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SPECTRUM OF INTRACRANIAL PATHOLOGY: TUMORS VERSUS INFECTIONS AT A TERTIARY CARE HOSPITAL

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ABSTRACT

Introduction: Aga Khan University Hospital Neurosurgery Department has evolved into a high-volume centre for treatment of neurosurgical diseases. We aimed to compare the relative outcomes of intracranial tumors and CNS infections seen at our facility. **Methods:** Hospital records of patients admitted under the neurosurgery service between 1994-2003 were evaluated. Cases with a principal diagnosis of an intracranial lesion were identified for further study. Demographic, clinical, and surgical variables were extracted from the medical record. Length of hospital stay, ICU utilization, and in-hospital mortality were the primary outcome indicators. Data were analyzed through descriptive statistics and comparisons of means and proportions. **Results:** The mortality rate was 8.7% for intracranial tumors and 18.8% for intracranial infections. Average age for tumor patients was 39.4 years and 26.5 years for patients with infections. Male predominance was seen in the tumor group (55%; p=0.02) and marginally in the infection group (51.6%; p=0.52). Mortality, length of stay and ICU utilization did not decrease significantly in either group over the ten-year period of our study. In both groups, electively admitted patients were associated with better outcomes as compared to emergent admissions. **Conclusion:** There is a need for better awareness and education among referring physicians to be on the lookout for patients requiring early neurosurgical referral. Careful selection of patients for surgical intervention should be practiced to ensure low mortality rates and more meaningful outcomes.

Advances in intracranial imaging have made the detection of intracranial lesions relatively accurate,[1,2] enabling us to focus on the etiology of these space-occupying lesions. Non-traumatic intracranial lesions are broadly grouped into tumors, infections and vascular lesions. This study focuses on intracranial pathology due to tumor and infectious etiologies.

In the United States, the country for which the best data are available, the incidence of primary brain tumors is 14 per 100,000, and brain tumors are the second leading cause of cancer-related deaths in males aged 20-39, which is a highly economically productive age group.[3,4]

Tuberculosis (TB) and mycoses are the two CNS infections commonly seen in our setting. Brain tuberculomas make up 5 to 8 per cent of intracranial masses in developing countries.[5] Before effective chemotherapy was available for tuberculosis, tuberculomas made up to 20 percent of all intracranial lesions.[6] Moreover, the incidence of CNS mycoses is on the rise,[7] mainly due to immunocompromise following organ transplantion or because of HIV/AIDS.

As in other parts of the world, neurosurgical facilities in Pakistan are mainly concentrated in large cities that accommodate high-volume tertiary care hospitals. At Aga Khan University Hospital in Karachi, neurosurgery services have evolved into a high-volume centre catering to a variety of neurosurgical diseases. As clearly defined by Long et al,[10] high-volume neurosurgical centers are characterized by affiliation with a medical teaching facility; a well-established neurosurgical residency program; 24-hour radiology service; round-the-clock operating room and anesthesia resources; and a craniotomy load of 50 cases per year. Our center, which is located in Pakistan's largest city with a population exceeding 12 million, fulfills all these criteria. Studies worldwide have supported the concept of specialized centers for advanced surgical specialties as it is shown to improve both mortality and morbidity.[11,12]

This study provides an analysis of outcome indicators for intracranial tumors and infections in a developing country setting. We also present trends in outcome over time, as well as important differences between electively and emergently admitted cases.

METHODS

Hospital records of patients admitted to the neurosurgery service during a 10-year period (1994-2003) were evaluated. Cases with a principal diagnosis of intracranial lesion(s) were included in this study. Information was collected on the following variables: age, sex, place of residence, primary diagnosis (benign, primary malignant, secondary malignant, infectious), intensive care unit admission, source of admission (emergency room or outpatient clinic), and surgical procedure(s) performed.

Length of hospital stay (LOS), ICU utilization and inpatient mortality were the designated outcome indicators in our study. Data were analyzed by assigning cases into one of two groups - tumor or infection. Cases that could not be clearly assigned into either group were excluded from further study.

RESULTS

The 10-year data was divided into two segments of 5 years each (1994-1998 and 1999-2003). Additionally, each segment was divided into groups - either tumor or infection. Total admissions to the neurosurgical service during the study period were 7,844. Of these, 733 (9.3 %) had intracranial tumors and 276 (3.5 %) had intracranial infections. The pathological spectrum of tumors and infections is shown in Tables 1 and 2, which demonstrates (i) equal frequency of benign and malignant tumors; and (ii) TB as the dominant intracranial infection.

