Dr. Hugo Salvador Navarrete Báez.
RFC: NABH550416IJ6 *CURP: NABH550416HSPVZG05 REG. PAT. IMSS A08 33 135 10-4
CEDULA PROFESIONAL: 515643. S.S.A. 64239 Cert. Consejo de Neurología No. 338 Cedula de Especialidad
No. AECEM 17582 CTA. EDO. 2-52486-6 Especialidad: Neurología. Calle Abelardo L. Rodríguez # 2916 A-2
Zona Rio C. P. 22320 Tel.- 664 684 06 87 Tijuana Baja California México

Tijuana, Baja California, México April 17th, 2019

To Whom it May Concern:

This is a clinical summary and for my long standing patient Narendra Jana, who suffers from Multiple Sclerosis and was under my care since May of 2017.

The Clinical Summary

Background:

Narendra Jana is a 34-year-old university graduate, who is an engineer by profession and presented with relapse remitting multiple sclerosis historically but secondary progressive MS now due to length of clinical course (approximately 12 years).
His records indicate normal developmental milestones and above average aptitude prior to clinical presentation of MS.
He is a non drinker and non recreational drug user and never has been historically.

Clinical History:

Narendra Jana, patient since mid 2017 presented with the first radiological signs of MS in 2008, as a T1 intensity in the globus pallidi bilaterally and a small region of hypointensity noted to the right of the fourth ventricle on T2 weighted images in a December 18th 2008 MRI.
As reported, he presented with a lack of physical feeling along his inner palms, face, and legs with occasional immobility from late 2008 to 2012.

There was little follow up except with interim non steroidal anti-inflammatory medications given in IV during this period of time (2009-2012), which didn't produce a positive response in his clinical condition.
He repeatedly reports persistent headaches during this time period from what is as of yet not radiologically imaged between 2009 and 2012 from inflammatory lesions in his cervical column.

A follow up MRI is taken in 2012 of the brain that shows T2 intensity in the posterior brain in the occipital lobe and signs of atrophy in the parietal lobe. The atrophy is advanced for his age of 28 when the MRI is taken and isn't present in former MRI series. He also reports optic neuropathy since 2008. An image of his optic nerve taken in July 20th 2012 shows the typical presentation of optic neuropathy, the optic disk being pale in both eyes.

Dr. Hugo Salvador Navarrete Báez.
RFC: NABH550416IJ6 *CURP: NABH550416HSPVZG05 REG. PAT. IMSS A08 33 135 10-4
CEDULA PROFESIONAL: 515643. S.S.A. 64239 Cert. Consejo de Neurología No. 338 Cedula de Especialidad
No. AECEM 17582 CTA. EDO. 2-52486-6 Especialidad: Neurología. Calle Abelardo L. Rodríguez # 2916 A-2
Zona Rio C. P. 22320 Tel.- 664 684 06 87 Tijuana Baja California México

FDG pet imaging is done in March 23rd 2016 indicates a dementia secondary to the effects of MS. It reveals decreased metabolic patterns over posterior bilateral parietal lobes, bilateral antero-mesial temporal lobes. Posterior cingulate gyrus and precuneus also show a decreased metabolic pattern.

The subcortical grey matter and frontal and occipital cortices maintain a normal metabolic pattern. The metabolic pattering is unique to MS since is doesn't effect metabolism to the grey matter.

An EEG is done in March 16th 2016 in Malaysia shows a posterior occipital slow wave transitions (POSTs), vertex sharps, and sleep spindles with random sharp waves arising from the right occipital lobe in sleep. Indicating a focal point of seizure in the occipital lobe even if a full seizure isn't recorded. It correlates with the October 27th 2012 MRI (posterior brain intensity).

A two day EEG is repeated in May 2016 that "shows interictal epileptiform discharges from the right hemisphere of the brain with a predominance to fronto-temporal region" (focal points of seizures even if the full seizure isn't recorded)

Epilepsy is a secondary effect of MS in his case.

The first cervical and thorasic MRI is taken in January 10th 2017, which shows atrophy from a long term presentation of MS along the cervical column from C3 to C7, indicating the condition has been progressive since 2008. Between C3 and C4 the atrophy is almost 3 mm. T1 and T2 lesions are reported in ER reports in November 13th 2017 in the cervical column and readily apparent in the MRI images.

The region around thoracic vertebra 12 in the January 10th 2017 MRI shows a central intensity typical of MS which is eventually reported as a region of atrophy in a September 25th 2017 MRI report and again seen in a sequential MRI of the January 10th 2017 MRI in August 28th 2018 (same image sequences in the same MRI machine).

