



Neuro-Ophthalmic Manifestations of Intracranial Space Occupying Lesions in Adults

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Abstract

Objectives: The purpose of this study is to evaluate the epidemiology, neuro-ophthalmic, and clinical characteristics of intracranial space occupying lesions (ICSOLs) in adult patients.

Methods: All patients above 16 years presenting with brain tumors confirmed by magnetic resonance imaging and treated surgically in our institute were included in this study. Epidemiology of the patients along with neurological and ophthalmic manifestation was evaluated.

Results: A total of 252 patients were included in the study ranging from 18 years to 79 years. Supratentorial location was more common than infratentorial location. The most common neurological symptom in our study was headache followed by seizures. Ophthalmic manifestations were present in (73.4%) of patients. The most common visual symptoms and signs were visual loss, strabismus, papilledema, and visual field defects. The most common histopathological diagnosis seen in our study was meningiomas followed by high-grade gliomas.

Conclusion: Ocular signs and symptoms can be considered as a window to the brain through which ICSOLs can be detected. The most common neurological manifestation of ICSOL in our study was headache with or without true localizing signs and symptoms. More frequently, these patients present to an ophthalmologist before a neurosurgeon with related ocular manifestations. Hence, through our study, we emphasize the importance of a detailed ophthalmological examination in these patients which can aid in early diagnosis and prompt management of such lesions.

Keywords: Intracranial space occupying lesions, neurological features, neuro-ophthalmic manifestations, ophthalmic signs, ophthalmic symptoms

Introduction

Intracranial space occupying lesions (ICSOLs) constitute a major reason for seeking neurological and ophthalmic consultations worldwide (1). Understanding the clinical manifestations of these lesions is complicated due to the extreme heterogeneity among these patients and management depends on various factors which include the size, location, duration, pathology, and rate of growth of these lesions (2).

Neurological symptoms may be caused by their mass effect on the surrounding structures, raised intracranial pressure, and expression or suppression of various hormones by the tumors or due to hydrocephalus (3,4).

Eye is considered as the window to look into the brain as developmentally, the visual system is an outgrowth from the central nervous system. Morphologically and functionally, the visual system as a whole can be called as the "Lit-

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tle brain” (5). Ophthalmic manifestations in intracranial tumors such as decreased visual acuity, visual field defects, ophthalmoplegia, papilledema, and optic atrophy may occur as an initial presentation in about 46.8%–88.6% of the patients due to raised intracranial pressure, compression on the visual pathway, cranial nerves, or orbito-ocular tissues or tumor infiltration of intraocular structures or adnexa (1,6).

About 60% of these patients present to an ophthalmologist with ocular complaints (1). Thus, they have an important role in the early diagnosis of these cases for immediate referral and prompt management. The purpose of this study is to evaluate the epidemiology, neuro-ophthalmic, and clinical characteristics of ICSOLs in adult patients presenting to our institute.

Methods

This prospective and observational study was carried out over a period of 2.5 years from June 2017 to December 2019. The study was approved by the Institutional Ethical Clearance Committee and has followed the tenets of the Declaration of Helsinki. All patients above 16 years presenting with ICSOLs which were confirmed by magnetic resonance imaging (MRI) and treated surgically in our institute were included in this study. Patients who had received chemotherapy or radiotherapy before surgery or with coexistent primary neoplasm elsewhere were excluded from the study. Patients age, gender, neurological symptoms including history of headache, nausea/vomiting, anosmia, seizures, anosmia, symptoms and signs of endocrine involvement, and neurological signs which included cerebellar signs, speech involvement, motor deficit, altered sensorium, and cranial nerve palsies were evaluated by the neurosurgical team.

Ophthalmic features which include diminution of vision, visual field defects including type of defect on perimetry, ocular pain, red eye, proptosis, papilledema, disc pallor, shunting of vessels, ptosis, pupil abnormality, nystagmus, and strabismus were evaluated by the ophthalmologist.

Other parameters which were evaluated were location of the tumor by contrast-enhanced MRI, type of surgical intervention, and post-operative histopathological diagnosis.

Results

A total of 252 patients were included in the study. Ages ranged from 18 years to 80 years and the mean age was 45.14 years. One hundred and twenty-eight (50.8%) of patients were males and 124 (49.2%) of patients were females. The frequency of the patients according to their age group is described in (Table 1) where maximum patients were in the age group of 41–50 years.

