Scientific Research Publishing

Neuroscience & Medicine, 2021, 12, 79-89
https://www.scirp.org/journal/nm
ISSN Online: 2158-2947
ISSN Print: 2158-2912

Comparative Analysis of Post-Rehabilitation Neuropsychological Profile of a Patient with Susac Syndrome—A Case Report

Jimmy Zúñiga-Márquez[1*], Nataly Gutierrez-Ávila[1], Patricia Quintero-Cusgüen[1], José Traslaviña-Sierra[2], Leidy Salazar-Tapiero[2], Lady Carrillo-Alba[2], Lina Caquimbo-Salazar[2], Claudia Murillo-Espinosa[2], Michel Hernández[1]

[1]Hospital Universitario de la Samaritana, Bogotá, Colombia
[2]Neuropsychological Assessment and Diagnosis Specialization Program, School of Psychology, Universidad San Buenaventura Bogotá, Bogotá, Colombia
Email: *jirazuma@hotmail.com, neuropsicologia@hus.org.co

How to cite this paper: Zúñiga-Márquez, J., Gutierrez-Ávila, N., Quintero-Cusgüen, P., Traslaviña-Sierra, J., Salazar-Tapiero, L., Carrillo-Alba, L., Caquimbo-Salazar, L., Murillo-Espinosa, C. and Hernández, M. (2021) Comparative Analysis of Post-Rehabilitation Neuropsychological Profile of a Patient with Susac Syndrome—A Case Report. *Neuroscience & Medicine*, **12**, 79-89.
https://doi.org/10.4236/nm.2021.123007

Received: August 9, 2021
Accepted: September 21, 2021
Published: September 24, 2021

Abstract

Susac Syndrome (SS) is an autoimmune disease characterized by the clinical triad of encephalopathy, hearing loss and retinal arterial occlusions, with prevalent structural changes identified on brain magnetic resonance imaging (white matter, corpus callosum, basal ganglia region and the thalamic region extending to the midbrain) in the majority of cases, which lead to cognitive manifestations of which there is a paucity of descriptions in the literature. The objective of this case study is to compare to post-rehabilitation neurocognitive profile of a 29-year-old woman with SS presenting with compromised intellectual and motor skills and cognitive functions, together with neuropsychiatric symptoms. Better performance was found in the neuropsychological assessment, with changes in the structural cerebral network evidenced on Diffusion Tensor Imaging (DTI) performed following the therapeutic and pharmacological intervention.

Keywords

Susac Syndrome, Demyelinating Disease, Neuropsychological Assessment, Rehabilitation

1. Introduction

Susac Syndrome (SS) is considered an orphan autoimmune disease that affects the microvasculature of the brain, the retina and the ear [1] [2], secondary to CD8 T-cell mediated inflammatory endotheliopathy. It compromises the main

blood-brain barrier functions due to leukocyte and other blood flow restrictions as a result of brain endothelial inflammation and microvascular occlusion [3] [4]. High quantities of CD4 immunoglobulins are found in more than 50% of the capillaries in brain biopsies; these deposits suggest antibody-mediated microvascular lesions [5] [6]. Susac syndrome is characterized by the clinical triad of subacute encephalopathy, hearing impairment including sensorineural hearing loss, neural hearing loss or vestibulopathy, and visual deficit associated with branch Retinal Artery Occlusions (RAO) [7] [8] [9] which respond to pharmacological treatment with immunosuppressants [10].

Typical SS findings on brain imaging include microinfarcts in the central portion of the corpus callosum, with hyperintense signals on T2 weighted images and FLAIR; later, during a subacute phase, hypointense signals of snowball appearance are seen on T1-weighted images [11] which, over time, may have the shape of a hole. Miliary lesions can also be found throughout the deep and cerebellar peripheral white matter as well as in the cerebellar peduncles, the thalamic region and the brainstem [12] [13].

Cerebrospinal Fluid (CSF) analysis in patients with SS shows higher amounts of protein with or without lymphocytic pleocytosis, as well as anti-endothelial cell serum antibodies in cases of encephalopathy [14]. Additionally, expected findings on ophthalmological fluorescein angiography include acute RAO, arterial wall segmental focal staining or damage to the internal retinal layers involving nerve fibers ranging from the nerve fiber layer to the external plexiform region, leak due to blood vessel lesions and loss of junctions. These characteristics can be observed even if the patient is asymptomatic [7] [15].

