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Classifying Pediatric Central Nervous System Tumors through near Optimal Feature Selection and Mutual Information: A Single Center Cohort

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Abstract

Background: Labeling, gathering mutual information, clustering and classification of central nervous system tumors may assist in predicting not only distinct diagnoses based on tumor-specific features but also prognosis. This study evaluates the epidemiological features of central nervous system tumors in children who referred to Mahak's Pediatric Cancer Treatment and Research Center in Tehran, Iran.

Methods: This cohort (convenience sample) study comprised 198 children (≤15 years old) with central nervous system tumors who referred to Mahak's Pediatric Cancer Treatment and Research Center from 2007 to 2010. In addition to the descriptive analyses on epidemiological features and mutual information, we used the Least Squares Support Vector Machines method in MATLAB software to propose a preliminary predictive model of pediatric central nervous system tumor feature-label analysis.

Results: Of patients, there were 63.1% males and 36.9% females. Patients' mean±SD age was 6.11±3.65 years. Tumor location was as follows: supra-tentorial (30.3%), infra-tentorial (67.7%) and 2% (spinal). The most frequent tumors registered were: high-grade glioma (supra-tentorial) in 36 (59.99%) patients and medulloblastoma (infra-tentorial) in 65 (48.51%) patients. The most prevalent clinical findings included vomiting, headache and impaired vision. Gender, age, ethnicity, tumor stage and the presence of metastasis were the features predictive of supra-tentorial tumor histology.

Conclusion: Our data agreed with previous reports on the epidemiology of central nervous system tumors. Our feature-label analysis has shown how presenting features may partially predict diagnosis. Timely diagnosis and management of central nervous system tumors can lead to decreased disease burden and improved survival. This may be further facilitated through development of partitioning, risk prediction and prognostic models.

Keywords: Pediatric CNS tumors, Epidemiology, Mutual information, Classification

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Introduction

Central nervous system (CNS) tumors are considered the second most common childhood malignancies after acute leukemia.[1, 2] These tumors comprise 15%-20% of all neoplasms, and affect children of all ages and ethnicities. The estimated incidence of CNS tumors amongst Americans less than 20 years of age is approximately 2000 individuals/year.[1-3]

The annual global incidence of CNS tumors is 3.7 for males and 2.6 for females per 100,000 children between the ages of 0-15 years. The mortality rate is 2.8% for males and 2% for females.[1,2] Medulloblastoma (MB), glioma and ependymoma account for the most prevalent pediatric CNS tumors. Meanwhile, one-third of CNS tumors amongst children less than 3 years of age are of the embryonic type. Up to 5% of children with MB may suffer from systemic metastases.[2,4,5]

In developing countries, childhood malignancies are considered the second most common cause of death beyond the neonatal age.[6-13] Timely diagnosis as well as multidisciplinary therapeutic approaches are known to be pivotal factors that lead to increased long-term survival and improved quality of life in children who suffer from CNS tumors.[6,7,9,14] With the advent of precise diagnostic measures and therapeutic modalities, efforts should be made to further improve the outcome of childhood CNS tumors.

Based on local epidemiological insights, the resources, strategies and interdisciplinary work paradigms can be re-adjusted and customized to approach these tumors in a more timely and efficient manner.

There are pediatric CNS tumors registry reports in Iran,[6-10] however a local comprehensive epidemiological mapping on childhood CNS tumors seems to be lacking. Our aim, in part, is to extract epidemiological features of childhood CNS tumors in patients at MAHAK's Pediatric Cancer Treatment and Research Center (MPCTRC) who have referred for diagnosis and treatment. MPCTRC is one of the main tertiary referral centers for childhood malignancies in Iran. Although this is a single institutional study, factors such as the diversity of patients' profiles and number of evaluated cases, in addition to the varied geographical and ethnic origins of referring children may make the outcome of this report an additional epidemiological point of reference for childhood CNS malignancies in Iran.

This study tried to employ analytical methods to define near optimal feature selection of the tumors, linking "presenting features" to possible "diagnoses". The mutual information analysis is an attempt to distinguish specific correlates of presenting signs and symptoms in children with possible CNS tumors which are linked to a particular diagnosis at a distinct likelihood value.