Table 1: Tumor Distribution

TUMOR	NO. OF PATEINTS	% OF PATIENTS
Primary Malignant	308	42.01
Benign	332	45.2
Secondary Malignant	93	12.68

Table 2: Infection Distribution

INFECTION	NO. OF PATEINTS	% OF PATIENTS
Fungal	18	6.5
Bacterial Meningitis	76	27.5
Tuberculous Meningitis	104	37.6
Intracranial Abscess	41	14.8
Tuberculoma	10	3.6
Encephalitis	27	9.8

Tumors

Table 4 shows intracranial tumor patients divided on the basis of elective versus emergency admissions. There is an approximate doubling of tumor-related neurosurgical admissions over the years. Demographics of these tumor patients indicate that the group of intracranial tumors is male-preponderant and dominated by relatively young patients (Table 3).

Most tumor patients underwent surgical intervention (craniotomy being the commonest procedure) but there is a small group managed conservatively (Table 4). Although the number of craniotomies doubled over the years, as a proportion of patients admitted there was no significant difference (53.8% to 54.9%; p=0.59).

Length of stay (LOS) in electively admitted tumor patients slightly decreased over the years from 11 days to 10.1 days but LOS for emergently admitted tumor cases decreased significantly from 14.6 days to 11.9 days in admissions. Intensive Care Unit (ICU) utilization for patients with intracranial tumors also decreased over the years, both in electively admitted patients (from 11.2 % to 8.6 %) as well as emergency admissions (from 16.4 % to 13.9 %), which may be indicative of improved prognosis in

Table 3: Demographics of Tumor Patients

YEAR GROUP	AGE(yrs)			Gender				
				Males		Females		
	ELECTIVE	EMERGENCY	p-VALUE	ELECTIVE	EMERGENCY	ELECTIVE	EMERGENCY	p-VALUE
1994-1998	37.9	40.5	-	88(32.7%)	70(26%)	77(28.6%)	34(12.6%)	0.02
1999-2003	37	42.4	0.99	171(36.6%)	90(19.27%)	136(29.1%)	70(14.9%)	0.9

Table 4: Surgical Procedures performed on Tumor Patients

	1994-1998 (269 patients)		1999-2003 (467 patients)		
	ELECTIVE	EMERGENCY	ELECTIVE	EMERGENCY	p-VALUE
Craniotomy	95(35.3%)	50(18.5%)	175(37.4%)	82(17.5%)	0.59
Transphenoidal Surgery	31(11.5)	01(0.37%)	54(11.5%)	07(1.5%)	0.16
Biopsy	02(0.47%)	03(1.1%)	09(1.9%)	08(1.7%)	0.6
VPS	03(1.1%)	08(2.9%)	17(3.6%)	10(2.1%)	0.04
No Procedure	34(12.6%)	41(15.2%)	52(11.1%)	53(11.3%)	0.57

Table 5: Mortality procedures in Tumor Patients

	1994-1998		1999-2003		
	ELECTIVE	EMERGENCY	ELECTIVE	EMERGENCY	p-VALUE
Craniotomy	05(5.2%)	10(20%)	13(7.4%)	14(17%)	0.35
Transphenoidal Surgery	01(3.2%)	00	01(1.8%)	01(14.2%)	0.38
Biopsy	00	00	01(11.1%)	00	NA
VPS	00	00	00	03(30%)	NA
No Procedure	02(5.8%)	11(26.8%)	00	06(11.3%)	0.3

Table 6: Demographics of Infection Patients

1994-1998			1999-2003				
ELECTIVE	EMERGENCY	p-VALUE	ELECTIVE	EMERGENCY	ELECTIVE	EMERGENCY	p-VALUE
24.0	27.5		17(14.6%)	43(37%)	13(11.2%)	43(37.0%)	0.52
28.8	26.0	0.62	17(10.6%)	70(43.7%)	21(13.1%)	55(34.3%)	0.2

recent years. Inpatient mortality among tumor patients electively admitted has remained the same over the years, although it decreased in emergent admissions from 21% to 15%. Of the various interventions, craniotomy was associated with the highest mortality as compared to other procedures. This pattern has not changed over time (Table 5).

Infections

Numbers of patients with intracranial infections increased slightly when compared across the two 5-year segments. The gender distribution remained unchanged, but a very young population suffers from intracranial infections with an average age of around 25 years, which is much less than the intracranial tumor population in our study, who have an average age of around 38 years.

In contrast to those with tumors, intracranial infection patients underwent shunt procedures more often than craniotomies. Moreover, as noted earlier, emergent shunt procedures dominated in both 5-year groups although the difference did not reach significance ($p=0.22$; Table 7).

