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PRESENCE OF ANTI-CARDIOLIPIN ANTIBODY AND ITS ASSOCIATION WITH NEUROPSYCHIATRIC MANIFESTATIONS IN PAEDIATRIC SLE PATIENTS

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ABSTRACT

Background: Neuropsychiatric (NP) manifestation is one of the most critical and severe presentations in paediatric SLE (pSLE) patients. It comprises a wide range of neurological symptoms affecting the central, peripheral, autonomic nervous systems and psychiatric symptoms. One of the most intriguing issue is the association of neuropsychiatric manifestation with anti-cardiolipin (aCL) antibody. **Objectives:** To identify the anti-cardiolipin antibody frequency, its association with NP manifestations and MRI of brain findings in pSLE patients. **Methods:** This was a cross-sectional study conducted in the Department of Paediatrics, Bangabandhu Sheikh Mujib Medical University (BSMMU), from June 2017 to May 2018. Newly diagnosed 50 pSLE patients who fulfilled the ACR criteria were enrolled in this study. Clinical information and laboratory investigations, including aCL antibody were measured and recorded in a pre-designed questionnaire. MRI of the brain was also done in all NP-SLE cases. **Result:** Neuropsychiatric manifestations were found in 40% of pSLE patients. Headache, convulsion, and mood disorder were common NP manifestations. This study found that aCL antibody positivity was present in 52% of pSLE patients. Abnormal MRI findings were observed in 55% of NP-SLE patients and cerebral atrophy was the commonest abnormality. A significant association with aCL antibody and MRI findings was found. **Conclusion:** Anti-cardiolipin antibody was present in 52% of pSLE patients. Associations between NP manifestations with MRI findings was found significant.

KEYWORDS: Anti-cardiolipin (aCL) antibody, Neuropsychiatric manifestation, paediatric SLE.

INTRODUCTION

Neuropsychiatric SLE (NP-SLE) is one of the significant and most severe presentations of pSLE. It comprises a wide range of neurological symptoms affecting the central, peripheral, and autonomic nervous systems as well as psychiatric symptoms.[1] pSLE has a more aggressive clinical course than adult-onset SLE and neuropsychiatric lupus is more frequent in the paediatric age group.[2] Manifestations of NP-SLE vary in severity, ranging from mild headache to life-threatening coma.[3] The prevalence of NP-SLE, ranges from 21% to 95%, and the prognosis following a neuropsychiatric event is highly variable.[4] Rahman et al. in a Bangladeshi study, found that 26% of pSLE patients had neuropsychiatric involvement.[5] The etiopathogenesis of neuropsychiatric manifestations in SLE patients remains largely unknown and has been attributed to autoantibody-mediated neural dysfunction, vasculopathy and coagulopathy. Anti-cardiolipin (aCL), anti-ribosomal p protein, anti-neuronal, anti-ganglioside, and anti-endothelial antibodies have been implicated in the pathogenesis of NP-SLE. One of the most intriguing issues is the association of neuropsychiatric manifestation with aCL antibody.[6] This study aimed to identify the frequency of anti-cardiolipin antibody and their association with NP manifestations and brain MRI findings in pSLE patients.

METHODOLOGY

This Cross-sectional study was carried out in the department of paediatrics, Bangabandhu Sheikh Mujib Medical University (BSMMU), from June 2017 to May 2018. Fifty newly diagnosed paediatric SLE cases fulfilling the ACR classification criteria[7] were enrolled in this study. NP manifestations were classified according to the 1999 ACR case definitions for neuropsychiatric lupus syndromes.[8]

Data were collected in a pre-designed structured questionnaire. Relevant clinical examination and necessary laboratory investigations for SLE diagnosis were done after taking consent from parents. Baseline laboratory investigations like Hb%, total white cell count, differentials, platelet count, ESR, serum creatinine, serum ALT, chest x-ray, urine routine examination, lipid profile, 24- hour urine total protein (UTP), C3, C4, coomb's test, ANA, anti ds-DNA and aCL antibody were done. Anti-cardiolipin antibody was detected by a commercially available ELISA kit (Orgentec, Germany) and performed at the time of diagnosis. The value >15 U/mL was considered as positive. MRI of the brain was performed in pSLE patients with NP manifestations by MAGNETOM AVANTO (Germany) TIM [76X18]. Prior approval of the Institutional Review Board (IRB) of BSMMU, Dhaka, Bangladesh, was taken for the study.