Patients and Methods

Out of 1517 children afflicted with malignancies who were primarily referred and admitted to MPCTRC for diagnosis and treatment during 2007 to 2010, there were 198 (13.05%) patients with CNS tumors. These patients underwent the appropriate diagnostic and therapeutic procedures. From this cohort, we reported the epidemiological features of pediatric CNS tumor patients as well as a near optimal feature selection based on mutual information, with the intent to classify these tumors in terms of the possible relation between presenting signs, symptoms, demographic particulars (features), and diagnosis-related specifics (labels).

Epidemiological evaluation

Patients or their legal guardians signed informed consents before study entry. A comprehensive, multifaceted questionnaire was designed by our investigator and administered to each patient enrolled in the survey. Additionally, the data registry system was used to gather and record data that pertained to sex, age at diagnosis, signs and symptoms, tumor location and histology, prior malignancy, cancer history in first degree family members, parental consanguinity and ethnicity. Parents' socioeconomic status was evaluated by responsible social workers upon admission and the data subsequently incorporated

Table 1. Supra- , infra-tentorial and spinal tumor locations according to sex and age groups.

Age	< 1 year n (%)			1 – 5 years n (%)			5 – 10 years n (%)			10 – 15 years n (%)			Total of
Tumor location	Supra	Infra	Spinal	Supra	Infra	Spinal	Supra	Infra	Spinal	Supra	Infra	Spinal	sex groups
Male	3(60)	2(40)	0	10(62.5)	29(63)	1(100)	15(62.5)	40(67.8)	1(100)	7(46.7)	15(62.5)	2(100)	125(63.1)
Female	2(40)	3(60)	0	6(37.5)	17(37)	0	9(37.5)	19(32.2)	0	8(53.3)	9(37.5)	0	73(36.9)
Total	5(100)	5(100)	0	16(100)	46(100)	1(100)	24(100)	59(100)	1(100)	15(100)	24(100)	2(100)	
Total of age group		10 (5.1)			63 (31.8)			84 (42.4)			41(20.7)		198(100)

into the patients' registry. We primarily categorized all patients based on their age at diagnosis into four age groups: <1 year, 1-5 years, 5-10 years and 10-15 years.

Data analysis

Descriptive analysis

Collected data were analyzed with SPSS version 19 software. The Kolmogorov-Smirnov test with 95% confidence interval was employed to determine the distribution of variables in normal or abnormal patterns. Chi-square and Spearman methods were used to analyze parametric and non-parametric data, respectively and the t-test to compare the mean values.

Analytical methods for feature selection and mutual information

We applied information theoretic criteria to distinguish some of the main childhood CNS tumor features, which have the most adequate information regarding class-labels or distinct diagnoses. This mutual information analysis provides such a model to link feature X to the label (diagnosis-related specific) Y, with a defined probability (predictability) level. We re-assessed the results of mutual information analysis by the Least Squares Support Vector Machine (LS-SVM) classification method, which is known as a strong statistical tool for classification and regression problems.[15] In non-linear relations, mutual information has been shown to retain the ability to find the most appropriate and relevant subset of features which strongly correlate with the labels, or in this study the diagnoses-related particulars.[15, 16]

Using these analytical methods, one can propose a paradigm to possibly achieve significant improvements in complex classification tasks such as distinct tumor type and histology prediction based on the modified mutual information of the presenting signs (features) of children with CNS tumors.

Data analysis was performed using Matrix Laboratory (MATLAB) version 7.13 software which is a powerful numerical computing environment and fourth-generation programming language that is frequently employed for these analyses. The programming codes have been adjusted to allow the data to undergo mutual information analysis with subsequent verification by the LS-SVM classification method.

Results

Descriptive results

Sex, age, tumor location and histology

Out of 198 patients, there were 125 (63.1%) males and 73 (36.9%) females. The M/F ratio was 1.71:1. There were 60 (30.3%) supra-tentorial tumors, 134 (67.7%) infra-tentorial tumors and 4 (2%) spinal tumors. Males prevailed in all age groups, with the exception of patients less than one year of age who were diagnosed with infra-tentorial tumors and in those older than 10 years of age with supra-tentorial tumors (Table 1).

Patients' mean age at diagnosis was 6.11±3.65 years (range: 1-14 years). The mean age of patients according to tumor diagnosis was: 6.33±4.08 years for supra-tentorial (range: 1-14 years), 5.96±3.41 years for infra-tentorial (range: 1-14 years) and 7.75±4.99 years for spinal (range: 1-12 years) tumors.