Table 1. Frequency of patients according to age group

AGE GROUP	Frequency	Percent
18–20	6	2.4
21–30	47	18.7
31–40	45	17.9
41–50	63	25
51–60	56	22.2
>60	35	13.9
Total	252	100.0

In our study, according to the location of the tumor, supratentorial location was present in 202 (80.1%) patients and infratentorial location was present in 46 (18.2%) patients and both supratentorial with infratentorial location was present in 4 (1.6%) of patients. The neurological manifestations according to the location are mentioned in Table 2. The most common neurological symptom in our study was headache which was present in 83.7% of patients followed by seizures which was seen in 45.6% of patients.

Ophthalmic manifestation was present in (73.4%) of patients. Ophthalmic symptoms and signs are illustrated in Table 3. The most common visual symptom was diminution of vision which was present in 30.2% of patients followed by strabismus which was present in 10.3% of patients. Papilledema was the most common ophthalmic sign which was seen in 41.3% of patients followed by visual field defects which was seen in 20.6% of patients.

The most common field defect seen in our study was bitemporal hemianopia which was seen in 29 (11.5%) patients. The various types of field defects with respect to their location are described in Table 4.

Sellar region was the most common location of the tumor followed by the frontal lobe.

The histopathological diagnosis with respect to the location of the ICSOL is mentioned in Table 5.

The most common histopathological diagnosis seen in our study was meningioma followed by high-grade gliomas. Histopathology-wise distribution of cases is mentioned in Table 6.

Discussion

Primary brain tumors are a group of neoplasms arising from the brain parenchyma and its surrounding structures and constitute to approximately 2% of all malignancies. Although the incidence of these tumors is relatively low, the associated mortality and morbidity of affected young and middle aged individuals has a major impact on the death-adjusted life years compared to other malignancies (7).

Table 2. Neurological manifestations of the patients according to the location of the tumor

Clinical features	Infratentorial	Supratentorial	Supra + infratentorial	Total
Headache	43 (17.1%)	165 (65.5%)	3 (1.2%)	211 (83.7%)
Nausea/vomiting	21	72	3	96 (38.1%)
Ophthalmic involvement	40	142	3	185 (73.4%)
Cerebellar signs	39	0	1	40 (15.9%)
Cranial nerve involvement	32	19	1	52 (20.6%)
Cranial Nerve I	0	8	0	8 (3.2%)
Cranial Nerve II	29	136	3	168 (66.7%)
Cranial Nerve III	1	9	0	10 (4%)
Cranial Nerve IV	2	9	0	11 (4.4%)
Cranial Nerve V	17	3	1	21 (8.3%)
Cranial Nerve VI	11	18	0	29 (11.5%)
Cranial Nerve VII	21	0	0	21 (8.3%)
Cranial Nerve VIII	20	0	0	20 (7.9%)
Lower Cranial Nerves	8	0	0	8 (3.2%)
Seizures	1	111	3	115 (45.6%)
Speech involvement	3	15	0	18 (7.1%)
Altered sensorium	1	37	0	38 (15.1%)
Ataxia	8	3	0	11 (4.4%)
Motor deficit	0	56	1	57 (22.6%)
Endocrine involvement	0	14	0	14(5.5%)
Acromegaly	0	1	0	1 (0.4%)
Acromegaly with DM	0	3	0	3 (1.2%)
Galactorrhea amenorrhoea	0	7	0	7 (2.8%)
Cushings features	0	2	0	2 (0.8%)
Neurocutaneous markers	0	1	0	1 (0.4%)

DM: Diabetes mellitus.

This study was undertaken to observe a particular cohort of patients who were clinically and radiologically diagnosed with ICSOLs managed by the neurosurgical team along with ophthalmological examination done by ophthalmology team.

In this study, the age of patients included ranged from 18 to 80 years and the mean age was 45.14 years (Table 1). This was similar to the study by Deshmukh et al. where the mean age observed in their study was 43.17 years (1). In contrast, this was higher than some other studies in the literature as we have excluded pediatric patients from our study (8,9). Peak age group in our study was 40–50 years, accounting 63 (25%) of the cases. This was similar to the Indian studies by Mondal et al. and Masoodi et al. (10,11) The age-related spectrum was also comparable to similar Indian study by Jaiswal et al. where the authors collected data of 4295 cases from a hospital based brain tumor registry (12). Out of the 252 patients, 124 patients were females and 128 were males. Male: female ratio was 1.03:1 which showed

negligible difference in male: female distribution which was similar to the study carried out by Nalawade et al. (6) However, meningioma cases had a female preponderance (Male: female: 12:34) which is consistent with various studies in the literature (10-13).