A case of a female patient diagnosed with Susac syndrome is presented. The patient was assessed by neurology and neuropsychology and treated with immunosuppressants and comprehensive rehabilitation. Workup included brain Magnetic Resonance Imaging (MRI) and Diffusion Tensor Imaging (DTI) with follow-up over more than 8 years, describing changes following pharmacological intervention and comprehensive rehabilitation.

2. Case Presentation

A 23-year-old female patient with incomplete professional education, a clinical picture of 5 days of holocranial headache associated with memory loss, bradypsychia and altered gait, with a probable diagnosis of Central Nervous System (CNS) demyelinating disease including Multiple Sclerosis (MS), Devic's disease or acute disseminated encephalomyelitis.

Brain MRI performed in 2013 showed evidence of hyperintense miliary lesions involving mainly white matter of the corona radiata, centrum semiovale, corpus callosum, basal ganglia region in the posterior segment of the right medial and lateral ipsilateral capsule, right thalamic region with midbrain to pontine extension, and at the level of the cerebellum (see **Figure 1**). The diagnosis of Susac syndrome was made based on the findings. Pharmacological treatment was

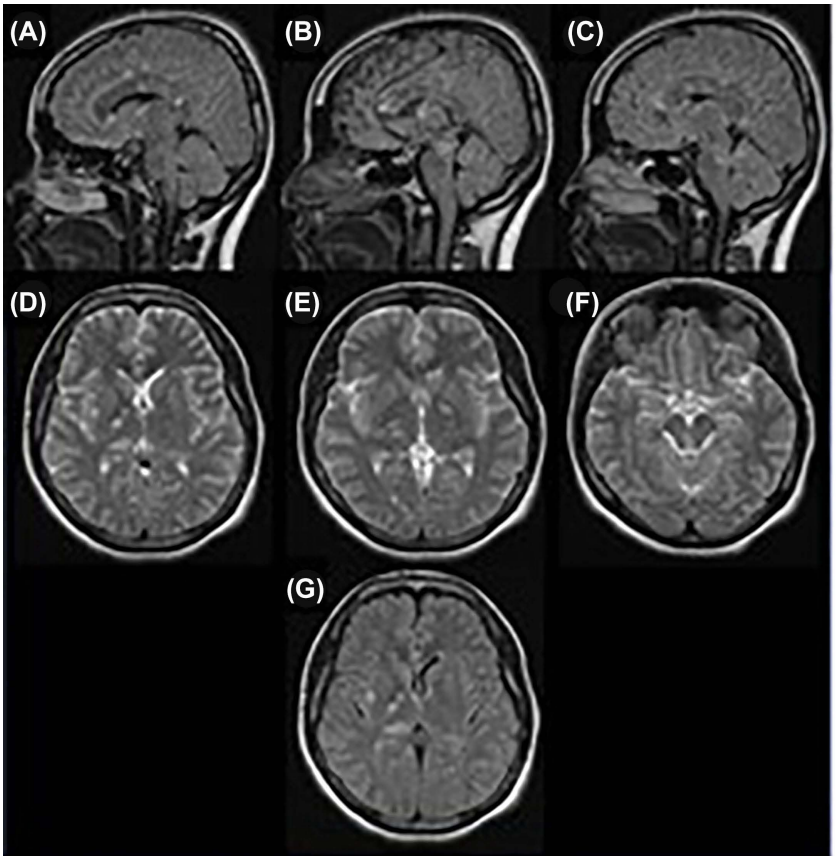

Figure 1. Brain MRI in 2013: (A-C) Sagittal section, T1-weighted image; (D-F) axial section, T2-weighted image; (G) axial section, FLAIR sequence. Hyperintense miliary lesions involving mainly white matter of the corona radiata, centrum semiovale, corpus callosum, basal ganglia region in the posterior segment of the right medial and lateral ipsilateral capsule, right thalamic region with midbrain to pontine extension, and at the level of the cerebellum.

initiated with methylprednisolone bolus 1000 mg/day for 5 days, immunoglobulin 400 mg/kg/day for 5 días, followed by rituximab 1000 mg infusion and new bolus after 15 days, and then 1000 mg infusion every 6 months.

Contrast brain MRI was performed one year later (see **Figure 2**).

Digital Fluorescein Angiography (FA) (see **Figure 3**).