Glioma was the most frequent supra-tentorial tumor (n=36, 59.99%) whereas MB was the most prevalent infra-tentorial tumor (n=65, 48.51%) as seen in Table 2. According to the compiled

Table 2. Supra- and infra-tentorial tumors according to their histology.

Tumor histology	Tumor location n (%)		Total
	Supra-tentorial	Infra-tentorial	
Medulloblastoma	-	65 (48.51)	65 (33.51)
Glioma	36(59.99)	25 (18.66)	61 (31.44)
Astrocytoma	-	27 (20.15)	27 (13.93)
Ependymoma	6 (10)	14 (10.43)	20 (10.31)
PNET	8 (13.33)	1 (0.75)	9 (4.64)
Optic nerve glioma	4 (6.67)	-	4 (2.06)
Atypical Teratoid Rhabdoid Tumor	2 (3.33)	1 (0.75)	3 (1.55)
Germ cell tumor	1 (1.67)	1 (0.75)	2 (1.03)
Craniopharyngioma	1 (1.67)	-	1 (0.51)
Primary CNS malignant lymphoma	1 (1.67)	-	1 (0.51)
Histiocytosis	1 (1.67)	-	1 (0.51)

data, MB (n=65, 33.51%), glioma (n=61, 31.44%) and astrocytoma (n=27, 13.93%) were the most frequent overall tumor types in our under-study cohort.

A thorough descriptive analysis revealed that 100 (50.5%) children presented with specific signs and symptoms one to six months prior to their diagnoses. The most prevalent clinical complaints were vomiting (n=106, 53.5%); headache (n=102, 51.5%); disturbances in gait and balance (n=51, 25.8%); strabismus (n=27, 13.6%); impaired vision (n=24, 12.1%); seizures (n=19, 9.6%); hemiparesis (n=18, 9.1%); diplopia (n=16, 8.1%); papilledema (n=15, 7.6%) and vertigo (n=14, 7.1%).

The majority of infra-tentorial tumor cases presented with vomiting (n=72, 53.7%), headaches (n=65, 48.5%) and disturbances in gait and balance (n=37, 27.6%). On the other hand, headaches (n=36, 60.3%) and vomiting (n=33, 55%) were the most common presenting features in patients diagnosed with supra-tentorial tumors. Chi-square and Spearman tests showed a significant correlation between vomiting(P=0.037) and diplopia (P=0.027) with gender. There was also a significant correlation between nystagmus and age (P=0.002).

Local tumor recurrence was observed in 31 (15.7%) patients while under treatment, out of which 13(41.9%) were supra-tentorial, 16 (51.6%) infra-tentorial and 2 (6.5%) were spinal tumors. There was a significant correlation between tumor site and local recurrence (P=0.037).

There were metastases in 47 (23.7%) patients. Amongst these, 41 (20.7%) tumors showed evidence of spread to the CSF and one case had spleen involvement. In patients who had relapsed, the mean age upon relapse was 1.9±2.38 years. The mean age of relapse with regard to tumor site was 2.1±2.67 years (supra-tentorial), 1.5±1.89 years (infra-tentorial), and 4±4.24 years (spinal).

There were 76 (38.4%) patients who completed the assigned therapeutic protocol regimens. Out of 198 children, 82 (41.4%) died during or after treatment. The frequency of death with regard to tumor site was 24 (29.3%) for supra-tentorial tumors and 58 (70.7%) for infra-tentorial tumors. The median survival was 3.36 years. According to the survival data, together, the roughly expected five-year survival rate was 36%. Analysis regarding the mutual information values for baseline predictive factors and the treatment outcome in terms of survival data is not outlined in the current report.

Amongst all evaluated cases, 4 (2%) had co-morbidities. Of these, there were 3 patients with neurofibromatosis type 1 and 1(0.5%) patient with concurrent tuberous sclerosis.

Data on familial cancer history demonstrated that 50 patients had positive family histories of cancer; 19 (9.6%) with CNS malignancies and 31 (15.7%) with other malignancies in a first degree family member. Parental consanguinity was reported in 77 (38.9%) parents. Low socio-

Table 3. The level of probability by which each subjective feature predicts the occurrence of the given diagnosis-related labels.