Along with ophthalmological manifestations, these patients present with varied neurological signs and symptoms but the first point of contact of these patients is usually an ophthalmologist. Hence, an ophthalmologists have to be aware of these neurological symptoms to avoid delay in diagnosis and definitive management.

Headache was the most frequently reported symptom which was seen in 83.7% of cases (Table 2). This was higher than other similar studies in the literature (10,14). The higher incidence of headache can be attributed to the delay in approaching a specialist and arriving at a diagnosis which is predominant in developing countries. The classic brain tumor headache is a global headache often radiating to the

Table 3. Ophthalmic manifestations of the tumors according to infratentorial location and supratentorial location of the tumor

Ophthalmic symptoms	Infratentorial	Supratentorial	Supra + infratentorial	Total
Decreased Visual acuity	3	73	0	76 (30.2%)
Bilateral	3	63	0	66 (26.2%)
Unilateral	0	10	0	10 (4%)
Diplopia	7	17	0	24 (9.5%)
Strabismus	10	16	0	26 (10.3%)
Ptosis	1	8	0	9 (3.6%)
Ophthalmic Signs				
Papilledema	26	75	3	104 (41.3%)
Ophthalmoplegia	11	18	0	29 (11.5%)
Nystagmus	34	4	0	38 (15.1%)
Disc Pallor	3	46	0	49 (19.4%)
Foster Kennedy Syndrome	0	10	0	10 (4%)
Visual field defects	0	53	0	53 (21%)
Proptosis	0	5	0	5 (2%)
Red Eye	0	5	0	5 (2%)
Ocular pain	0	5	0	5 (2%)
Pupillary Abnormality	1	6	0	7 (2.8%)

vertex or periorbital region which wakes the patients in the early hours of the morning, associated with nausea and vomiting due to secondary CO₂ retention and vasodilation and less frequently associated with visual obscurations which are transient fogging of vision usually on rapid changes in posture (15). The incidence of associated nausea and vomiting was 38.1% which confirms the well-known predominance of raised intracranial pressure in these cases (Table 2). Hence, all patients presenting with non-migrainous headaches with or without associated nausea and vomiting should have careful examination of fundus and visual fields.

According to the literature, seizure may occur as an initial symptom in 30–50% of patients. Consistent with the literature, the incidence of seizure in our study was 45.6% (Table 2). An epileptic attack occurring in a patient past the age of 20 years with no prior history of epilepsy should raise the suspicion of an intracranial tumor. Seizures occur secondary to irritation of the cerebral cortex either from the tumor itself or from the surrounding peritumoural edema. Seizures can occur from lesions in any area of the cerebral cortex but are more commonly seen in patients with lesions in the frontal or temporal lobes and is rarely seen in patients with lesions of the brainstem and cerebellum (16). Furthermore, patients with low-grade tumors are more likely to present with seizures than patients with high-grade tumors (16). Consistent with the literature, all these findings collaborat-

ed with our study where 80 out of the 115 (69.5%) patients who presented with seizures had lesions in the frontal and temporal lobes and 74 out of 115 (64.3%) patients had a benign lesion.

Motor deficits associated with intracranial lesions include partial or complete weakness of one or more limbs due to lesions located in or around the pre-central cortex which was seen in 22.6% of patients. Other motor symptoms including ataxia were seen in 4.4% of patients and incoordination due to involvement of the cerebellum was seen in 15.9% of patients (Table 2).

Cranial nerve involvement in intracranial lesions can present as single or multiple cranial nerve palsies either by local compression and direct infiltration or by paraneoplastic process (17). Cranial nerve involvement excluding optic nerve was seen in 52 (20.6%) of patients out of which 32 patients had infratentorial tumors, 19 patients had supratentorial tumors, and one patient had presence of both supra and infratentorial tumors (Table 2).