In 2017, the patient was seen by the neuropsychology service for higher cognitive function assessment. On admission to the service, the patient was in physical therapy and receiving pharmacological treatment with rituximab 1000 mg infusion every 6 months, prednisolone 5 mg/day, levetiracetam 500 mg/day, sertraline 50 mg/day, risperidone 1 mg/day, calcium carbonate 600 mg/day, bromocriptine 2.5 mg /day. Follow-up by inter-disciplinary team during a 3-year period was decided, in order to strengthen basic and complex cognitive processes that include functional skills.

The neuropsychological assessment protocol used with the patient consisted of: Mini Mental State Examination (MMSE), perception, language and praxis subtests of the Barcelona Test revised version, Brief Test of Attention (BTA),

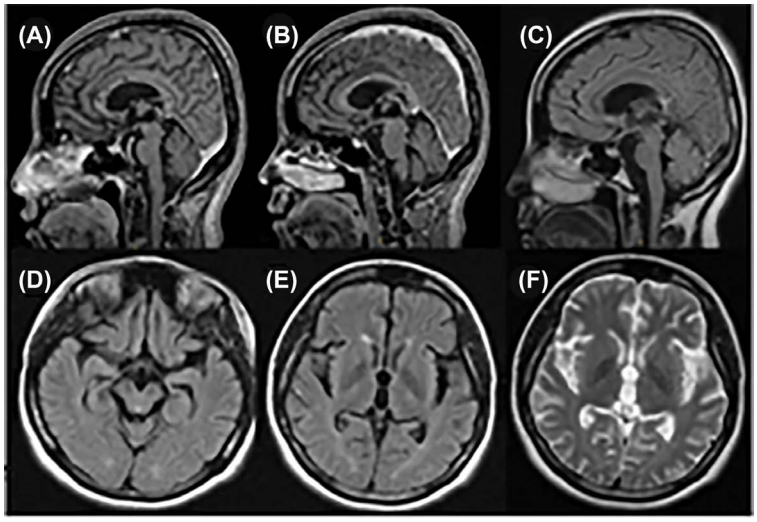

Figure 2. Brain MRI 2014: (A-C) Sagittal section, T1-weighted image; (D-E) axial section on T1; (F) axial section on T2-weighted scan, showing no signal enhancement to suggest an inflammatory demyelinating process. However, loss of volume is observed, with increased subarachnoid space between the Gyri of both convexities, significant midbrain, callosal and cerebellar volume loss, greater than expected for the age. Moreover, small hypointense oval-shaped lesions were seen on T1, involving mainly the Genu and stem of the corpus callosum.