Features/ Labels	Tumor location	Supra-tentorial tumor histology	Infra-tentorial tumor histology	Glioma grade	Tumor type
Sex	0	0.09303376	0.07279279	0	0
Age	0.02218408	0.14177559	0.05548487	0.12603528	0.07988289
Age at diagnosis	0.02378428	0.02942488	0.11341056	0.11828352	0.03328327
Geographical location	0.00889318	0.10274425	0.09325237	0	0
Parent relation	0	0	0.00449638	0.00137491	0
Familial cancer	0	0.08348207	0	0.04482414	0
Prior malignancy	0.01031004	0	0	0	0
Delivery route	0.01127802	0	0	0	0.01699034
Back pain	0.01084928	0	0	0.01209735	0
Seizure	0.00789531	0	0.0155234	0.04047938	0.00432578
Weight loss	0	0	0	0.01209735	0
Appetite loss	0.01474822	0	0	0.01209735	0

economic status was noted in 102 (51.5%) as noted by social workers at MPCTRC. With regards to ethnicity, all 198 patients were Caucasians. There were 167 Iranian children from various geographical locations across the country and 18 Iraqi children.

Analytical assessments on mutual information

Tables 3 and 4 demonstrate the overall features evaluated in each child who presented with CNS tumors as well as the class-labels which presumably correlated with various features to develop a "mutual information-based" predictive model. Table 3 outlines the level of probability by which each subjective feature can predict the

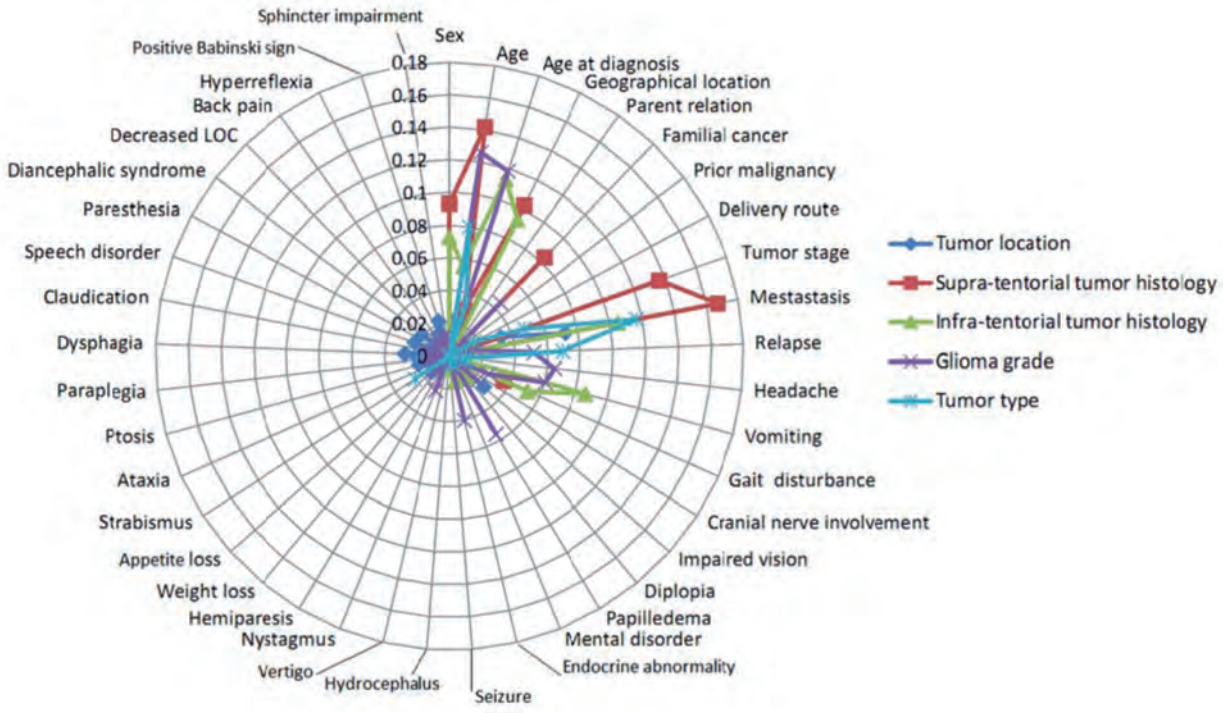

Table 4. The level of probability by which each objective feature predicts the occurrence of the given diagnosis-related labels.

