its correlation with the ABO blood group

Blood Group		Type			Total
		C	D	L	
A	Count	32	3	1	36
	% within type	43.8%	23.1%	100.0%	
AB	Count	8	1	0	9
	% within type	11.0%	7.7%	0.0%	
B	Count	19	4	0	23
	% within type	26.0%	30.8%	0.0%	
O	Count	14	5	0	19
	% within type	19.2%	38.5%	0.0%	
Total	Count	73	13	1	87
	% within type	100.0%	100.0%	100.0%	
Chi-square tests.					
		Value	df	p-Value	
Pearson Chi-square		4.669	6	0.587	
Likelihood ratio		4.924	6	0.554	
Number of valid cases		87			

Abbreviations: C, classical; D, desmoplastic; L, large cell; df, degree of freedom.

Table 3 Prevalence of medulloblastoma subtype and its correlation with Rh factor

Rh		Type			Total	
		C	D	L		
Negative	Count	3	0	0	3	
	% within type	4.1%	0.0%	0.0%	3.4%	
Positive	Count	70	13	1	84	
	% within type	95.9%	100.0%	100.0%	96.6%	
Total	Count	73	13	1	87	
	% within type	100.0%	100.0%	100.0%	100.0%	
Chi-square tests.						
		Value	df	p-Value		
Pearson Chi-square		0.596	2	0.742		
Likelihood ratio		1.073	2	0.585		
Number of valid cases		87				

Abbreviations: C, classical; D, desmoplastic; L, large cell; df, degree of freedom.

study (Amit et al), suggesting a best-fitted representative control group for this study.⁸ In our study, the distribution of the blood group in the patients was 21.8, 26.4, 10.3, and 41.4% for O, B, AB, and A and; in comparison to the control group, there is a reduction in the prevalence for O and B group by 36% and 27%, while an increase in the prevalence by 128 and 188% for AB and A groups, respectively (►Table 1). Interestingly, our study suggests a higher incidence of medulloblastoma in individuals with blood group A and the lowest incidence with blood group O compared with the control group, suggesting an association of blood group A with medulloblastoma. However, no significant association was established between Rh factor and its distribution with medulloblastoma (►Table 1). Previous studies have shown conflicting results regarding the association between ABO blood groups and medulloblastoma. Sowbhagya et al studied 94 patients of medulloblastoma and found a significantly higher frequency in patients with blood group B.⁹ Mehrazin studied 26 patients of medulloblastoma and found no significant association with the ABO blood group.¹⁰ In contrast, Atwell studied 48 patients with medulloblastoma and found a higher incidence in blood group O (46%); however, a comparison with controls was not disclosed in their study.¹¹ Pearce et al (1965) have studied 102 patients with medulloblastoma and with the similarity of our results, they also have unveiled an association of blood group A with the medulloblastoma incidences (48%).¹² In a systematic meta-analysis for the correlation of the blood group and cancer, Zhang et al have also established a significant relationship with the blood group A and suggested a significantly higher associated risk as compared with the non-A blood group.¹ As we have enrolled only pediatric medulloblastoma cases from the north Indian population and medulloblastoma cases are prevalent in the pediatric population, this investigation has an advantage over another study with its demography and selected age group.⁷ Our study provides supporting evidence about the possible association of ABO blood group antigens in the development of medulloblastoma.

Further, we investigated the prevalence of subtype of medulloblastoma in the pediatric population and we found mostly classical (83.9%) and desmoplastic (14.9%) subtypes. Furthermore, the association of the subtype of medulloblastoma (classical and desmoplastic) with the blood group type ABO was also investigated. We find that the classical subtype was prevalent with the A blood group (43.8%), while the desmoplastic subtype was associated with the blood group O (38.5%); however, the association was statistically insignificant ($p=0.587$; ►Table 2). Further, on investigating the association of Rh factor with the prevalence of medulloblastoma and its subtype prevalence in the pediatric population, we find no clear link between Rh factor and medulloblastoma or its subtypes (►Tables 1 and 3).

The mechanisms by which the ABO blood groups lead to cancer development and progression are still unclear. Many hypotheses have been proposed in this regard (►Fig. 2), including the modulatory role of ABO blood group

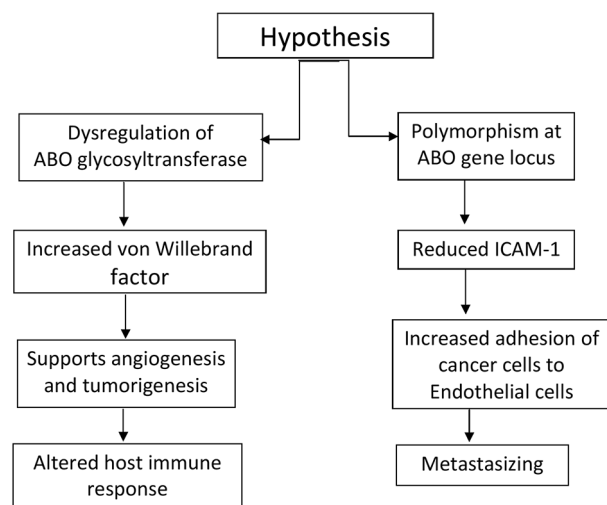


Fig. 2 Diagrammatic representation of the hypothesis suggesting the role of the ABO blood group in cancer causation.