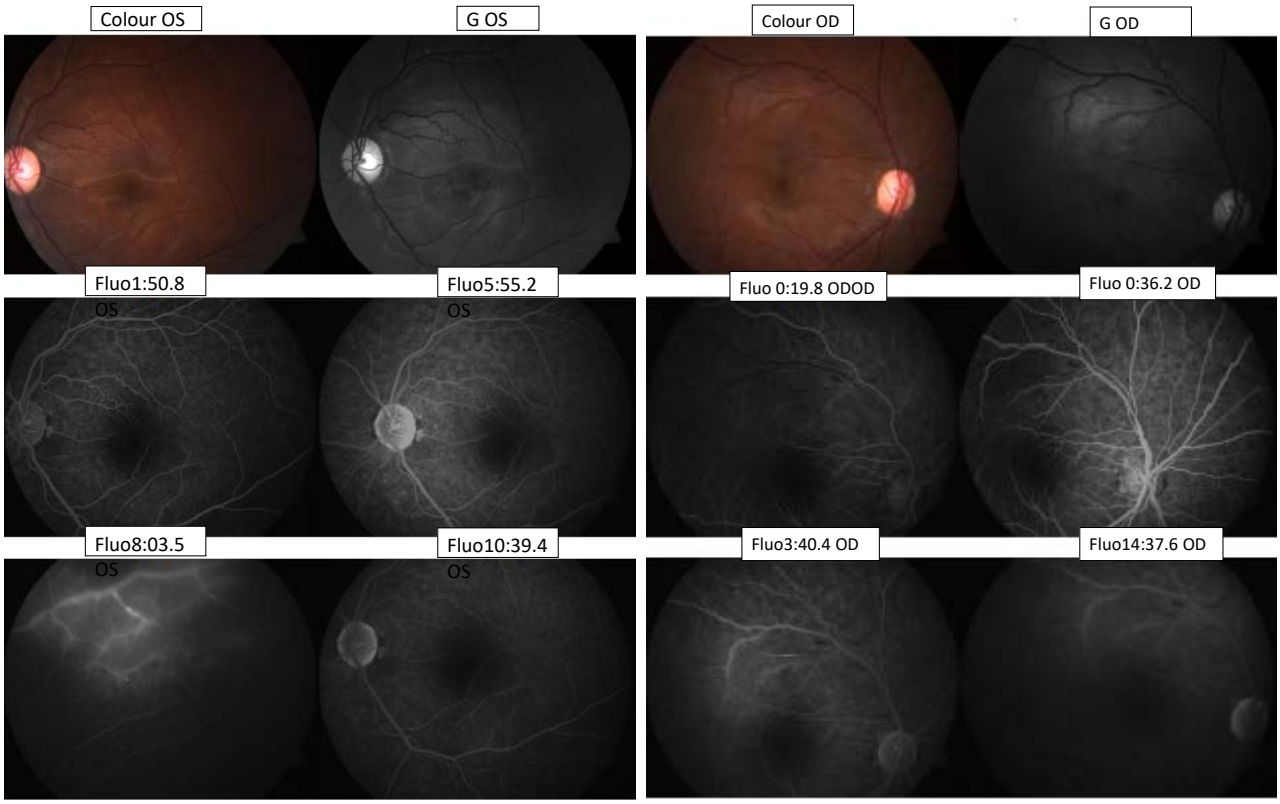

Figure 3. Bilateral Fluorescein Angiography examination in 2015, shows an area of retinal pallor close to the superior temporal arcade of the right eye, with arteriolar branch occlusion, nerve fiber layer hemorrhage and old retinal infarct lesions. In contrast, the left eye shows poor capillary perfusion and hyperfluorscent vessel walls in the superior temporal periphery, leading to the conclusion of vasculitis and recurrent arteriolar occlusions consistent with Susac syndrome.

Ardila memory curve, Rey Auditory Verbal Learning Test (RAVL), Rey-Osterrieth Complex Figure, Semantic and Phonologic Verbal Fluency Test, Boston Naming Test, Towers of Hanoi, Stroop Color and Word Test, and Wechsler Adult Intelligence Scale (WAIS IV).

3. Results

The neuropsychological assessment conducted in 2017 showed significant decline in complex attention, memory (short and long term), presence of simultagnosia, altered up-beat and down-beat ocular saccades, speech characterized by the presence of dysarthria, and failure to comprehend complex directions, with involvement of executive function, childish behavior and challenges with functional skills, requiring constant support. The patient's total IQ score on the Wechsler Adult Intelligence Scale (WAIS IV) was 79.

In the neuropsychological assessment performed in 2019 after the combined therapeutic process, there were changes as compared to the initial assessment, with no evidence of decline. Percentages in visual and auditory learning abilities were higher, close to normative values. The fine motor component improved significantly, associated with a higher level of independence. As for performance on the WAIS IV, the total IQ score was 85 (6 points higher than the previous test) (see Table 1).

Table 1. Results of neuropsychological tests 2017-2019.

Year	2017		2019	
	Mini-Mental State Examination (MMSE)			
	Score	Score Normal	Score	Score Normal
Natural Score	28	30	30	30
	Brief Test of Attention (BTA)			
Percentile	15	90	15	90
	Trail Making Test A (TMT-A)			
Percentile	10	90	60	90
	Trail Making Test B (TMT-B)			
Percentile	10	90	85	90
	Ardila's Visual Memory Curve			
Initial Volume	3	7 ± 2	6	7 ± 2
Maximum Volume	8	10	10	10
Trails	10	4	5	4
Evocation 3 (20) Minutes	7 (5)	10	7 (8)	10
	Rey Auditory Verbal Learning Test (RAVL)			
Learning Capacity	33%	50% - 75%	47%	50% - 75%
Evocation 3 (20) Minutes	3 (3)	7 - 15	7 (6)	7 - 15

Continued

	Rey-Osterrieth Complex Figure (ROCF)			
Copy (Percentile)	20	90	85	90
Evocation (Percentile)	40	90	55	90
	Phonologic Fluency Test			
Percentile	F = 15, A = 20, S = 25	90	F = 25, A = 55, S = 45	90
	Semantic fluency test (Fruits Animals)			
	Score	Score Normal	Score	Score Normal
Fruits (Percentile)	40	90	70	90
Animals (Percentile)	30	90	45	90
	Subtests-Integrated Neuropsychological Exploration Program—Revised Barcelona Test (natural scoring)			
Orophonatory Praxis	9	20	16	20
Symbolic Gesture—Order	Right = 7, Left = 5	10	Right = 10, Left = 9	10
Object Use Mimic	Right = 7, Left = 6	10	Right = 10, Left = 10	10
Overlay Images	8	20	16	20
	Wechsler Adult Intelligence Scale (WAIS-IV)			
CIT	79	90 - 110	85	90 - 110

Two Diffusion Tensor Imaging (DTI) brain MRI scans were performed in 2018 and 2019 in order to observe potential CNS structural effects after the combined therapeutic approach.

