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CLINICAL SPECTRUM AND NEURO IMAGING FINDINGS OF PATIENTS WITH CEREBRAL ARTERIOPATHY

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ABSTRACT

Objective: To determine the association between the clinical spectrum and neuroimaging findings of patients with cerebral arteriopathy.

Study Design: Prospective cross-sectional study.

Place and Duration of Study: The Institute of Child Health and the Children Hospital Ferozepur Road Lahore, from Jan 2016 to Jun 2016.

Material and Method: The study was carried out on sixty patients who were less than 16 of age years and admitted in neurology department during this period of six months. They were all confirmed cases of cerebral arteriopathy on the basis of history, examination, investigations and imaging findings. Arteriopathy on imaging was defined as focal or segmental narrowing of arterial blood vessels. While patients with other causes of arterial ischemic stroke were excluded from the study.

Results: Out of these 60 patients, majority of them were females (55%) and again majority of them were under the age of 5 years (38%). Recurrent episodes of stroke were noted in (56%), hemiplegia (96.7%) followed by fits (53.3%) was the frequently occurring feature. The radiological finding showed that both acute as well as chronic infarction was a frequent feature (46.7%) and commonly involved artery was middle cerebral artery.

Conclusion: Hemiplegia followed by fits was the most occurring clinical findings and middle cerebral artery was found to be most commonly involved. The diagnosis of cerebral arteriopathy is important because of the long-term morbidity in the form of neurological and behavioral complications. Timely treatment and multidisciplinary approach is needed for these complications. Recurrence can also be prevented in this way.

Keywords: Cerebral arteriopathy, Clinical spectrum, Magnetic resonance angiography.

INTRODUCTION

The frequency in children of arterial ischemic stroke and cerebral arteriopathy was found to be 53% and was a frequently occurring risk factor in children[1]. Arteriopathies are of different types, it can be progressive or non-progressive. Moya Moya, sickle cell, primary angitis of CNS are the progressive forms while transient cerebral arteriopathy and arterial dissection are the non progressive forms[2]. The diagnostic criteria was made by Se'bire and his colleagues in 2004 for Moya Moya, other vasculitis, cases of transient cerebral arteriopathy, post varicella arteriopathy and arterial dissection[3]. Cerebral arteriopathy is a well-known entity amongst inflammatory brain diseases in children. Inflammation involving the cerebral blood vessels can be idiopathic, which occurs in healthy children called as childhood primary angiitis of the central nervous system (cPACNS)[4]. Children who are younger than 16 years develop long term sequels of stroke[5]. There is increased risk of death in children with bilateral involvement of cerebral blood vessels[6]. Focal cerebral arteriopathy is described as a separate entity in a newly published classification of arterial ischemic stroke[7]. In all healthy children about 1/3 of anterior circulation stroke are because of transient cerebral arteriopathy[2]. It can occur secondary to varicella infection. Transient cerebral arteriopathy is non-progressive and unilateral involvement of arteries especially supra clinoid portion of internal carotid artery and its proximal branches[11]. Transient cerebral arteriopathy usually progresses in the first few weeks followed by static state for another 6 months

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ultimately leading to improvement[2]. Other causes like aortic dissection[8], fibromuscular dysplasia[9], post radiation vasculopathy[10] can also present like transient cerebral arteriopathy (TCA). The neuroimaging findings of involvement of parenchymal and blood vessels are helpful in differentiating between the types of arteriopathy[11]. The CNS angitis can present in children with severe neurological, psychiatric and cognitive decline[2] and proper rehabilitation is needed to prevent these complications[5]. Primary angitis usually involves the medium and small sized vessels. The cerebral arteriopathy can present with stroke and, cranial nerve involvement[11].

Cerebral arteriopathy is focal or segmental narrowing of blood vessel with irregularity in arterial wall, while sudden blockage of cerebral arteries is due to thrombus or emboli[2]. The rationals of my study is to determine the association between the clinical spectrum and neuroimaging findings of patients with cerebral arteriopathy.

PATIENTS AND METHODS

Total sample size of 60 patients was collected, these patients were admitted in neurology ward either through emergency or outpatient department of Children hospital Lahore during a period of six months from January 2016 to June 2016, through a prospective cross-sectional study. The sample size of patients fulfilling the criteria for cerebral arteriopathy was randomly selected by using non-probability consecutive sampling technique.