	Tumor location	Supra-tentorial tumor histology	Infra-tentorial tumor histology	Glioma grade	Tumor type
Headache	0	0	0	0.06439415	0.01029526
Vomiting	0	0	0.08640104	0.06039517	0.00974539
Gait disturbance	0	0.03622965	0.05210944	0.02647024	0
Cranial nerve involvement	0.00654266	0	0.00359828	0.00453867	0
Impaired vision	0.02817039	0	0.01742589	0.02257452	0
Diplopia 0	0	0.01597488	0	0	
Papilledema	0	0	0.01543471	0.0555964	0
Mental disorder	0	0	0	0	0.00538184
Tumor stage	0.03315984	0.1361494	0	0.00006374	0.04831054
Endocrine abnormality	0.00699137	0.00559034	0	0	0.00110357
Hydrocephalus	0	0	0	0	0
Vertigo	0.00181613	0	0.0083215	0	0
Nystagmus	0.00323738	0	0	0.02260708	0
Hemi paresis	0.00860185	0	0	0.00550027	0
Metastasis	0.07196196	0.16721635	0.10495572	0.01668869	0.1165873
Relapse	0	0	0	0.05149247	0.06906262
Strabismus	0.01131529	0	0.0024282	0.00640841	0.0254771
Ataxia	0	0	0	0.01209735	0
Ptosis	0.01976063	0	0	0	0
Paraplegia	0.01923929	0	0	0.01209735	0
Dysphagia	0.02769879	0	0	0.01209735	0
Claudication	0.01319164	0	0	0.01209735	0
Speech disorder	0.023149	0	0	0	0
Paresthesia	0.00167998	0	0	0	0
Diancephalic syndrome	0.02137622	0	0	0.01209735	0
Decreased Level of consciousness	0.00335468	0	0	0	0
Hyper-reflexia	0.0147865	0	0	0	0
Positive Babinski	0.02213358	0	0	0.01209735	0.00032169
Sphincter impairment	0.00960917	0	0	0.01209735	0

occurrence of the given labels (diagnoses). Table 4 summarizes the objective features for the same.

Although not the intent of this study, we have provided a detailed explanation of the concept of mutual information analysis.

The definition of mutual information lies in the Shannon entropy[17] and information theory.[15,16,18] The mutual information of two random variables X (the presenting feature in the current study) and Y (the label or diagnosed tumor type in this study) is defined as:

$$I(X;Y) = H(X) - H(X \mid Y) = H(Y) - H(Y \mid X) = H(X) + H(Y) - H(X;Y) \quad (1)$$

Where H(X) and H(Y) are the entropies (properties toward average) of X and Y, and H (X | Y), H (Y | X) are the conditional entropies. H (X; Y) is the joint entropy of X and Y defined as:

$$H(X) = -\int_x p_X(x) \log p_X(x) dx \quad (2)$$

$$H(Y) = -\int_y p_Y(y) \log p_Y(y) dy \quad (3)$$

$$H(X;Y) = -\int_x \int_y p_{X,Y}(x,y) \log p_{X,Y}(x,y) dx dy \quad (4)$$

Where p X,Y (x,y), pX (x) and pY (y) are joint probability density functions and marginal density functions of X and Y, respectively. The marginal density functions are given by:

$$p_X(x) = \int_y p_{X,Y}(x,y) dy \quad (5)$$

$$p_Y(y) = \int_x p_{X,Y}(x,y) dx \quad (6)$$

By substituting equations (2) to (4) into (1), the mutual information equation becomes:

$$I(X;Y) = \int_x \int_y p_{X,Y}(x,y) \log \frac{p_{X,Y}(x,y)}{p_X(x)p_Y(y)} dxdy \qquad (7)$$

In discrete form, the integrations are substituted by summation of overall possible values that appear in the dataset. Consequently, in order to estimate the mutual information between X and Y, it is only required to estimate pX,Y(x,y). Mostly in biomedical research, histogram- and kernel-based methods are employed to assess the probability-density functions.[18] However, their usage is usually restricted to one- or two-dimensional probability-density functions.

In the present analytical report, although all calculations were performed by MATLAB data analyzer, the above details have been addressed to explain the concept and rationale as to why we chose the mutual information and LS-SVM methods. Our aim was to arrive at a model that possibly proposed a predictive paradigm to define tumor location (supra- vs. infra-tentorial), histology and grade based on the 43 subjective and objective presenting features in this study as outlined in Tables 3 and 4, at a distinct precision level.

This preliminary proposed model may become more sophisticated in such a way to develop software for possible use in the clinical setting, which is suggestive of tumor class-labels according to the input features. This would reveal predictions at distinct probability levels.