For DTI, tract segmentation was performed based on the diffusion pattern, with a total of 32 sampling directions, B value of 800 s/mm^2, resolution plane 1.75 mm and slice thickness of 2 mm. When calculating the tensor, a deterministic fiber tracking algorithm was used, based on the DSI Studio, version 2019-05, http://dsi-studio.labsolver.org. Post-processing parameters included fractional anisotropy threshold of 0.3, angular threshold of 45 degrees, randomly selected tracking size between 0.5 and 1.5 voxels. Fibers with a length of less than 10 or more than 300 mm were discarded.

Tract segmentation was performed in accordance with the clinical condition. Figure 4 shows segmentation of the corpus callosum, forceps minor and uncinate fasciculus (A: year 2018 y B: year 2019). There is evidence of demyelination progression in callosal structures but with increase in other fibers (see Table 2).

Figure 5 shows fronto-pontine, frontal lobe oblique fibers, inferior fronto-occipital, arcuate fascicle and cingulum tract segmentation. Greater volume is found in 2019 as compared to 2018 (see Table 2). A: posterior coronal section 2018, B: anterior coronal section 2018, C: posterior coronal section 2019, D: anterior coronal 2019. Also, sagittal section, E: left 2018, F: right 2018, G: left 2019 and H: right 2019.

Reconstruction of the connectome with fiber reorganization findings and greater homogeneity in both hemispheres after pharmacological intervention and cognitive rehabilitation (see Figure 6).

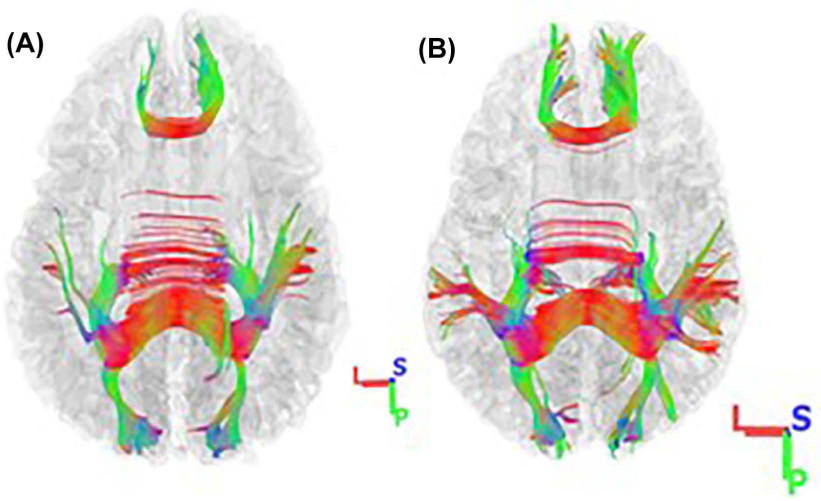

Figure 4. Tract segmentation of the corpus callosum, forceps minor and uncinate fasciculus ((A) 2018 and (B) 2019). Progression of Susac's disease in the white matter, comparison in one year of evolution with combined treatment.

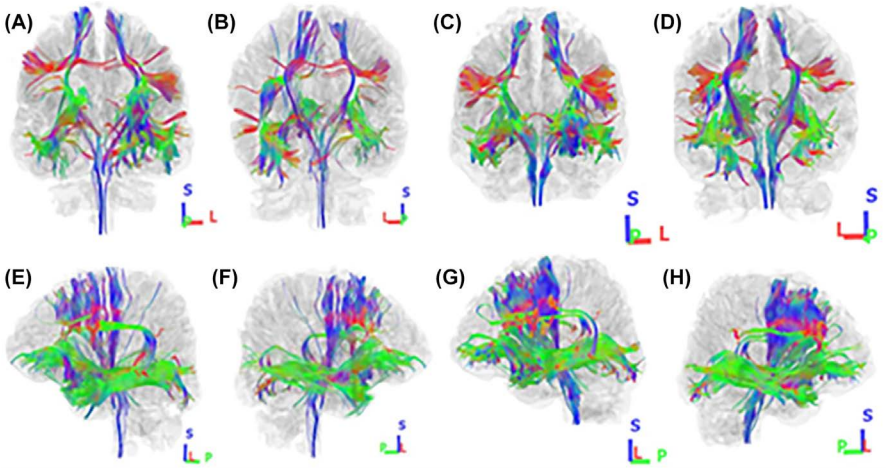

Figure 5. Tract segmentation 2018-2019. Progression of Susac's disease in the white matter, comparison in one year of evolution with combined treatment.