Under My Care (Dr Hugo Navarrete)

Narendra has been under my care since March of 2017, presenting with the typical features of MS, optical neuropathy and neuro spinal degeneration (which wasn't determined to be progressive in 2017 but eventually is realized to be) effecting mentation, mobility, and sensory responses.

A lumbar MRI is done in August 9th 2017 which shows signs of neurodegeration between L3-L5, and L5-S1 shows 7 mm of atrophy.

The first ER presentation where appropriate medications are given is in September 19th 2017 in Hospital Angeles, Mexico City preceded by a brain, cervical MRI with contrast on

Dr. Hugo Salvador Navarrete Báez.
RFC: NABH550416IJ6 *CURP: NABH550416HSPVZG05 REG. PAT. IMSS A08 33 135 10-4
CEDULA PROFESIONAL: 515643. S.S.A. 64239 Cert. Consejo de Neurología No. 338 Cedula de Especialidad
No. AECEM 17582 CTA. EDO. 2-52486-6 Especialidad: Neurología. Calle Abelardo L. Rodríguez # 2916 A-2
Zona Rio C. P. 22320 Tel.- 664 684 06 87 Tijuana Baja California México

August 25th 2017. The August 25th 2017 MRI shows T1 enhanced lesions in the cervical spine and a T1 intensity in the globus pallidi (basal brain) with T2 intensities in the cervical spine.

The patient presenting with "acute pain 9/10, low back. And left thoracic limb, associated to numbness and paraesthesia in the same distribution" and "difficulty for walking and sitting discomfort, with only tolerance of laying position".
Methylprednisolone is administered for 5 days to a positive response in the ER.
A MRI is done immediately thereafter in September 25th 2017 with contrast that shows a reduction of T1 intensities in the cervical column and basal brain (thus showing drug response).
There are T2 intensities in the FLAIR image sequences along the corpus callosum and posterior brain (occipital lobe) in this series with mild features of Dawson's fingers (unique and typical in MS)
The next ER appointment is in November 13th 2017 with the same presentation: hypoactive reflexes, slowed finger to nose, altered physical sensitivity and difficulty walking. The ER doctor notes the clear T1 and T2 lesions in the former MRIs along both cervical spine and occipital brain. This ER is preceded by trials with Rebif and Gylenia (Gylenia for a month and a half with an initial hospitalization) under the care of me, who is the long term treating neurologist since March 2017 when he lived in San Diego, CA, US.

Methylprednisolone is administered for 5 days to a positive response.
A MRI is done in December 5th 2017 showing the same response and the same features as in the September 25th 2017 MRI.
Another ER is repeated in January 12th 2018 with the same presentation and same positive response with methylprednisolone.

An ER appointment in Berlin (Bundeswehrkrankenhaus) takes place in the 17th of March 2018 presenting with "fixation disturbance and nystagmu of the entire left facial half, hypoesthesia entire left body halftone, decreased reflex status left" and "finger-pointing" difficulties.
The repeated ER appointments (four where methylprednisolone is administered) is reported as a result of insufficient outpatient medications to manage his condition, which is eventually determined to be secondary progressive MS.
The treatment started in ER (IV methylprednisolone) was completed with three more days of IV methylprednisolone given 1 gram each day outpatient under the care of Dr. Stefanie Klaffke in Berlin Germany.
Rebif 20 mcg was prescribed thereafter taken every other day trialed for a period of 5 months with limited efficacy, from March 2018 to July 2018.

Dr. Hugo Salvador Navarrete Báez.
RFC: NABH550416IJ6 *CURP: NABH550416HSPVZG05 REG. PAT. IMSS A08 33 135 10-4
CEDULA PROFESIONAL: 515643. S.S.A. 64239 Cert. Consejo de Neurología No. 338 Cedula de Especialidad
No. AECEM 17582 CTA. EDO. 2-52486-6 Especialidad: Neurología. Calle Abelardo L. Rodríguez # 2916 A-2
Zona Rio C. P. 22320 Tel.- 664 684 06 87 Tijuana Baja California México

Due to limited efficacy the patient was switched to Tecfidera 240 mg twice a day from July 2018 to January 14th 2019.