Figure 1 summarizes the mutual information values for each feature. As illustrated, patient's sex, age, geographical origin, tumor stage and presence of metastasis are the five cardinal features that predict (at a 10%-18% precision level) supra-tentorial tumor histology.

Out of the 29 objective features outlined in Table 4, the presence of headache, vomiting, gait disturbances, diplopia, papilledema, mental disorders, hydrocephalus, ptosis and relapse did not seem to predict tumor location (i.e., supra- vs. infra-tentorial or spinal). Other objective features in addition to a history of prior malignancy, delivery route, presence of back pain and appetite loss predicted tumor location at various probability levels.

Based on our analysis, age, age at diagnosis, and the presence of weight and appetite loss were of predictive value for glioma grade. However other features such as the presence of diplopia, mental disorders, endocrine abnormalities, hydrocephalus, vertigo, ptosis, speech disorders, paresthesia, loss of consciousness and hyper-reflexia were not predictive of glioma grade. Age at diagnosis and the presence of seizures were shown to be predictive of infra-tentorial tumor histology.

Mutual information analysis showed that tumor type was primarily predicted by the presence of headaches, vomiting, mental disorders, strabismus, a positive Babinski sign, tumor stage, endocrine abnormality, metastasis and relapse.

Treatment

All patients underwent preoperative laboratory and imaging procedures, surgical tumor biopsy or removal, post-surgical chemo-and radiotherapy (linear accelerator) and were closely followed.

Discussion

CNS tumors comprise 15%-20% of all childhood malignancies and are the second most frequent childhood malignancy worldwide. They are the leading cause of morbidity and mortality in children suffering from malignant diseases.[1-3,22] Afro-American children with CNS tumors have a higher mortality risk compared to Caucasians (13%-40%).[1] In the current study, the four-year follow up of registered patients with CNS tumors shows a mortality rate is as high as 41.4% (n=82 from 198).

The current survey aimed to evaluate epidemiological features of CNS tumors among patients admitted to MPCTRC for diagnostic procedures, and treatment who were referred for consequent follow-up. Our information source was the MPCTRC Cancer Registry System.

The estimated annual incidence of cancer amongst Iranian children aged 0-15 years old is 150 per 100,000 (3000-3500 new cancers annually) which is higher than reported from developed countries.[1-3,19-21] However, recent reports have also shown an increasing cancer incidence in these countries as well.[20]

MAHAK is a charitable institution that provides support to all children who suffer from cancer in Iran. We estimate that approximately 60% of these patients are currently registered with MAHAK.

In our database at MPCTRC from 2007 to 2010, there were 1517 cancer cases of which 198 patients were known to have CNS tumors. This incidence of 13.05% was less than other local surveys.[6-10] One reason for this disparity might be the primary management of these patients by adult neurosurgeons, radiotherapists and/or the failure to submit the pathology report to health authorities (as required by law), as well as the loss of patients.

Our data indicated that, at equal age, there was an overall higher incidence of CNS tumors in males compared to females, with a ratio of 1.7:1. This supported results from other international reports that suggested a M/F prevalence ratio of approximately 2:1.1-3,[6, 19, 20-22] however, both high and low grade gliomas have been shown to prevail in females. Our study showed that in infants CNS tumor incidence was independent of sex, with a M/F ratio of 1:1.

The overall incidence of CNS tumors was highest in children less than 8 years of age. The mean age was 6.11±3.65 years old in our studied population which complied with other reports.[6-13]

According to reports from different centers,[6-8,10-12] infra-tentorial tumors have a higher prevalence compared to supra-tentorial tumors. Likewise, our data has indicated a greater frequency of infra-tentorial tumors, with a ratio of 2:1. These tumor types include MB (33.5%), astrocytoma (13.93%), glioma (12.89%) and ependymoma (10.31%). Consistently in all reports, MB is considered the most common infra-tentorial CNS tumor. The occurrence of other infra-tentorial tumors including astrocytoma, glioma and ependymoma varies from center to center. The incidence and frequency of supra-tentorial tumors in the current study confirms the results of other reports.[1-3,6-8,10]

Based on the MPCTRC's structured questionnaire used in the current study, the most common complaints included vomiting, headaches and disturbances of gait and balance in children who suffered from CNS tumors. Diplopia, papilledema and vertigo were the least frequent symptoms. Reports from other centers in our region agreed with the above findings.[6-8, 11, 12]