LOS in the intracranial infection patients is comparatively higher than in intracranial tumor patients, and this difference is more pronounced in the emergency admissions with LOS of around 20 days for emergently admitted intracranial infection patients. However, LOS has decreased significantly over the years in electively admitted intracranial infection patients, implying a better prognosis in this subgroup.

Emergently admitted patients with intracranial infections are more likely to spend time in the ICU than those admitted electively. Similar to a lack of any significant decrease in mortality in tumor patients, we did not find any significant decrease in mortality in infection patients in either elective or emergent groups, over the years.

The highest in-hospital mortality after surgical intervention was seen in emergent craniotomies for intracranial infection (31.5%). The lowest surgical mortality was in intracranial infection patients undergoing ventriculo-pertioneal shunting (7.1% for elective and 17% for emergent procedures, as shown in Table 8).

DISCUSSION

Intracranial pathology in developing countries such as Pakistan differs from the spectrum seen in the developed world. Infective pathology makes a significant part of the intracranial case-load in our country. Our data showed a preponderance (27.3%) of infective pathology, which is slightly higher than the 23% reported in a study[13] conducted at a public-sector tertiary care hospital that is also in Karachi.

Tumors

We compared our results in the tumor category with a study analyzing the effect of specialized neurosurgical centers in United States on the outcome of brain tumor patients.[10] Brain tumor distribution in our center is quite similar to tertiary care centers in the US, but our patients experience longer hospital stay and higher mortality. Overall, in-hospital mortality of tumor patients at our centre is 8.7%, which is significantly higher than observations from North America[10,14,15] showing mortality rates ranging from 2.5-3.1%. The higher mortality may be attributable to late tumor presentation in the developing world.[16] This discrepancy underscores the importance of early tumor diagnosis and prompt treatment in decreasing both morbidity and mortality. Moreover, the average age of tumor presentation in our patients was much less, and the proportion of males higher, than that in the US.[10,17]

Mortality, length of stay and ICU utilization in tumor patients did not decrease significantly over the years (in either elective or emergent admissions), compared with data from the US.[17] However, electively admitted tumor patients had shorter length of stay, lower rates of ICU utilization, and lower mortality. This can be attributed to clinical stability, better surgical preparation, and better neurological status at the time of admission.

Infections

We found tuberculous involvement of the brain to be the most common intracranial infection (37.6%), an observation in keeping with clinical experience across Pakistan. In comparison, the frequency of neurotuberculosis in the United States is less than 0.5 %.[18] Tuberculosis is associated with poor socioeconomic conditions and is endemic in South Asia.19 In our study, in-hospital mortality in intracranial infection patients (18.8%) was similar to that reported by earlier investigators.[19,20] Although isolated studies of particular infection types are available, we were unable to find any other hospital-based study providing an epidemiology of intracranial infections and their outcome analysis.

The number of infection admissions increased by 37.9% across the two 5-year segments, which is less than that of tumor admissions. Most of these patients were admitted through the ER. An important point is that the average age of intracranial infection patients (26.5 years) was much less than that of intracranial tumor patients in this study. The most common surgical intervention performed in this etiology group was ventriculo-peritoneal shunting for relief of elevated intracranial pressure. Craniotomies performed

Table 7: Surgical procedures performed on Infection Patients

	1994-1998 (269 patients)		1999-2003 (467 patients)		
	ELECTIVE	EMERGENCY	ELECTIVE	EMERGENCY	p-VALUE
Craniotomy	07(6.0%)	19(16.3%)	175(37.4%)	82(17.5%)	0.00002
Biopsy	01(0.86%)	04(3.4%)	02(1.25%)	07(4.3%)	0.92
VPS	14(12.0%)	41(35.3%)	14(8.7%)	61(38.1%)	0.35
No Procedure	04(3.4%)	19(16.3%)	12(7.5%)	20(12.5%)	0.10

Table 8: Mortality and Procedure In Infection Patients

	1994-1998		1999-2003		
	ELECTIVE	EMERGENCY	ELECTIVE	EMERGENCY	p-VALUE
Craniotomy	1(14.2%)	6(31.5%)	00	08(22.8%)	0.46
Transphenoidal	00	00	00	00	NA
Biopsy	00	00	00	01(14.2%)	NA
VPS	01(7.1%)	07(17%)	00	11(18%)	0.22
No Procedure	00	03(15.7%)	01(8.3%)	02(10%)	0.5

in this group were mainly for biopsies or intracranial abscess drainage. Craniotomy as a surgical intervention in patients with intracranial infection carried much higher mortality than that for intracranial tumor patients (Tables 4 and 8). Length of stay, ICU utilization and mortality remained stable over the years in infectious patients.