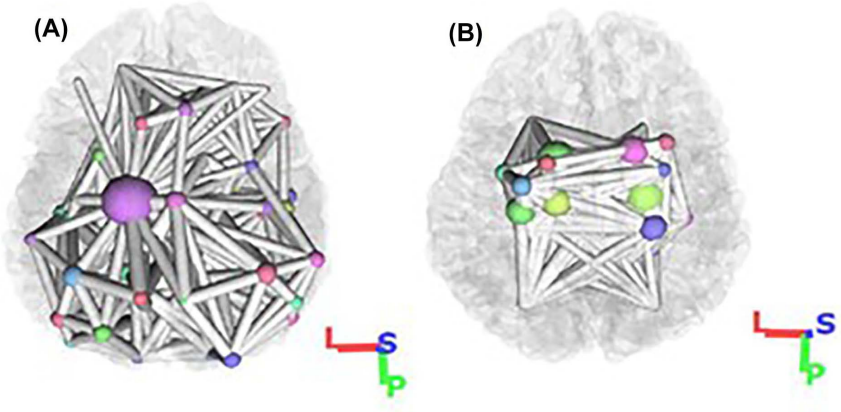

Figure 6. Connectome, (A) 2018 before combined treatment; (B) 2019 after combined treatment.

Table 2. Comparative values DTI in 2018 before combined treatment to 2019 after combined treatment.

Tract	Number		Length		Volume (mm^3)		FA	
	2018	2019	2018	2019	2018	2019	2018	2019
Corpus callosum	3739	2464	91.31	100.34	27452.3	36,658.1	0.54	0.49
Left fronto-pontine	95	909	93.73	100.27	5157.25	7172.38	0.56	0.53
Right fronto-pontine	97	851	90.59	92.12	6817.13	9107.88	0.50	0.50
Left arcuate	137	721	86.06	68.28	4673.38	4618.25	0.46	0.41
Right arcuate	0	44	0	83.09	0	2780.75	0	0.43
Left cingulum	470	2149	39.20	44.33	8470.88	5034.75	0.42	0.46
Right cingulum	353	2493	38.31	55.58	7343.88	6388.38	0.41	0.44
Left frontal oblique	130	2021	61.16	59.84	4893.88	5824.88	0.42	0.40
Right frontal oblique	213	1278	51.89	52.77	4373.25	4109.88	0.39	0.40
Left inferior fronto-occipital	126	10,528	123.21	108.33	5187.88	2682.75	0.46	0.42
Right inferior fronto-occipital	29	6148	118.42	126.71	3166.63	5555.38	0.43	0.42

4. Discussion

Susac Syndrome (SS) is considered an underdiagnosed disease condition, due to its multiple clinical involvements. Identification and diagnosis may take up to 2 years [12] [16], posing a challenge because of symptom variability consistent with other demyelinating diseases of the CNS or diseases that include retinal and auditory compromise.

The case described in this study meets the characteristic clinical triad of the disease, and imaging results are consistent with what has been reported in the literature, with white matter involvement, marked bilateral cortical deterioration of the front-parietal region and cerebellum, and corpus callosum hypotrophy [17] [18] [19]. Disturbances of the motor component and of other neuropsychological functions correlate with these findings, highlighting cerebellar participation in visuospatial processing and executive function components of the dorsolateral type such as divided attention, planning, and working memory. Likewise, distinct connection networks that favor communication with cortical and subcortical structures of the brain are recognized, significantly influencing cognitive processes [20] [21].

Structures in which significant atrophic process is observed, such as midbrain, corpus callosum, cerebellum, prefrontal areas and the neuronal networks integrating these centers explain to a great extent the deficits observed in the patient in terms of sustained attention, visuospatial construction tasks, speech production, planning, learning, skills acquisition, processing speed and motor component. It is also found that these areas lend themselves to combined therapy because of improvement in the neurocognitive profile in terms of motor function

and greater functional ability which will ultimately lead to slight improvement of overall intellectual capacity, with a structural neuronal reorganization to support the improvement in the clinical picture [22].

