DOI Number: 10.5958/0976-5506.2018.01894.6

Association between Papilledema and Guillian - Barré Syndrome

Mohammad A.S. Kamil[1], Aqeel K. Hatem[2], Adel M. Abbass[3], Sajidli. Alhussaini[4]

[1]Fallujah University/ College of Medicine,[2]Baghdad University College of Medicine, [3]AL.hr-rssaiarrl eaching Hospital.Thiear, [4]Nursing Home Hospital/Medical City

ABSTRACT

Background: Guillain barre syndrome is monophasic acute polyradiculoneuropathy autoimmune in nature, it appears as rapid developing areflexia and motor weakness with or without sensory and autonomic disorder, it reaches nadir in less than 4 weeks. Papilledema is rare and usually asymptomatic finding in patient with GBS, the CSF protein is usually elevated in GBS with papilledema, and high protein level will cause a disorder in the appropriate absorption of CSF at the arachnoid villi.

Aim of the study: To determine the percent of papilledema in GBS, the causes of papilledema in GBS, the correlation of papilledema to different clinical presentations of GBS.

Patients and method: A cross sectional study was made on seventy patients who have GBS during 4 weeks hospitalization, males are thirty seven and females are thirty three, that admitted to neurological ward and Respiratory Care Unit in Baghdad Teaching Hospital between 1st January- 2017 to 1st January- 2018. All patients were newly diagnosed by consultant neurologist and selected according to criteria by Asbury and Cornblath 1990 and meet with Brighton Collaboration Diagnostic Criteria Level 1and 2.Regarding patients who have papilledema diagnosed by consultant neurologist by fundoscopic examination and supported by consultant ophthalmologist by slit lamp examination .

Results: There is a correlation between GBS and papilledema, in this study 3 patients had papilledema, the percent of papilledema in GBS was (4.29%) and the cause appears to be high CSF protein.

Conclusions : Regarding the patients who had elevated CSF protein, there is significant association between the presence of papilledema and need for mechanical ventilation. There is more correlation between AIDP and papilledema as compared with (AMAN, AMSAN).

Keywards: *Gullian berre syndrome, papilledema, cerebrospinal fluid protein, Acute inflammatory demyelinating Polyneuropathy.*

INTRODUCTION

Guillain Barré syndrome is an acute monophasic polyradiculoneuropathy autoimmune in nature. It manifests as rapidly evolving areflexic motor paralysis with or without sensory disturbance and autonomic manifestation. The usual pattern is an ascending paralysis, it may be severe and fulminant[1] .Two-thirds of patients can recall a preceding illness, most frequently upper respiratory in 58% or gastrointestinal infection in 22%, respiratory and gastrointestinal illness in

10%, surgery in 5%, or immunization 1 - 4 weeks before the onset of neurological symptoms in 3% [2]. its begins commonly with acroparesthesia, followed 7–10 days later by symmetric ascending type weakness, associated with severe radicular pain in up to two thirds of patient, proximal and distal weakness is usually the predominant feature, Hyporeflexia or areflexia may be delayed one week. Most reach weakness nadir by 2 weeks, but 80% by 3 weeks and 90% by 4 weeks, The disease ranges

Corresponding author :
Dr. Mohammad A.S. Kamil
Fallujah University/ College of Medicine
E-mail: mohkamil68@gmail.com 009647707216142.

Indian Journal of Public Health Research & Development, December 2018, Vol. 9, No. 12 from mild weakness to flaccid quadriplegia and up to one-third progress to respiratory failure, AIDP accounts for 80% of GBS cases,CSF protein is elevated in most patients[3].

Protein elevated in 90% in the absence of white blood cell elevation (less than 20 per mm_3), called albuminocytologic dissociation, CSF protein elevation may be delayed; a repeated lumbar puncture in 5 to 7 days may be supportive of the diagnosis,CSF pressure typically normal but may be raised and high protein cause papilloedema [4].