Elective versus emergency

Intracranial tumor and infection patients show similar trends when elective versus emergency admissions are compared in each category. Acute presentation through the ER was a significant predictor of worse outcome in both groups. Emergently admitted patients spent more time in the hospital and were more likely to utilize ICU facilities, compared with electively admitted patients; mortality in emergently admitted patients has also been consistently higher throughout the ten years under study. This difference is more marked in infection patients than tumor patients. These observations are comparable with earlier data[14] showing that patients admitted through the ER had significantly higher mortality.

CONCLUSION

The neurosurgical service at Aga Khan University Hospital in Karachi has evolved over the years into a specialized high-volume center. Our data, particularly the preponderance of young patients, underscore the need to establish and maintain a well-equipped service, which can potentially translate into saving productive years for the nation. There is a need for yearly analysis of cases to look at neurosurgical outcomes in our setting and identify predictors of poor prognosis. Careful selection of patients for surgical intervention will ensure low mortality rates.

REFERENCES:

1. Desmeules M, Mikkelsen T, Mao Y. Increasing incidence of primary malignant brain tumors: influence of diagnostic methods. *J Natl Cancer Inst* 1992; **84**:442-445
2. Modan B,Wagener DK, Feldman JJ, et al. Increased mortality from brain tumors: a combined outcome of diagnostic technology and change of attitude towards the elderly. *Am J Epidemiol* 1992; **135**:1349-1357
3. CBTRUS 1995-1999 Data: http://www.cbtrus.org/reports/reports.html
4. American Cancer Society 2002: http://www.cancer.org/docroot/STT/content/STT_1x_Cancer _Facts__Figures_2002.asp
5. Bouchama A, Al-Kawi MZ, Kannan I. Brain biopsy in tuberculoma: The risks and benefits. *Neurosurgery* 1991; **28**:405
6. Rammamurthi B, Varadarajan M. Diagnosis of tuberculoma of the brain. *J Neurosurg* 1961; **18**:1
7. Jamjoom AB et al. Intracranial mycotic infections in neurosurgical practice. *Acta Neurochir (Wien)* 1995; **137(1-2)**:78-84
8. Smith SF, Simpson JM, Sekhon LH. A quarter of a century of neurosurgery: the value of a relational database to document the trends in neurosurgical practice of a tertiary referral hospital. *J Clin Neurosci* 2004; **11(1)**:31-6
9. Pickard JD, Bailey S, Sanderson H, Rees M, Garfield JS. Steps towards cost-benefit analysis of regional neurosurgical care. *BMJ* 1990; **29**:629-35
10. Long DM, Gordon T, Bowman H, Etzel A, Burleyson G, Betchen S, Garonzik IM, Brem H. Outcome and cost of craniotomy performed to treat tumors in regional academic referral centers. *Neurosurgery* 2003; **52(5)**:1056-63
11. Flood AB, Scott WR, Ewy W. Does practice make perfect? Part II: The relation between volume and outcomes and other hospital characteristics. *Med Care* 1984; **22(2)**:115-25
12. Gordon TA, Burleyson JP, Tielsch JM, Cameron JL. The effects of regionalization on cost and outcome for one general high-risk procedure. *Ann Surg* 1995; **221**:43-49, 1995
13. Irfan A, Qureshi A. Intracranial space occupying lesions-review of 386 cases. *J Pak Med Assoc* 1995; **45(12)**:319-20
14. Cowan JA Jr, Dimick JB, Leveque JC, Thompson BG, Upchurch GR Jr, Hoff JT. The impact of provider volume on mortality after intracranial tumor resection. *Neurosurgery* 2003; **52(1)**:48-53
15. Barker FG 2nd. Craniotomy for the resection of metastatic brain tumors in the U.S., 1988-2000: decreasing mortality and the effect of provider caseload. *Cancer* 2004; **100(5)**:999-1007
16. Kaplan FJ, Levitt NS, De Villiers JC, Soule SG. Acromegaly in the developing world-a 20-year teaching hospital experience. *Br J Neurosurg* 2001; **15(1)**:22-7
17. Barker FG 2nd, Amin-Hanjani S. Changing neurosurgical workload in the United States, 1988-2001: craniotomy other than trauma in adults. *Neurosurgery* 2004; **55**:506-518
18. Sheller J R, des Prez R M. CNS tuberculosis. *Neurol clin* 1986; **4**:143
19. Hosoglu S, Geyik MF, Balik I. Predictors of outcome in patients with tuberculous meningitis. *Int J Tuberc Lung Dis* 2002; **6(1)**:64-70
20. Qureshi HU, Merwat SN, Nawaz SA. Predictors of inpatient mortality in 190 adult patients with tuberculous meningitis. *J Pak Med Assoc* 2002; **52(4)**:159-63