A VEP was done in August 10th 2018 showing "left optic neuropathy" and "conduction deficit in the left visual pathway", indicating demyelinating optic neuropathy.
A visual field test and optic disk tests were also done on August 10th 2018 showing significant optic neuropathy in both eyes with images to correlate the neuropathy.
A FDG pet trial is done in August 7th 2018 where brain functioning is measured before and after methylprednisolone is given using a FDG pet machine. There is still a dementia secondary to MS but better metabolic activity due to medication (IV methylprednisolone) showing drug response with "lesser hypometabolic activity" in several regions of the brain.

A neuropsychological report dated August 11th 2018 indicates reduced processing speed with his executive functioning and decision making mostly preserved. Tests for visual attention and task switching is below cut off. Tests with
respect to global functioning, memory functioning, attention span, and language are average.
A SEP isn't needed to demonstrate the relative latency of his left limbs (it's readily apparent in the ER appointments that he has a conduction deficit in his left limbs) and its easy to correlate with the cervical and thoracic MRIs and general neurology tests repeatedly done in medical appointments.
He has the data to show it, which collates with the cervical/thoracic MRI.
Three days of IV methylprednisolone were administered in July 2018 by Dr. Luis Amaya in Mexico City again.
Due to limited efficacy of Tecfidera and methylprednisolone, plasmapheresis was performed for three days (two volume replacements with 5% immunoglobulin 2 bottles per liter) to September 14th 2018 by Dr. Luis Amaya and to a positive effect (reducing his EDSS from 4.5 to 3.0). It was also reported to improve the efficacy of Tecfidera for a period of two months.
But despite the medications given the positive effects were only transient (lasting only a few months); it was determined why this was the case. In a comparison between the MRIs taken in January 10th 2017, September 25th 2017, May 30th
2018, and August 28th 2018 it was shown that the patient has progressive atrophy of the cervical column, indicating that it is a progressive form of MS that would only have temporary relief and limited efficacy from medications for relapse remitting MS. The diagnosis of Secondary Progressive MS is reiterated by Dr. Francisco Manjarrez, Dr. Luis Amaya, and me in Mexico and by Dr. Stefanie Klaffke in Germany.

Dr. Hugo Salvador Navarrete Báez.
RFC: NABH550416IJ6 *CURP: NABH550416HSPVZG05 REG. PAT. IMSS A08 33 135 10-4
CEDULA PROFESIONAL: 515643. S.S.A. 64239 Cert. Consejo de Neurología No. 338 Cedula de Especialidad No. AECEM 17582 CTA. EDO. 2-52486-6 Especialidad: Neurología. Calle Abelardo L. Rodríguez # 2916 A-2 Zona Rio C. P. 22320 Tel.- 664 684 06 87 Tijuana Baja California México

Another VEP is done to verify this in the next hospital setting.

With the given information the patient researched Rituximab by consulting several hospitals in Europe and presented his clinical history to a clinician in India, Dr. Pushpendra Renjen, and the neurology team in Apollo Hospital, New Delhi.
Rituximab was administered following a blood test and JC Virus test at a dose of 1 gram separated by two weeks (two times) as the starting dose.
The neurologist also did a VEP test to show the progressive optic neuropathy, which shows latency in both eyes now (only left eye before) due to demyelinating optic neuropathy, correlating well with the diagnosis of secondary progressive MS.
The medication produced a positive response within 4 weeks, indicating that he does have a more aggressive form of MS, namely secondary progressive MS, but that he does respond to the more clinically effective medications as well, specifically monoclonal antibodies like Rituximab, Natalizumab and Alemtuzumab.

A brain, cervical, thoracic , and lumbar MRI was done in January 20th 2019 with contrast that shows the same features as former MRIs and the slow progressive features of MS (specifically along the cervical column).
With his clear progressive recovery since Rituximab, he is scheduled to receive another IV in July or August of 2019.

Best Regards,

DR. HUGO NAVARRETE
NEUROLOGIA
D.G.P. 515643 S.S.A. 64239
CERTIFICADO 338

Dr. Hugo Salvador Navarrete Báez.
NEUROLOGY
Mexican Board Certified
Med. Lic. # 515643 Cert. 338
Neurólogo. Certificado por el Consejo Mexicano de Neurología.
Egresado de la Universidad Nacional Autónoma de México
Post-grado en Centro Médico de Occidente, I.M.S.S.
Av. Abelardo L. Rodríguez 2916-A2. Zona del Río. Tijuana, B.C. c.p. 22320 Tel.(664) 684 0687
Cert. No. 338 Cédula Profesional No. 515643 S.S.A. 64239
R.F.C. NABH550416IJ6 Cédula de Especialista: AECEM 17582