CNS tumors in children are characterized by a high tendency to metastasis and local recurrence for which the frequency ranges from 23%-64% for metastasis and 10%-60% for local recurrence.[5] Systemic metastasis in MB is reported in 3%-5% of children.[5, 10, 14] In the current study, 25.3% of patients had evidence of metastasis and 15.7% experienced relapse. This agreed with other published studies.[5, 10, 14]

Certain genetic disorders such as neurofibromatosis, tuberous sclerosis and Li-Fraumeni are suggested to predispose patients to CNS tumors.[1] Other predisposing risk factors include familial cancer history and parental consanguinity.[1-3] In our study cohort two distinct groups were more predisposed to develop cancer, those with a well-known genetic cancer predisposition, namely neurofibromatosis type 1 (four patients) and tuberous sclerosis (one patient), and another group comprised of 50 (25.3%) patients with a familial cancer history of CNS tumors (n=19; 9.6%) and other malignancies (n=31; 15.7%). Of note, a predisposing risk factor is possibly the high numbers of parental consanguinity (n=77; 38.9%). Parental consanguinity may result in unmasking and activation of genetic factors which possibly predispose the offspring to cancer. These results re-emphasize the need for surveillance of family members of cancer victims.

We performed a mutual information and LS-SVM-based analysis using MATLAB software which led to the present results on selective features predictive of the diagnosis of distinct

tumor types, their location and histology.

The development of this model in a greater scale and under a more sophisticated approach may possibly result in the preparation of feature-label predictive software for CNS tumors. According to our survey, selective objective features as well as a history of prior malignancy, for example, are predictive of tumor location. On the other hand sex, age, patients' place of birth, tumor stage and presence of metastasis are predictive of supra-tentorial tumor histology.

Predicting the occurrence of a distinct CNS tumor based on the presenting features may possibly lead to more timely and efficient diagnostic or therapeutic measures.[23]

New treatment modalities that have prolonged survival and higher cure rates recommend preoperative chemotherapy, followed by surgery and subsequent chemo/radio therapy with a linear accelerator. However, most pediatric oncologists remain hesitant to apply preoperative chemotherapy. Additionally, the majority of pediatric oncology centers have a selective policy for admission and refuse to accept patients with CNS tumors. MPCRTC follows an open-door policy in this regard.

As with other Middle Eastern countries, Iran has a high rate of consanguineous marriage, possibly as high as 30% in urban areas and 64% in rural locations.[24] This should be considered a crucial public health issue that contributes not only to inheritable disorders such as thalassemia but also possibly increases the cancer incidence, which imposes an immense psychological and financial burden on the involved families and public health services.

Conclusion

Despite considerable achievements in diagnosis and tailored or targeted treatment of children afflicted with malignancies, including brain tumors, management of CNS tumors in developing countries remains a dilemma. Late diagnosis, surgical intervention by adult neurosurgeons, outdated radiotherapy techniques, delayed or improper chemotherapy, the lack of a proper inter-disciplinary approach and brain tumor networks, along with inconsistent follow-up may result in low survival rate and poor quality of life in these patients. Apart from minor epidemiological differences compared to earlier reports, the high rate of familial cancer history and parental consanguinity were the hallmarks of our survey. Present data have demonstrated the same prevalence of CNS tumors in children less than 15 years old who referred to MPCTRC compared to earlier reports. Based on the mutual information, near optimal selective features can be used to predict tumor location and histology. This, in turn, may lead to offer more timely and efficient diagnostic or therapeutic measures. Putting these feature-label insights together with survival data may also further lead to the development of a survival prediction model.

Our future reports from the same cohort will focus on the mutual information values for CNS tumor predictive treatment-related factors such as time to diagnosis, tumor type, histology, location, chemotherapy and radiotherapy protocols used, extent of surgical removal, presence of post-surgical residual tumor, and performance status as well as the treatment outcome in terms of overall survival, progression-free survival and quality of life.

Ethical standards

In full compliance with ethical standards, this study protocol followed the Ethical Guidelines for the Clinical Research, Tehran University of Medical Sciences, Tehran, Iran. The study was assessed by the Ethical Review Board at MPCTRC by which granted the approval.

Disclosure

Clinicians and authors participating in the clinical management of patients, data collection and evaluation did not have any conflict of interest in the preparation of this report.

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