Papilledema mean optic nerve head swelling caused by increased intracranial pressure with absent spontaneous venous pulsations, usually bilateral but may be asymmetric[5] .It is primarily due to a rise of pressure in the optic nerve sheath, which produces axoplasmic flow stasis in the optic nerve fibers in the surface nerve fiber layer and prelaminar region of the optic nerve head, Axoplasmic flow stasis then results in swelling of the nerve fibers, and consequently of the optic disc, Swelling of the nerve fibers and of the optic disc secondarily compresses the fine, low-pressure venules in that region, resulting in venous stasis and fluid leakage; that leads to the accumulation of extracellular fluid[6]. Papilledema caused by brain mass like tumor or pseudotumor include: Idiopathic intracranial hypertension, cerebral venous thrombosis, meningeal diseases include infections, gliomatosis cerebri, drugs include hypervitaminosis A, administration or withdrawal of corticosteroids, metabolic disturbances, hyper- and hypoadrenalism, myxedema, hypoparathyroidism, GBS, spinal tumor such as oligodendroglioma, systemic lupus erythematosus, severe systemic hypertension, and hypersecretion of CSF by a choroid plexus tumor [7].

Papilledema and raised intracranial pressure have been reported in association with GBS, The cerebrospinal fluid protein is usually reported to be high. In most of these reports the papilledema appeared after established limb weakness and very rare the papilledema preceded the limb weakness, These elevated proteins will cause a defect in the proper absorption of CSF at the arachnoid villi, giving rise to increase intracranial pressure[8].

The Pseudotumor cerebri also been rarely reported with (AIDP), where the CSF protein level was normal and papilledema develop [8].The papilledema in patients with Guillain Barré syndrome may be very rarely secondary to cerebral edema and hypernatremia [9].

Aim of the study: To determine the percentage and causes of papilledema in GBS, correlation of papilledema to different clinical presentations of GBS.

Patients and methods:

A cross sectional study was made on seventy patients have GBS during 4 weeks hospitalization, who were admitted to neurological ward and Respiratory Care Unit of Baghdad Teaching Hospital between 1_{st} of January- 2017 to 1_{st} January- 2018. The age of patients ranged from 18–75 years, males are thirty seven and females are thirty three. All patients gave their consent to participate in the study.

The inclusion criteria: All patients selected according to criteria by Asbury and Cornblath 1990, and meet with Brighton Collaboration Diagnostic Criteria Level 1and 2 [10,11] .All patients were newly diagnosed by consultant neurologist and were investigated by Electromyography and Nerve

Conduction Studies, CSF opening pressure and analysis was done after at least seven days from the onset of the disease. All patients who had papilledema were diagnosed by consultant neurologist by fundoscopic examination and classified according to Frise´n Papilledema Grading Scale, supported by consultant ophthalmologist by slit lamp examination and Optical Coherence Tomography (OCT) to excluded pseudopapilloedema and to approve finding.

The exclusion criteria: The patients with secondary causes of papilledema.[7] .The following investigations were done for every patient with papilledema to exclude secondary causes:1-Brain and Spine Magnetic Resonance Imaging (MRI)**,** Magnetic Resonance Venography (MRV) .2-CSF pressure and analysis.3-Serum calcium and sodium.4-Liver and renal function test.5-Complete blood count, erythrocyte sedimentation rate and C reactive protein.6-Antinuclear antibody, anti-double stranded DNA antibody, lupus anticoagulant, anticardiolipin antibody.

Statistical analysis: SPSS 20.0.0 software package applied to do the statistical analysis, p value considered when suitable to be significant if less than 0.05.

RESULTS

In this study, the age of patients range from (18-75) years with mean age of (36.1 ±16.2) years, 33 (47.1%) are female while 37 (52.9%) of patient are male.

Forty four patients had antecedent infection (few weeks) preceding onset of the weakness, being most frequent respiratory tract infection (RTI) in 33 (47.1%), diarrhea in 7 (10.0%) of patients and 26 (37.1%) of patients had no previous infection.

The sensory symptoms was obsereved in 45 patients(64.3%),bulbar involvement in 24 patients (34.3%),involvement in 18 respiratory patients (25.7%),requirement for mechanical ventilation in 10 patients(14.3),facial weakness in 29 patients (41.4%),as shown in table 1

Three patients (4.29%) of GBS developed papilledema, while the remaining 67 (95.71%) did not had papilledema,as illustrated in table 2.