These patients were admitted in ward with the suspicion of arterial ischemic stroke. After taking biodata, complete history, clinical examination and MRI findings (including T1 weighted, T2 weighted, fluid inversion recovery sequences and diffusion restriction images). The following investigations were carried out, complete blood count, peripheral blood smear, serum ferritin levels, total iron binding capacity, Hb electrophoresis, bleeding time, prothrombin time and activated partial thromboplastin time, echocardiography and carotid doppler to rule out other causes of ischemic stroke. Once they all turned out to be normal magnetic resonance angiography (MRA) of these patients was carried out which available in our hospital. The findings of arteriopathy on MRA were in the form of narrowing or beading of vessels, there might be irregularities in vessel wall. Other available investigations for inflammation like C reactive protein, erythrocyte sedimentation rate and antinuclear antibody were also carried out. All patients between the ages of 1 month to 16 years were included, while those patients with developmental delay, central nervous system infections like meningitis, encephalitis, and other causes of ischemic stroke were excluded from the study. The study was approved by the hospital ethical committee. After taking informed consent from the parents and the guardians data was collected with the help of a designed proforma which includes the bio data, mode of admission, recurrence of stroke, clinical findings of patients in the form of history including neurological deficit, speech difficulty, altered sensorium and fits while the examination findings include pallor, papilledema, bulging fontanelle and cranial nerve involvement. MRI findings including acute infarction, chronic infarction, both acute and chronic infarcts. Magnetic resonance angiography included involvement of middle, anterior or posterior cerebral arteries their unilateral and bilateral involvement, involvement of middle cerebral artery with anterior cerebral artery, posterior cerebral artery or internal carotid artery. Data was then analyzed by SPSS version 19 to observe the significance of clinical and radiological findings with clinical examination and associated variables. Quantitative variables like age was presented as mean and standard deviation while qualitative variables like MRA and MRI findings were presented in frequencies and percentages. Chi-square test (x^2) was used to compare the variables. A *p*-value of <0.05 was taken as statistically significant.

RESULTS

This study was conducted on total 60 patients admitted in neurology ward children

hospital. Out of these 55% were females (n=33) and 45% were males (n=27). Seventy percent of them were admitted through emergency department while 30% were admitted through outpatient department. Fifty six percent of these patients came with recurrent episodes and remaining 43.3% came with first episode. The patients were divided into three groups according to the ages, group 1 included 1 month to 5 years, group 2 included 5 to 10 years, while group 3 had patients more than 10 years and found that patients <5 years were in larger number (38%) followed by group 2 (15%) and patients in group 3 (7%). The mean ± standard deviation of sample age group was 3.92 ± 3.59. Their clinical spectrum was determined by hemiplegia (96.7%) speech difficulty (38.3%), fits (53.3%), and altered sensorium (41.7%). Altered sensorium was assessed with the help of Glassgow Coma Scale. On examination 66.7% were well and 33.3% were sick. A total of 53.3% patients had cranial nerve involved, bulging fontanelle was found in (6.7%) children below the age of one year. Six point seven percent had papilledema on fundus examination. Amongst the MRI findings 38.3% had acute infarction, 15% chronic infarction while 46.7% both acute as well as chronic infarction. MRA showed unilateral involvement of middle cerebral artery the most common (25%) followed by bilateral middle cerebral artery (21%), 13% of each found with involvement of middle cerebral artery with anterior cerebral artery or posterior cerebral artery, 6.7% of middle cerebral artery with internal carotid artery. Bilateral posterior cerebral artery (10%) and bilateral internal carotid artery (10%). Rest of the investigations were not significant in any patients.

Table-I: Frequencies and association between the radiological finding with altered sensorium.

MRA Findings	Altered Sensorium		Total	*p*-value
	Yes	No		
Unilateral middle cerebral artery	5 (33.3%)	10 (66.7%)	15 (100%)	(p=0.00007)
Bilateral middle cerebral artery	13 (100%)	0	13 (100%)	
Both middle and internal carotid artery	2 (50%)	2 (50%)	4 (100%)	
Both middle & anterior cerebral artery	3 (37.5%)	5 (62.5%)	8 (100%)	
Both middle & posterior cerebral artery	1 (12.55%)	7 (87.5%)	8 (100%)	
Bilateral posterior cerebral artery	0	6 (100%)	6 (100%)	
Bilateral internal carotid artery	1 (16.7%)	5 (83.3%)	6 (100%)	
Total	25 (41.7%)	35 (58.3%)	60 (100%)	

Table-II: Frequencies and association between the radiological findings with fits.