Data were checked, verified, and analyzed by SPSS (statistical program for social science) software 20**.** Mean and standard deviation (SD) were used for reporting. Chi-square test was used to see the association between categorical data. A p-value of less than 0.05 was considered significant.

RESULT

A total of 50 SLE cases were enrolled in this study. Most of the patients were female (82%), and the mean age was 11.56 ± 2.73 years. Mean duration of the disease was 5.58±3.6 months (Table- I). The most common clinical manifestation was constitutional (96%), followed by mucocutaneous (82%), renal (60%), and musculoskeletal (58%) manifestation. Forty percent of patients had neuropsychiatric manifestations; among them headache was most common (65%) followed by convulsion, mood disorder and psychosis. (Table-II) Anti-CL antibody positivity was found in 52 % of pSLE patients. Among the total 20 NP-SLE patients 60% had aCL positivity and 40% were aCL negative. This association was not significant (Table-III). MRI of the brain was done in all the 20 NP-SLE patients and 55% had abnormal findings. Among them, cerebral atrophy (35%) was the commonest, followed by white matter ischemic change, ischemic infarct, and dysmyelinating disease (Table-IV). Among the 20 NP-SLE patients, 60% was aCL positive, of which 81.82% of patients had abnormal MRI findings. On the other hand, 40% NP- SLE was aCL negative; of them, only 18.18% had abnormal MRI findings. The association between aCL positivity and MRI changes was significant (Table-V).

Table I: Demographic data of the paediatric SLE patients (n=50).

Variable	Number of patients	Percentage (%)
Female, n (%)	41	82.0%
Male, n (%)	9	18.0%
Age in years (mean± SD)	11.56±2.73	
Disease duration in months (mean± SD)	5.58±3.6	

Table II: Different clinical presenting features among paediatric SLE patients (n=50).

Clinical manifestation Total number (%)		Number of Patients	Percentage (%)
Constitutional 48 (96%)	Fever	46	95.8
	Fatigue	44	91.6
	Lymphadenopathy	25	52.0
Musculoskeletal 41(58%)	Arthritis	29	100.0
	Myositis	10	34.5
Skin 30 (82%)	Malar rash	34	68.3
	Photosensitivity	28	61.0
	Oral ulcer	26	83.0
	Alopecia	25	63.4
Renal 29 (60%)	Hypertension	23	56.6
	Oedema	17	50.0
	Haematuria	15	46.6
	Proteinuria	14	76.6
Gastrointestinal 27 (54%)	Hepatosplenomegaly	27	100.0
	Ascites	7	26.0
Neuropsychiatric manifestation 20 (40%)	Headache	13	65.0
	Convulsion	11	55.0
	Mood disorder	7	35.0
	Psychosis	5	25.0
	Cerebrovascular disease	3	15.0

Table III: Association between neuropsychiatric manifestation with aCL antibody in pSLE patient (n=50)

Neuropsychiatric status	aCL		
	+ve for aCL (n=26)	-ve for aCL (n=24)	P value
	n (%)	n (%)	
+ve for NP manifestations (n=20)	12 (60)	08 (40)	0.335

P value reached from chi square test

Table IV: Different MRI changes in NP-SLE patients (n=20).

MRI findings	Number	Percentage
Normal	09	45%
Abnormal	11	55%
1) Cerebral atrophy	7	63.3%
2) White matter ischemic changes	5	45.4%
3) Ischemic infarct	5	45.4%
4) Dysmyelinating disease	4	36.3%
5) Haemorrhagic infarct	1	9%

Table V: Association of MRI finding with aCL in paediatric NP-SLE patients (n=20).

aCL	MRI findings				
	Abnormal MRI findings (n=11)		Normal findings (n=9)		P value
	N	%	N	%	
+ve for **aCL (n=12)**	9	81.82	3	33.34	0 .05
-ve for **aCL (n=8)**	2	18.18	6	66.66	
Total	11	100	9		

By applying x^2-test, a statistically significant difference was found ($p<0.05$).

DISCUSSION

NP involvement in pSLE patients develops approximately 70% of children in the first year after initial diagnosis. These complications seem to be more severe in children and are accompanied by higher morbidity and mortality rates.[9] Early recognition of symptoms is crucial in preventing permanent neurological sequel and patients quality of life.

In the present study, the mean age of the children was 11.56 ±2.73 years, and female: male ratio was 4.5:1. It is well established that females are more prone to develop SLE than males.