antigens on several inflammatory and adhesion molecules that are important for tumorigenesis.¹³ Another hypothesis suggests the dysregulation of the enzymatic activity of ABO glycosyltransferases, which is involved in the processes of intercellular adhesion and cell membrane signaling, may promote the process of malignancy.^{14,15} ABO glycosyltransferases help in modulating the circulating plasma levels of von Willebrand factor (vWF), which is an important mediator of angiogenesis and apoptosis, which, in turn, are processes involved in cancer formation.^{16,17} Levels of plasma vWF increases substantially in various types of cancers, and a positive correlation has been found between these increase and the severity of the disease. Individuals with non-O blood groups have significantly higher levels of plasma vWF compared with individuals with blood group O and thus are more vulnerable to malignancies.^{18,19}

Conclusion

We have demonstrated an association between the distribution of ABO blood group antigens and the prevalence of pediatric medulloblastoma in the north Indian population. Individuals with blood group A have a higher risk of developing medulloblastoma in contrast to individuals with blood group O. These findings suggest that the blood group antigens should be considered as a non-modifiable preclinical risk factor for the development of medulloblastoma in a pediatric population. We highly recommend a comprehensive pan India surveillance and study of the prevalence of medulloblastoma in the pediatric population and a possible link with the blood group, its risks, and outcomes.

Conflict of Interest

None declared.

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References

- Zhang BL, He N, Huang YB, Song FJ, Chen KX. ABO blood groups and risk of cancer: a systematic review and meta-analysis. *Asian Pac J Cancer Prev* 2014;15(11):4643–4650
- Liumbruno GM, Franchini M. Beyond immunohaematology: the role of the ABO blood group in human diseases. *Blood Transfus* 2013;11(04):491–499
- Liumbruno GM, Franchini M. Hemostasis, cancer, and ABO blood group: the most recent evidence of association. *J Thromb Thrombolysis* 2014;38(02):160–166
- Franchini M, Liumbruno GM, Lippi G. The prognostic value of ABO blood group in cancer patients. *Blood Transfus* 2015;6:1–7
- Allouh MZ, Al Barbarawi MM, Hiasat MY, Al-Qaralleh MA, Ababneh EI. Glioblastoma and ABO blood groups: further evidence of an association between the distribution of blood group antigens and brain tumours. *Blood Transfus* 2017;15(06):543–547
- Kumarguru BN, Pallavi P, Sunila, Manjunath GV, Vasana TS, Rajalakshmi BR. Histopathological study of central nervous system lesions: emphasizing association of neoplasms with ABO blood groups. *J Clin Diagn Res* 2017;11(04):EC15–EC20
- Muzumdar D, Deshpande A, Kumar R, et al. Medulloblastoma in childhood-King Edward Memorial hospital surgical experience and review: comparative analysis of the case series of 365 patients. *J Pediatr Neurosci* 2011;6(Suppl 1):S78–S85
- Agrawal A, Tiwari AK, Mehta N, et al. ABO and Rh (D) group distribution and gene frequency; the first multicentric study in India. *Asian J Transfus Sci* 2014;8(02):121–125
- Sowbhagya P, Kolluri VR, Krishna DK, Das S, Das BS, Reddy GN. Intracranial tumours and blood groups. *Eur J Cancer* 1991;27(02):221–222
- Mehrazin M. ABO blood group frequency and brain tumors. *Asian Pac J Cancer Prev* 2006;7(04):582–584
- Atwell JD. Distribution of ABO blood groups in children with embryonic tumours. *BMJ* 1962;1(5271):89–90
- Pearce KM, Yates PO. Blood groups and brain tumours. *J Neurol Sci* 1965;2(05):434–441
- Hsiao LT, Liu NJ, You SL, Hwang LC. ABO blood group and the risk of cancer among middle-aged people in Taiwan. *Asia Pac J Clin Oncol* 2015;11(04):e31–e36
- Hakomori S. Antigen structure and genetic basis of histo-blood groups A, B and O: their changes associated with human cancer. *Biochim Biophys Acta* 1999;1473(01):247–266
- Roseman S. Reflections on glycobiology. *J Biol Chem* 2001;276(45):41527–41542
- Franchini M, Crestani S, Frattini F, Sissa C, Bonfanti C. ABO blood group and von Willebrand factor: biological implications. *Clin Chem Lab Med* 2014;52(09):1273–1276
- Franchini M, Frattini F, Crestani S, Bonfanti C, Lippi G. von Willebrand factor and cancer: a renewed interest. *Thromb Res* 2013;131(04):290–292
- Jenkins PV, O'Donnell JS. ABO blood group determines plasma von Willebrand factor levels: a biologic function after all? *Transfusion* 2006;46(10):1836–1844
- Nowacki P, Tabaka J. Human von Willebrand factor (factor VIII-related antigen) in glial neoplastic cells of brain gliomas. *Folia Neuropathol* 2003;41(01):23–27