MRA Findings	Fits		Total	*p*-value
	Yes	No		
Unilateral middle cerebral artery	6 (40%)	9 (60%)	15 (100%)	p=0.55
Bilateral middle cerebral artery	9 (69.2%)	4 (30.8%)	13 (100%)	
Both middle and internal carotid artery	2 (50%)	2 (50%)	4 (100%)	
Both middle & anterior cerebral artery	6 (75%)	2 (25%)	8 (100%)	
Both middle & posterior cerebral artery	4 (50%)	4 (50%)	8 (100%)	
Bilateral posterior cerebral artery	2 (33.3%)	4 (66.7%)	6 (100%)	
Bilateral internal carotid artery	3 (50%)	3 (50%)	6 (100%)	
Total	32 (53.3%)	28 (46.7%)	60 (100%)	

Data was analyzed and *p*-value was found to be highly significant with altered sensorium (table-I), It was insignificantly associated with fits (p=0.55), while significantly associated with general wellbeing (p<0.01) of the child as shown in table-II & III respectively. Highly significant values were also found in papilledema as shown in table-IV and cranial nerve involvement

(p<0.001) as discussed in (table-V). Middle cerebral artery was most frequently involved in patients with hemiplegia as shown in table-VI.

DISCUSSION

Our study shows slight female predominance which is in contrast to the two studies showing male dominance[12,13]. While another study conducted in India showed equal distribution of disease between both male and female gender[14]. Among the clinical spectrum we found hemiplegia as the most commonly occurring feature in our population followed by fits, which is very much similar to a study where they found focal deficit (80%) and fits (15%). Middle cerebral artery was also found to be the most commonly involved artery similarly in another study[12]. MRA is an important tool in the diagnosis of cerebral arteriopathy and it reveals area of stenosis[15]. Intracranial vessel wall imaging will be the best future option to rule out the underlying cause and is especially important if the cause is not found in heart or extra cranial arteries[14,16]. Ninety percent of patients with reversible cerebral arteriopathy have good outcome[17]. Recurrences are more common in patients of cerebral arteriopathy[18] and the recurrence rate was found to be 66% in study[13]. A study by Ameli *et al* showed the median age of patients with cerebral arteriopathy was (5.7%) which is very much close to our study in which patients less than 5 years were in large no (38%) similarly unilateral involvement was more common in that study (72%) and anterior circulation was involved commonly (78%)[18].

Reversible cerebral vasoconstriction syndrome is one of the causes which improves with time and thunder clap headache is one of the important symptoms followed by seizures[19]. In cases of involvement of small vessels of cerebrum the neuroimaging findings may be normal or may show diffuse involvemen and is usually diagnosed on brain biopsy[20]. Conventional angio-

Table-III: Frequencies and association between the radiological findings with general wellbeing of patients.

MRA Findings	Examination		Total	p-value
	Well	Sick		
Unilateral middle cerebral artery	9 (60%)	6 (40%)	15 (100%)	p=0.013
Bilateral middle cerebral artery	4 (30.8%)	9 (69.2%)	13 (100%)	
Both middle and internal carotid artery	2 (50%)	2 (50%)	4 (100%)	
Both middle & anterior cerebral artery	6 (75%)	2 (25%)	8 (100%)	
Both middle & posterior cerebral artery	7 (87.5%)	1 (12.5%)	8 (100%)	
Bilateral posterior cerebral artery	6 (100%)	0	6 (100%)	
Bilateral internal carotid artery	6 (100%)	0	6 (100%)	
Total	40 (66.7%)	20 (33.3%)	60 (100%)	

Table-IV: Frequencies and association between the radiological finding with papilledema.