In the current study three cases had papilledema, two of them male and one female were presented below are their characteristics, which in summary; 2/3 had grade 2 papilledema presented within the 3rd week, with 1/3 presented in the 2nd week had grade 1 papilledema. All three cases were asymptomatic, as illustrated in table 3.

There was no significant difference in age, gender, limb weakness, sensory symptom, bulbar weakness, respiratory involvement, requirement for mechanical ventilation, bifacial weakness and cells in CSF among patients presented with or without papilledema. On the other hand, the CSF protein level and pressure was significantly elevated in GBS with papilledema compared to those without, with p value (0.004),(0.001) respectively, as illustrated in table 4.

In this study 47(67.1%)of patients had high CSF protein level ,there was no significant difference in age ,gender and various presentations (limb weakness ,sensory symptoms ,bulbar weakness, respiratory involvement and bifacial weakness)among patients presented with or without papilledema w, but on other hand there was significant association between requirement for mechanical ventilation and patient had papilledema with p value (0.016), as illustrated in table5.

In the current study four cases were AMAN and two cases were AMSAN, the CSF protein was lower than that in patients with (AMAN, AMSAN) compared to those with AIDP with p value (0.002), Odd Ratio (0.978) and 95% Confidence Interval (0.955–0.999), i.e. there is negative relationship between CSF protein level and axonal variant (AMAN, AMSAN), as illustrated in table 6.

Table 1: Demographic and clinical characteristics (Descriptive data).

Variables	Value
Age (years), mean ± SD	36.1 ± 16.2
Gender, number (%)	
Female	33 (47.1%)
Male	37 (52.9%)
Antecedent infection, number (%)	
Respiratory tract infection (RTI)	33 (47.1%)
Diarrhea	7 (10.0%)
Others	4 (5.7%)
Negative	26 (37.1%)
Presentation	
MRC score of Limb weakness, mean ± SD	35.8 ± 10.5
Sensory Symptom, number (%)	45 (64.3%)
Bulbar involvement, number (%)	24 (34.3%)
Respiratory involvement, number (%)	18 (25.7%)
Requirement for mechanical ventilation, number (%)	10 (14.3%)

Table 2: Frequency of papilledema in GBS patients (n=70).

	NO.	%	95%CI
papilledema	3	4.29	3.81 – 4.76%
No papilledema	67	95.71	-

Table 3: Characteristic of the patients with papilledema.

ID	Timing	Grade	CSF pressure	CSF protein	CSF	Fate of
			(up to 250mm	(up to 45 mg/dl)	WBC	papilledema
			H2o)			after 3
						months
1	3rd week	Grade2	240	220	1	Recover
2	3rd week	Grade2	220	205	2	Recover
3	2nd week	Grade1	220	210	4	Recover

Table 4: GBS patients compared according to presentation with or without papilledema (n=70).

Variables	No papilledema	Papilledema		P value
	(n=67)	(n=3)		
Age (years), mean ± SD	35.33 ± 5.03	36.12 ± 16.49		0.935
Gender				0.599
Female	31 (46.3%)	2	(66.7%)	
Male	36 (53.7%)	1	(33.3%)	
Presentation				
MRC score of limb	44.00 ± 3.46	35.40 ± 10.62		0.169
weakness, mean ± SD				
Sensory Symptom	42 (62.7%)	3	(100.0%)	0.548
Bulbar weakness	22 (32.8%)	2	(66.7%)	0.269
Respiratory involvement	16 (23.9%)	2	(66.7%)	0.160
Requirement for	8 (11.9%)	2	(66.7%)	0.052
mechanical ventilation				
Bifacial weakness	26 (38.8%)	3	(100.0%)	0.067
CSF analysis				
Pressure, mean ± SD	168.43 ± 29.19	226.67 ± 11.55		0.001
Protein level , mean ± SD	108.79 ± 59.11	211.67 ± 7.64		0.004
Cells, mean ± SD	2.33 ± 1.53	1.64 ± 2.33		0.298
EMG study				
Demyelinating	61 (91.0%)	3 (100.0%)		1.0
Axonal	6 (9.0%)	0 (0.0%)		

Table 5: High CSF protein level GBS patients compared according to presentation with or without ›illedema (n=47).