DTI-MRI findings allow making connectome reconstructions (see **Figure 6**) showing continuing cortical atrophy, mainly of the corpus callosum, midbrain and cerebellum following rehabilitation. However, baseline imaging prior to the combined therapeutic intervention shows hyperconnectivity in primary motor and sensory regions which are found to have better distribution, greater tract homogeneity and improved inter and intra-hemispheric connectivity after the intervention. This allows for more efficient information transport through fiber bundles, specifically in the arcuate fasciculus, frontal lobe "u" fibers, inferior and superior longitudinal fasciculus, and spino-thalamic tract (see **Table 2**).

From the comparison between this case and literature reports on SS, neuropsychological deficits are found to be similar in terms of attention, processing speed, working memory, complex comprehension, reduced intellectual capacity in general, executive function deficit, and ataxia. Despite variations among individual cases of SS, there are similar neurocognitive derangements which allow the use of equivalent treatments with favorable results. Therefore, expanding the possibilities of comprehensive intervention including neuropsycology, neurology and other disciplines is considered relevant for the furtherance of a combined therapeutic approach.

In conclusion, the patient's neuropsychological profile and functional skills show changes related to structural reorganization, consistent with brain imaging findings. This could indicate that association fibers linked to cognitive processes may show a positive response to the combined approach of rehabilitation plus pharmacological therapy.

Acknowledgements

We are grateful to the patient and her family. We also thank radiology technician Edinson Jimenez, for his active participation during the process, and radiology specialists Dr. Gonzalo Larrota and Dr. Jorge Marin, for their advice.

Conflicts of Interest

The authors declare no conflicts of interest regarding the publication of this paper.

References

[1] Delgado, F.R., Monteiro, G.C., Margarit, B.P. and Izquierdo, A.Y. (2019) Encefalomielitis aguda diseminada. Leucoencefalitis aguda hemorrágica. Otras enfermedades desmielinizantes. *Medicine*, **12**, 4606-4615. https://doi.org/10.1016/j.med.2019.05.012

[2] Marrodan, M., Acosta, J.N., Alessandro, L., Fernandez, V.C., Contentti, E.C., Arakaki, N., *et al.* (2018) Clinical and Imaging Features Distinguishing Susac Syndrome from Primary Angiitis of the Central Nervous System. *Journal of the Neurological*

Sciences, **395**, 29-34. https://doi.org/10.1016/j.jns.2018.09.029

[3] Hardy, T.A., O'Brien, B., Gerbis, N., Barnett, M.H., Reddel, S.W., Brewer, J., *et al.* (2015) Brain Histopathology in Three Cases of Susac's Syndrome: Implications for Lesion Pathogenesis and Treatment. *Journal of Neurology, Neurosurgery & Psychiatry*, **86**, 582-584. https://doi.org/10.1136/jnnp-2014-308240

[4] Engelhardt, B., Vajkoczy, P. and Weller, R.O. (2017) The Movers and Shapers in Immune Privilege of the CNS. *Nature Immunology*, **18**, 123-131. https://doi.org/10.1038/ni.3666

[5] Magro, C.M., Harman, A.P., Klinger, D., Orosz, C., Adams, P., Waldman, J., Knight, D., Kelsey, M. and Ross, P. (2003) Use of C4d as a Diagnostic Adjunct in Lung Allograft Biopsies. *American Journal of Transplantation*, **3**, 1143-1154. https://doi.org/10.1034/j.1600-6143.2003.00152.x

[6] Gross, C.C., Meyer, C., Bhatia, U., Yshii, L., Kleffner, I., Bauer, J., Tröscher, A.R., *et al.* (2019) $CD8^+$ T Cell-Mediated Endotheliopathy Is a Targetable Mechanism of Neuro-Inflammation in Susac Syndrome. *Nature Communications*, **10**, Article No. 5779. https://doi.org/10.1038/s41467-019-13593-5

[7] Do, T.H., Fisch, C. and Evoy, F. (2004) Susac Syndrome: Report of Four Cases and Review of the Literature. *American Journal of Neuroradiology*, **25**, 382-388.