A lesion involving the cavernous sinus may affect the third, fourth, and sixth cranial nerves and cause dysfunction of the first and second divisions of the trigeminal nerve. Neoplastic considerations include meningioma, lymphoma, pituitary adenomas, metastases, trigeminal neuromas, chordomas, chondrosarcomas, and nasopharyngeal carcinomas (18). The incidence of cranial nerve III, IV, and VI involvement

Table 4. Type of field defect according to location of tumor

Type of visual field defect	Location of SOL	Number of cases
Bitemporal hemianopia	Sellar region SOL	28
	Multiple intracranial SOL	1
Left eye hemianopia with right eye blind	Sellar region SOL	4
Right eye temporal hemianopia with the left side involvement of three quadrants	Sellar region SOL	3
Left superior homonymous quadrantanopia	Temporal lobe SOL	2
Homonymous hemianopia	Temporal lobe SOL	1
Left eye blind spot enlargement with the right eye blind	Sellar region SOL	1
Left eye hemianopia with the right side involvement of three quadrants	Sellar region SOL	1
Left eye blind with the right eye unreliable fields	Sellar region SOL	1
Left incongruous homonymous hemianopia	Sellar region SOL	1
Left side central scotoma with the right superotemporal field defect	Basifrontal SOL	1
Macular sparing congruous homonymous hemianopia	Parieto-occipital SOL	1
Bilateral peripheral field constriction	Sellar region SOL	1
Bilateral three quadrant involvement	Sellar region SOL	1
Bilateral central scotoma	Occipital lobe SOL	1
Right eye hemianopia with the left eye blind	Sellar region SOL	1
Right incongruous homonymous hemianopia	Sellar region SOL	1
Right inferior homonymous quadrantanopia	Parieto-occipital SOL	1
Right Macular sparing congruous homonymous hemianopia	Parietooccipital SOL	1
Total		53

SOL: Space occupying lesion.

was more for tumors in the supratentorial region (Table 2). Combined involvement of the third fourth and sixth cranial nerves causing paralytic strabismus were seen in seven cases with supratentorial tumors out of which six patients had tumors in the sellar region with cavernous sinus involvement. The sellar region tumors included four cases of pituitary adenoma, and one case each of cavernous hemangioma and chordoma. According to Table 2, the incidence of cranial nerves V, VII, VIII, and lower cranial nerves is more for tumors present in the infratentorial region.

Other neurological manifestations in our study include altered sensorium (15.1%), speech involvement (7.1%), and endocrine involvement (5.5%) (Table 2).

Ophthalmic signs and symptoms sometimes form an early manifestation of ICSOLs and high index of suspicion of these features can aid in early diagnosis and prompt management and thereby reduce the morbidity and mortality associated with these lesions (19). Ophthalmic manifestations of intracranial tumors include diminution of vision, diplopia, ophthalmoplegia, pupillary abnormalities, proptosis, nystagmus, and optic nerve head changes and their presentation is largely affected by the type, location, and size of the tumors.

The reported incidence of neuro-ophthalmic involvement ranges from 46.8% to 88.6% (2). In our study, ophthalmic involvement was seen in 73.4% (Table 2). Higher incidence of ophthalmic involvement can be attributed to the poor referral network and poverty leading to delayed presentation of these cases in developing countries.

Patients from developing countries tend to present late with larger masses and this may affect the prevalence and pattern of ophthalmic manifestations at presentation. The most common ophthalmic symptom in our study was diminution of vision which was seen in 30.1% of the cases which is comparable to the study by Serova et al. (20) (Table 3). However, this was lesser as compared to other studies in the literature which may be due to the higher incidence of sellar region tumors in their study (2,21,22).

Ophthalmoplegia was seen in 29 (11.5%) of the patients on examination out of which diplopia which is a symptom of ocular cranial nerve involvement was seen in 9.5% of the cases which is comparable to a Kenyan study by Marco et al. (23) (Table 3). The frequency of double vision as a symptom may not represent all cases of ocular deviations and ocular cranial nerve involvement as patients with severe vi-

Table 5. The histopathological diagnosis with respect to the location of the ICSOL