MRA Findings	Papilledema		Total
	Yes	No	
Unilateral middle cerebral artery	0	15 (100%)	15 (100%)
Bilateral middle cerebral artery	0	13 (100%)	13 (100%)
Both middle and internal carotid artery	0	4 (100%)	4 (100%)
Both middle & anterior cerebral artery	1 (12.5%)	7 (87.5%)	8 (100%)
Both middle & posterior cerebral artery	0	8 (100%)	8 (100%)
Bilateral posterior cerebral artery	2 (33.3%)	4 (66.7%)	6 (100%)
Bilateral internal carotid artery	1 (16.7%)	5 (83.3%)	6 (100%)
Total	4 (6.7%)	56 (93.3%)	60 (100%)

graphy can be used safely in children[21]. This conventional angiography is the preferred mode of investigation of patients with cerebral arteriopathy especially involving the medium and large vessels. It can well appreciate the striae and beading pattern that is the area of stenosis followed by dilatation of distal arterial branches[22]. Among patients of arterial ischemic stroke arteriopathy is one of the chief causes but its mechanism is still not well understood[23], because of this poorly understood mechanism it is difficult to develop special treatment modalities[1].

Arteriopathy of medium and large sized vessels consists of both progressive and non-progressive forms, and its non-progressive form is more identical to that of transient cerebral arteriopathy[13]. In cases of small vessel vasculitis the magnetic resonance angiography findings are usually normal[22]. A study showed that the disease activity is higher in patients with small vessel vasculitis as compared to the patients with medium and large arteries involvement[24]. The causes of small vessel involvement could also be primary or secondary. The primary causes include primary angitis of central nervous system and secondary causes include systemic disorders[25]. The biomarkers of inflammation are helpful in patients with small vessel involvement along with MRA findings. MRA findings could be bilateral or diffuse with involvement of both white and deep gray matter[12]. It is reported that in 60% of patients these areas of diffusion restriction were seen, these biomarkers are not helpful in determining the disease outcome[13]. Full thickness brain biopsy is indicated in patients with small vessel involvement[25]. The Calabrese criteria for adult patients regarding primary angitis of central nervous system can also be used for pediatric patients with angitis and the aim of CASCADE criteria was used to

Table-V: Frequencies and association between the radiological findings with cranial nerve involvement.

MRA Findings	Cranial Nerves		Total	*p*-value
	Involved	Not Involved		
Unilateral middle cerebral artery	7 (46.7%)	8 (53.3%)	15 (100%)	*p*=0.0005
Bilateral middle cerebral artery	13 (100%)	0	13 (100%)	
Both middle and internal carotid artery	2 (50%)	2 (50%)	4 (100%)	
Both middle & anterior cerebral artery	3 (37.5%)	5 (62.5%)	8 (100%)	
Both middle & posterior cerebral artery	0	8 (100%0	8 (100%)	
Bilateral posterior cerebral artery	5 (83.3%)	1 (16.7%)	6 (100%)	
Bilateral internal carotid artery	2 (33.3%)	4 (66.7%)	6 (100%)	
Total	32 (53.3%)	28 (46.7%)	60 (100%)	

Table-VI: Frequencies and association between the radiological findings with Hemiplegia.

MRA Findings	Hemiplegia		Total
	Yes	No	
Unilateral middle cerebral artery	13 (86.7%)	2 (13.3%)	15 (100%)
Bilateral middle cerebral artery	13 (100%)	0	13 (100%)
Both middle and internal carotid artery	4 (100%)	0	4 (100%)
Both middle & anterior cerebral artery	8 (100%)	0	8 (100%)
Both middle & posterior cerebral artery	8 (100%)	0	8 (100%)
Bilateral posterior cerebral artery	6 (100%)	0	6 (100%)
Bilateral internal carotid artery	6 (100%)	0	6 (100%)
Total	58 (96.7%)	2 (3.3%)	60 (100%)

reduce the use of overlapping terms such as focal cerebral arteriopathy, transient cerebral arteriopathy and primary angitis of central nervous system[13].

Supportive management of stroke in the form of antithrombotic therapy is helpful[25]. Imuno modulatory drugs are more useful in patients of small vessel vasculitis with steroids and cyclophosphamide[25]. There are certain protocols consisting of steroids for 6 months combined with intra venous pulses of cyclophosphamide on monthly basis and further followed by oral azathioprim and oral steroids for additional 18 months[2]. Methotrexate and mycophenolate mophetin can also be used according to some studies[22].

CONCLUSION

Hemiplegia followed by fits were the most occurring clinical findings and middle cerebral artery was found to be most commonly involved. The diagnosis of cerebral arteriopathy is important because of the long-term morbidity in the form of neurological and behavioral complications. Timely treatment and multidisciplinary approach is needed for these complications. Recurrence can also be prevented in this way.

CONFLICT OF INTEREST

This study has no conflict of interest to declare by any author.

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