[8] Dörr, J., Radbruch, H., Bock, M., Wuerfel, J., Brüggemann, A., Wandinger, K.P., *et al.* (2009) Encephalopathy, Visual Disturbance and Hearing Loss-Recognizing the Symptoms of Susac Syndrome. *Nature Reviews Neurology*, **5**, 683-688. https://doi.org/10.1038/nrneurol.2009.176

[9] Kleffner, I., Dörr, J., Ringelstein, M., Gross, C.C., Böckenfeld, Y., Schwindt, W., *et al.* (2016) Diagnostic Criteria for Susac Syndrome. *Journal of Neurology, Neurosurgery & Psychiatry*, **87**, 1287-1295. https://doi.org/10.1136/jnnp-2016-314295

[10] Rennebohm, R.M., Asdaghi, N., Srivastava, S. and Gertner, E. (2020) Guidelines for Treatment of Susac Syndrome—An Update. *International Journal of Stroke*, **15**, 484-494. https://doi.org/10.1177/1747493017751737

[11] Raets, I. and Gelin, G. (2012) Susac's Syndrome: A Clinical and Radiological Challenge. *Journal of the Belgian Society of Radiology*, **95**, 355-356. https://doi.org/10.5334/jbr-btr.721

[12] Egan, R.A. (2019) Diagnostic Criteria and Treatment Algorithm for Susac Syndrome. *Journal of Neuro-Ophthalmology*, **39**, 60-67. https://doi.org/10.1097/WNO.0000000000000677

[13] Susac, J.O., Murtagh, F.R., Egan, R.A., Berger, J.R., Bakshi, R., Lincoff, N., *et al.* (2003) MRI Findings in Susac's Syndrome. *Neurology*, **61**, 1783-1787. https://doi.org/10.1212/01.WNL.0000103880.29693.48

[14] Vodopivec, I., Venna, N., Rizzo III, J.F. and Prasad, S. (2015) Clinical Features, Diagnostic Findings, and Treatment of Susac Syndrome: A Case Series. *Journal of the Neurological Sciences*, **357**, 50-57. https://doi.org/10.1016/j.jns.2015.06.063

[15] García-Carrasco, M., Mendoza-Pinto, C. and Cervera, R. (2014) Diagnosis and Classification of Susac Syndrome. *Autoimmunity Reviews*, **13**, 347-350. https://doi.org/10.1016/j.autrev.2014.01.038

[16] Feresiadou, A., Eriksson, U., Larsen, H.C., Raininko, R., Nygren, I. and Melberg, A. (2014) Recurrence of Susac Syndrome Following 23 Years of Remission. *Case Reports in Neurology*, **6**, 171-175. https://doi.org/10.1159/000362868

[17] Köhler, A.A., Alessandro, L., Calandri, I.L. and Fiol, M. (2015) Microangiopatía con afección del cuerpo calloso y retina secundaria a síndrome de Susac. *Neurología Argentina*, **7**, 92-193. https://doi.org/10.1016/j.neuarg.2015.01.003

[18] Roessler-Górecka, M., Mendel, T., Wiśniowska, J. and Seniów, J. (2017) Neuropsychological Characteristics of Encephalopathy in Susac's Syndrome?—Case Report. *Neurologia i Neurochirurgia Polska*, **51**, 174-179. https://doi.org/10.1016/j.pjnns.2017.01.001

[19] Barritt, A.W., Wickremaratchi, M. and Anderson, S.J. (2019) Neuropsychological Outcome of a Case of Susac Syndrome: A Two-Year Follow-Up Study. *Applied Neuropsychology*: *Adult*, **26**, 89-95. https://doi.org/10.1080/23279095.2017.1359178

[20] Tirapu-Ustarroz, J., Luna-Lario, P., Iglesias-Fernandez, M.D. and Hernaez-Goni, P. (2011) Contribucion del cerebelo a los procesos cognitivos: Avances actuales [Cerebellar Contribution to Cognitive Process: Current Advances]. *Revista de Neurología*, **53**, 301-315. https://doi.org/10.33588/rn.5305.2010747

[21] O'Halloran, C.J., Kinsella, G.J. and Storey, E. (2012) The Cerebellum and Neuropsychological Functioning: A Critical Review. *Journal of Clinical and Experimental Neuropsychology*, **34**, 35-56. https://doi.org/10.1080/13803395.2011.614599

[22] Ruiz-García, R.G., Chacón-González, J., Bayliss, L. and Ramírez-Bermúdez, J. (2021) Neuropsiquiatría del síndrome de Susac: A propósito de un caso [Neuropsychiatry of Susac Syndrome: A Case Report]. *Revista Colombiana de Psiquiatría*, **50**, 146-151. https://doi.org/10.1016/j.rcp.2019.10.007