Variables	No papilledema (n=44)	Papilledema (n=3)	P value
Age (years), mean ± SD	34.36 ± 16.25	35.33 ± 5.03	0.919
Gender			0.579
Female	19 (43.2%)	2 (66.7%)	
Male	25 (56.8%)	1 (33.3%)	
Presentation			
MRC score of limb weakness, mean ± SD	36.00 ± 10.20	44.00 ± 3.46	0.166
Sensory Symptom	29 (65.9%)	3 (100.0%)	0.541
Bulbar weakness	13 (29.5%)	2 (66.7%)	0.235
Respiratory weakness	8 (18.2%)	2 (66.7%)	0.110
Requirement for mechanical ventilation	2 (4.5%)	2 (66.7%)	0.016
Bifacial weakness	18 (40.9%)	3 (100.0%)	0.082

Table 6: Correlation between CSF protein level and GBS variant types.

	(AIDP)	(AMAN,AMSAN)	OR	95%CI	P value
Protein level	118.2 ± 61.7	59.5 ± 22.6	0.978	0.955–0.999	0.002

DISCUSSION

In this study there was association between Guillain Barré syndrome and papilledema, the percentage of papilledema in Guillain Barré syndrome was (4.29%). This agree with study done by Karkare in Bangalore (India) on sixty patients with Guillain Barré syndrome who found the percentage of papilledema was (3.3%)[12].And consisted with the Turkish study done by Güngör on thirty-two Guillain Barré syndrome patients which found the percent of papilledema was (3.1%)[13]. And also similar to the percent of papilledema in Guillain Barré syndrome reported by Canadian Ophthalmological Society 2015 which confirm the papilledema detected in (4%) of Guillain Barré syndrome cases[14].

In this study three cases were reported with papilledema, regarding the causes of papilledema in GBS, this study found that the CSF protein level and pressure was significant elevated in Guillain Barré syndrome with papilledema compared to those without. In the current study not all patients had high CSF protein, only (67.1 %) of the patients had high CSF protein level during first 2 weeks of disease, this agree with study done by Massachusetts General Hospital (Boston) on 110 patients with GBS which found the CSF

protein elevations in (73 %) of patients[15]. And agree with the Indian study done by Kalita between 2000 and 2012 on 328 Guillain Barré syndrome patients who found (68%) had CSF albuminocytological dissociation [16]. The possible explanation of high CSF protein was increase in permeability of the blood – nerve – barrier due to inflammation of the proximal nerve roots, thus will lead to defect in absorption of CSF at arachnoid villi and increase ICP[8].

Regarding other clinical feature of GBS in patients with papilledema, the follow up (after 3 months) also showed complete resolution of these finding, this agree with usual outcome of disease in general which was reported by Biomed Central Neurology in United Kingdom (BMC) 2013 in which (87%) of GBS experience full recovery [17].

This study showed there is significant correlation between (CSF Protein level and CSF pressure) with time of CSF aspiration, the CSF protein level and pressure increase with time, this agree with Turkish study by Sahin carried out between 2011 and 2015 on 24 patients in which the CSF Protein level could be normal in first week and start to elevated after that in 2nd and 3rd week [18] .And since the cause of papilledema is the high CSF protein, so give impression for increase possibility to find papilledema with time of disease progression.

CONCLUSIONS

There is correlation between GBS and papilledema, the percent of papilledema in GBS was 4.29%.

CSF protein level and pressure was significantly elevated in patients with papilledema comparing to those without. CSF protein level and pressure was elevated with time of disease progression.

No significant difference in the age, gender, limb weakness, sensory involvement, bulbar involvement, respiratory involvement, need for mechanical ventilation and facial palsy among patients presented with or without papilledema. But regarding the patients who had high CSF protein, there is significant association between papilledema and requirement for the mechanical ventilation.