Location	Histopathology With Number Of Cases	Total	Location	Histopathology With Number Of Cases	Total
Basal Ganglia	Abscess-1	3	Occipital Lobe	Low-grade Glioma-2	19
	High-grade Glioma-1			Metastasis-9	
Basifrontal	Low-grade Glioma-1	18	Orbital SOL With Intracranial extension	Epidermoid Cyst-1	2
	Meningioma-18			Meningioma-1	
Brainstem	High-grade Glioma	1	Parafalcine SOL	Adenocarcinoma-1	3
Cerebellum	Abscess-2	15		Parasagittal SOL	
	Hemangioblastoma-2		Parasagittal SOL	Lymphoma-1	2
Corpus Callosum	Low-grade Glioma-2	2	Parietal Lobe	Meningioma	11
	Medulloblastoma -3			High-grade glioma-3	
Cerebello pontine Angle	Atypical Meningioma-1	28	Parietooccipital lobe	Low-grade glioma-3	10
	Ependymoma-1			Meningioma-3	
Frontal Lobe	High-grade Glioma-2	15	Petroclival SOL	Tuberculoma-1	4
	Metastatic Adenocarcinoma-1			High-grade glioma-3	
Frontoparietal Lobe	Tuberculoma-1	32	Pineal gland SOL	Low-grade glioma-1	1
	Atypical Meningioma-1			Meningioma-1	
Frontotemporal Lobe	High-grade Glioma-5	11	Sellar region	Epidermoid cyst-1	3
	Low-grade Glioma -4			Pinocytoma-2	
Glomus Jugular Tumour	Meningioma-4	4	Temporoparietooccipital lobe	Pituitary adenoma-40	51
	Metastasis-1			Cavernous hemangioma-1	
Insular SOL	Sarcoidosis-1	2	Thalamic SOL	Chordoma-1	1
	Tuberculoma-2			Colloid cyst-1	
Jeffersons Type C SOL	Atypical Meningioma-1	1	Ventricular SOL	Craniopharyngioma-2	17
	High-grade Glioma-6			Invasive pituitary adenoma-1	
Multiple Intracranial SOL	High-grade Glioma-1	4		Lymphocytic hypophysitis-1	6
	Low Grade-3			Meningioma-1	
	Abscess-2			Rathke's cleft cyst-1	
	High-grade Glioma-6			Pituitary abscess-1	
				Abscess-2	
				Epidermoid cyst-1	
				High-grade glioma-7	
				Low-grade glioma-5	
				Meningioma-1	
				Trigeminal schwannoma-1	
				High-grade glioma-1	
				High-grade glioma-4	
				Colloid cyst-2	
				Low-grade glioma-2	
				Meningioma-1	
				Neurocysticercosis-1	

DNET: Dysembryoplastic neuroepithelial tumor, SOL: Space occupying lesion.

sual impairment or patients with altered mental status at the time of admission are difficult to assess (2). Intracranial tumors cause ocular nerve involvement either by infiltration or by mass effect. Although the third nerve palsy is the most common in sellar region tumors, sixth nerve involvement is seen more commonly as a manifestation of raised intracranial pressure due to the long intracranial course making it more prone to stretching over the tip of the petrous bone producing a false localizing sign (8). This is the cause for increased incidence of sixth nerve palsy as compared to third and fourth nerve palsies in our study.

Optic nerve head changes including papilloedema and pale disc were seen in 104 patients (41.3%) and 49 patients (11.5%), respectively, which is comparable to the study by Nalawade et al. (6) (Table 3). This reiterates the importance of ophthalmoscopy in the early diagnosis of intracranial tumors. Infratentorial mass lesions, which may obstruct the ventricular outflow at the relatively narrow Sylvian aqueduct, are more likely to produce papilledema than supratentorial mass lesions (24). This was confirmed in our study where papilledema was present in 26 out of the 46 patients (56.52%) with infratentorial tumors and 74 out of the 127 patients (37.12%) with supratentorial tumors (Table 3) The incidence of papilledema was more with intra-axial tumors (57.7%) than extra-axial tumors (42.3%) which can be attributed to the focal edema accompanying intra-axial tumors. Our results are in agreement with Hartmann and Guillauman who showed that incidence of papilledema was 76% and 40% in patients with gliomas and meningiomas, respectively (25).