Different studies in our country and neighboring countries also showed similar findings.[5,10]

In this study, the most common clinical manifestation was constitutional (96%) followed by mucocutaneous (82.0%), renal (60.0%), and musculoskeletal (58%). Musculoskeletal (68%) was the most common manifestation observed in an Eastern Indian study followed by constitutional, renal, and skin involvement.[11] Another study in our country also found that common clinical features were constitutional including fatigue (91%) and fever (83%), followed by arthritis (74%), and skin rash (71%).[5]

In this study, 40% of pSLE patients had neuropsychiatric involvement. Avcin et al. in their Canadian study found that 26 % of pSLE patients had neuropsychiatric manifestations.[6] A review article observed 65% neuropsychiatric involvement in their analysis.[12] Singh et al. in an Indian study, found 55.5% neuropsychiatric involvement in their study.[10] The reason for our lower incidence could be the non-reporting of neuropsychiatric involvement to rheumatology clinic due to lack of awareness.

Headache and seizure disorder were the most frequent NP manifestations found in the Indian study.[10] We found headache, convulsion, mood disorder, and psychosis as frequent NP manifestations in this study. Hajghaemi et al. in a study done in Iran also identified headache, cerebrovascular disease, and seizure as important NP manifestations.[13]

In the present study, 52% of pSLE patients had aCL positivity, and 40 % had neuropsychiatric involvement. On the other hand among NP-SLE cases 60% were aCL positive. An Egyptian study found that 16.7% aCL positive patients had neuropsychiatric involvement.[12] In a study done in Taiwan, it was also observed that 47.8% aCL positive pSLE patients had neuropsychiatric manifestations.[13] The frequency of NP manifestations with aCL positivity in different studies were more or less similar to our study.

MRI evaluation of the present study detected that 55% of NP-SLE patients had abnormal findings, among which cerebral atrophy was the most frequent finding. Cerebral atrophy, ischemic infarct, and hemorrhagic infarct were the significant MRI findings found in a study done in Taiwan.[15] A study conducted in KSA showed that 68% of NP-SLE patients had MRI abnormalities. White matter ischemic changes (92%), cerebral atrophy (23%), and basal ganglia calcification (7.69%) were the abnormal MRI findings described in their study.[16] All results were consistent with the present study.

Among 20 NP-SLE patients, 60% had aCL positivity, and 81.8% of them had abnormal MRI findings. On the other hand, 18.18% of NP-SLE patients had abnormal MRI findings, which were aCL negative. Abnormal MRI findings were much higher among those who had positive aCL antibody. The association between aCL seropositivity and MRI changes was found significant in this study. This finding was similar to the study conducted by Menon et al. where significant correlations between abnormal MRI results and the presence of aCL antibody was found.[17]

CONCLUSION

NP manifestations were found in 40% of pSLE patients and among them 46.2% had anti- cardiolipin antibody positivity. The most common neuropsychiatric manifestations were headache, convulsion and mood disorder. The association between aCL positivity and NP manifestations was not significant. MRI findings were found abnormal in 55% of NP-SLE patients and was significantly associated with aCL antibody positivity.

Key massage

What is already known about this subject?

- Neuropsychiatric manifestations are common in paediatric SLE patients and significantly associated with anti-cardiolipin antibody

What does this study add?

- MRI findings were found abnormal in NP-SLE patients and was significantly associated with aCL antibody positivity.

How might this impact on clinical practice?

- This study identified the NP manifestations, ensure effective treatment, and minimize this disease's morbidity.

Competing interests: None.

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Ethical approval information

Ethical clearance of this study was taken from the Institutional Review Board (IRB), Bangabandhu Sheikh Mujib Medical University, Dhaka on 31/07/2017 and reference no: BSMMU/2017/8026.