There is more correlation between papilledema and AIDP as compared to (AMAN, AMSAN).

Ethical Clearance- Taken from Iraqi Board for Medical Specialization /Ministry of Higher Education And Scientific Research /Republic of Iraq**.**

Source of Funding : Self

Conflict of Interst: Nil

REFERENCES

1. Hauser SL, Amato AA. Guillain-Barré Syndrome and other immune-mediated neuropathies. In: Hauser SL, Josephson SA. (eds.) Harrison‟s Neurology in Clinical Medicine. 4th ed. New York: McGraw-Hill; 2017.p.681-690.
2. Katirji B, Koontz D. Disorders of Peripheral Nerves. In: Daroff RB, Jankovic J, Mazziotta JC, Fenichel GM. (eds.) Bradley‟s Neurology in Clinical Practice. 6th ed. Philadelphia: Elsevier; 2011.p.1957-1958.
3. Dazen MM, Saperstein DS. Acquired immune demyelinating neuropathies. Continuum (Minneap Minn). 2014;20(5):1241–1260.
4. Lunn M, Hanna M, Howard R, Parton M, Rahman S, Reilly M, et al. Nerve and Muscle Disease. In: Clarke C, Howard R, Rossor M, Shorvon S. (eds.) A Queen Square Textbook of Neurology. 2nd ed. Black well: John Wiley & Sons, Ltd; 2016.p.414-416.
5. Baliga RR. (eds.) 250 cases in clinical medicine. 4th ed. Oxford: Elsevier Ltd; 2012.p.711-714.
6. Hayreh SS. Pathogenesis of optic disc edema in raised intracranial pressure. Prog Retin Eye Res. 2016 Jan;50:108-44.
7. Maurice V. Disturbances of Cerebrospinal Fluid, Including Hydrocephalus, Pseudotumor Cerebri, and Low-Pressure Syndromes. In: Ropper AH, Samuels MA, Klein JP.(eds.) Adams

and Victor's principles of neurology.10th ed. New York: McGraw-Hill Education; 2014.p.617-638.
8. Kharbanda PS, Prabhakar S, Lal V, Das CP. Visual loss with papilledema in Guillain-Barre syndrome. Neurology India. 2002; 50: 528-529.
9. Colls BM. Guillain-Barr´e syndrome and hyponatraemia. Internal Medicine Journal. 2004;34(4):218.
10. Asbury AK, Cornblath D H. Assessment of current diagnostic criteria for Guillain-Barre syndrome. Ann Neurology J. 2004; 27:21.
11. Donofrio PD. Guillain-Barre´Syndrome. Continuum (Minneap Minn).2017;23(5):1295–1309.

1. Karkare K, Taly AB, Sinha S, Rao S. Temporal profile of pain and other sensory manifestations in Guillain-Barre' syndrome during ten days of hospitalization. Neurology India. 2011;(5):712.
2. .Güngör L, Güngör İ, Öztürk HE, Onar MK. Visual Evoked Potentials in Guillain-Barré Syndrome. J Clin Neurol. 2011;7(1):34-39.
3. Bruce CT, McClelland CM, Van Stavern GP. Papilledema in an otherwise clinically typical case of Miller Fisher syndrome. Can J Ophthalmol. 2015; 50: e67–e69.
4. Ropper AH, Wijdicks EFM, Truax BT. Guillain-Barré Syndrome.
5. Contemporary Neurology Series. 1991; 34:57.
6. .Kalita J, Misra U, Goyal G, Das M. Guillain-Barré syndrome: subtypes and predictors of outcome from India. Journal of the Peripheral Nervous System. 2014; 19:36–43.
7. Gonza´ lez-Sua´ rez I, Sanz-Gallego I, Rodriquez de Rivera FJ, Arpa J. Guillain-Barre´ syndrome: natural history and prognostic factors: a retrospective review of 106 cases. BMC Neurol. 2013; 13:95.
8. Sahin S, Cinar N, Karsidag S. Are cerebrospinal fluid protein levels and plasma neutrophil/lymphocyte ratio associated with prognosis of Guillain Barré syndrome?. Neurology International. 2017;. 9(2):7032..