The pathognomonic signs of a chiasmal lesion include bilateral, usually bitemporal field defect that respect the vertical meridian but can frequently be asymmetrical and unpredictable in evolution (26,27). Ophthalmic manifestations are related to the anatomical location of the chiasm. Associated features of cranial nerve paralysis and diplopia may develop because of parasellar extension of the lesions. In our study, there were 51 cases of sellar region tumors which include pituitary adenoma (40 cases), craniopharyngioma (two cases), and one case each of cavernous hemangioma, chordoma, colloid cyst, hypothalamic glioma, lymphocytic hypophysitis, invasive pituitary adenoma, meningioma, pituitary abscess, and Rathke's cleft cyst (Table 5).

The extent of field loss at the time of presentation can range from minimal defect that the patient has not noticed and are discovered on perimetry to complete bilateral loss of the temporal fields or in the worst event can be catastrophic with binocular loss of all perception of light. Fifty-three (21%) patients had field defect confirmed by perimetry in our study. Out of the 53 field defects, the most common field defect seen was bitemporal hemianopia which was seen in 29(55.8%) of patients which is comparable to the study by Rajendran et al. (28) (Table 4).

Nystagmus was seen in 38 patients (15.1%) which was mainly seen in lesions affecting the cerebellum (Table 3). Three patients with pineal gland tumors presented with Perinaud's syndrome; a characteristic convergence-retraction nystagmus and one patient with third ventricular tumor presented with nystagmus retractorius.

Other ocular manifestations in our study include Foster Kennedy syndrome (4%), proptosis (2%), red eye (2%), ocular pain (2%), and papillary abnormality (2.8%) (Table 3).

After complete neuro-ophthalmic examination of these patients, neuroimaging was done in all the patients with suspected intracranial tumors. Contrast-enhanced MRI is the

Table 6. Histopathological diagnosis of cases

HPE	Frequency	Percent
Abscess	8	3.2
Adenocarcinoma	1	0.4
Cavernous hemangioma	1	0.4
Chordoma	1	0.4
Colloid cyst	3	1.2
Craniopharyngioma	2	0.8
DNET	1	0.4
Ependymoma	1	0.4
Epidermoid cyst	8	3.2
Fungal mass	1	0.4
Hemangioblastoma	2	0.8
High-grade glioma	47	18.7
Hypothalamic glioma	1	0.4
Invasive meningioma	1	0.4
Low-grade glioma	33	13.1
Lymphocytic hypophysitis	1	0.4
Lymphoma	1	0.4
Medulloblastoma	3	1.2
Meningioma	48	19
Metastasis	12	4.7
Neurocysticercosis	1	0.4
Pineocytoma	2	0.8
Pituitary abscess	1	0.4
Pituitary adenoma	41	16.3
Rathke's cleft cyst	1	0.4
Sarcoidosis	1	0.4
Schwannoma	24	9.5
Tuberculoma	5	2.0
Total	252	100.0

HPE: Histopathology, DNET: Dysembryoplastic neuroepithelial tumor.

investigation of choice which was done in all our cases. In addition, MRI angiogram and venogram to display vasculature alongside the tumor, MR spectroscopy to assess the metabolic activity of the tumor, and functional MRI with tactography to provide additional information on the course of important white matter tracts and their relationship with the tumor were done depending on the type and location of the tumor before planning surgical intervention (15,29).

Frontal lobe (12.7%) was the most common location of the tumor in our study followed by cerebellopontine angle (11.1%). Location-wise histopathological distribution of cases is mentioned in Table 5.

Surgical intervention was either diagnostic, curative, or palliative purposes depending on the type, location, and size of the tumor as well as the patients age and general health.

The largest proportion of tumors in our study was meningiomas (19%) followed by high-grade gliomas (18.7%). This was similar to the study by Jaiswal et al. (12) The other tumors seen in our study are mentioned in Table 6.

Conclusion

Ocular signs and symptoms can be considered as a window to the brain through which ICSOLs can be detected. The most common neurological manifestation of ICSOL in our study was headache with or without true localizing signs and symptoms. More frequently, these patients present to an ophthalmologist before a neurosurgeon with related ocular manifestations. Hence, through our study, we emphasize the importance of a detailed ophthalmological examination and knowledge of associated neurological manifestations in these patients which can aid in early diagnosis and prompt management of these lesions.

Disclosures

Ethics Committee Approval: The study was approved by the Institutional Ethical Clearance Committee and has followed the tenets of the Declaration of Helsinki.

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Conflict of Interest: None declared.

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