REFERENCES

1. Mak A, Ho RC, Lau CS. Clinical Implications of Neuropsychiatric Systemic Lupus Erythematosus. Advances in Psychiatric Treatment. 2009; 15(6): 451-58. DOI: 10.1192/apt.bp.108.005785
2. Khajezadeh AM, Zamani GR, Moazzami, Nagahi Z, Torshizi MM, Ziaee V. Neuropsychiatric Involvement in Juvenile-Onset Systemic Lupus Erythematosus. Neurology Research International 2018, Article ID 2548142:1-7 https://doi.org/10.1155/2018/2548142
3. Miyakis S, Lockshin MD, Atsumi T, Branch DW, Brey RL, Cervera RH et al. International Consensus Statement on An Update of The Classification Criteria for Definite Antiphospholipid syndrome (APS). Journal of Thrombosis and Haemostasis. 2006; 4(2):295-306. https://doi.org/10.1111/j.1538-7836.2006.01753.x
4. Hanly JG. Diagnosis and Management of Neuropsychiatric SLE. Nature Reviews Rheumatology. 2014; 10(6): 338-47. https://doi.org/10.1038/nrrheum.2014.15
5. Rahman SA, Islam MI, Talukder MK, Islam MM, Huque SS, Roy RR. Presentation of Childhood Systemic Lupus Erythematosus in a Tertiary Care Hospital. Bangladesh Journal of child health. 2014; 38(3): 124-29. https://doi.org/10.3329/bjch.v38i3.22819
6. Avčin T, Benseler SM, Tyrrell PN, Čučnik S, Silverman ED. A follow-up study of anti hospholipid antibodies and associated neuropsychiatric manifestations in 137 children with systemic lupus erythematosus. Arthritis Care & Research. 2008; 59(2): 206-13. DOI: 10.1002/art.23334
7. Hochberg MC. Updating the American College of Rheumatology revised criteria for the classification of systemic lupus erythematosus. Arthritis Rheum 1997; 40: 1725
8. ACR Ad Hoc Committee on Neuropsychiatric Lupus Nomenclature. The American College of Rheumatology nomenclature and case definitions for neuropsychiatric lupus syndromes. Arthritis Rheum 1999;42: 599–608
9. Kamphuis S, Silverman ED. Prevalence and Burden of Pediatric-Onset Systemic Lupus Erythematosus. Nature Reviews Rheumatology. 2010; 6(9): 538–46. https://doi.org/10.1038/nrrheum.2010.121

10. Singh S, Gupta MK, Ahluwalia J, Singh P, Malhi P. Neuropsychiatric Manifestations and Antiphospholipid Antibodies in Pediatric Onset Lupus:14 years of Experience From a Tertiary Center of North India. Rheumatology International. 2009; 29(12): 1455-61. DOI: 10.1007/s00296-009-0887-6
11. Mondal R, Nandi M, Ganguli S, Ghosh A, Hazra A. Childhood Lupus: Experience From Eastern India. Indian Journal of Pediatrics. 2010; 77(8): 889-91. DOI: 10.1007/s12098-010-0126-x
12. Levy DM, Kamphuis S. Systemic Lupus Erythematosus in Children and Adolescents. Pediatr Clin North Am. 2012; 59(2): 345-64. DOI: 10.1016/j.pcl.2012.03.007
13. Hajighaemi F, Etemadifar M, Bonakdar ZS. Neuropsychiatric Manifestations in Patients with Systemic Lupus Erythematosus: A study from Iran. Advanced biomedical research. 2016; 5: 43. DOI: 10.4103/2277-9175.178795
14. Mostafa GA, Ibrahim DH, Shehab AA, Mohammed AK. The Role of Measurement of Serum Autoantibodies in Prediction of Pediatric Neuropsychiatric Systemic Lupus Erythematosus. Journal of Neuroimmunology. 2010; 227(1-2):195-201. https://doi.org/10.1016/j.jneuroim.2010.07.014
15. Yu HH, Lee JH, Wang LC, Yang YH, Chiang BL. Neuropsychiatric manifestations in Pediatric Systemic Lupus Erythematosus: a 20-year Study. Lupus. 2006; 15(10): 651-57. DOI: 10.1177/0961203306070990.
16. Olfat MO, Al-Mayouf SM, Muzaffer MA. Pattern of Neuropsychiatric Manifestations and Outcome in Juvenile Systemic Lupus Erythematosus. Clinical Rheumatology. 2004; 23(5): 395-99. DOI: 10.1007/s10067-004-0898-3.
17. Menon S, Shortall EJ, Newman SP, Hall-Craggs MR, Chinn R, Isenburg DA. A Longitudinal Study of Anti Cardiolipin Antibody Levels and Cognitive Functioning in Systemic Lupus Erythematosus. Arthritis & Rheumatism.1999; 42(4): 735–41. https://doi.org/10.1002/1529-0131(199904)42:4<735::AID-ANR17>3.0.CO;2-L