

As Anne Frank once said “ If I haven't any talent for writing books or newspaper articles, well, then I can always write for myself”, I thought of penning down a lot from my personal experience, hoping to help others suffering from ***Isaac's Syndrome***.

➤ **Purpose of this Inscription**

This article provides a review of the clinical phenotypes & a record on Neuromyotonia. Recent investigations have led to an understanding of the autoimmune underpinnings of this condition and its specific associated antibodies, the do's & don'ts, holistic alternate supportive medication, medical qualified practitioners who have proved their credibility in this domain, some affiliated medical expressions & a handful but handy practical observation of facts . The case study review helps us understand the spectrum of the symptom associated with the peripheral nerve hyperexcitability syndrome.

➤ **In Layman's Language**

Neuromyotonia (NMT), also known as Isaacs Syndrome, is a diverse disorder. As a result of muscular hyperactivity, patients may present with muscle cramps, stiffness, myotonia-like symptoms (slow relaxation), associated walking difficulties, hyperhidrosis (excessive sweating), myokymia (quivering of a muscle), fasciculations (muscle twitching), fatigue, exercise intolerance, myoclonic jerks and other related symptoms.

➤ **Etiology**

Though the etiology of the disease remains unclear, some doctors say there may be 3 main causes: - Acquired, Hereditary or Consequence of cancer in the body. There is some evidence to suggest the role of autoimmunity and specifically, antibodies against the potassium channel in motor nerve terminals.

➤ **Common Symptoms**

Progressive stiffness, Diminished reflexes, Delayed muscle relaxation, Muscle twitching, Pain, Cramping, Weakness, Muscle wasting, Increased sweating, Calf muscle hypertrophy, Muscle fibrillation, Weight loss.

These symptoms generally persist throughout the day, even during sleep or when under general anesthesia. Speech and breathing may also be affected if the muscles of the throat are involved. Smooth muscles and cardiac (heart) muscles typically are spared.

➤ **Pathology**

A doctor may conduct a basic neurological exam, including coordination, strength, reflexes, sensation, etc. A doctor may also run a series of tests that include blood work and MRIs.

From there, a patient is likely to be referred to a neurologist or a neuromuscular specialist. The neurologist or specialist may run a series of more specialized tests, including needle electromyography EMG/ and nerve conduction studies (NCS) (these are the most important tests), chest CT (to rule out paraneoplastic) and specific blood work looking for voltage-gated potassium channel antibodies, acetylcholine receptor antibody, and serum immunofixation, TSH, ANA ESR, EEG etc.

In a study by Nagashima et al in 1985, a complex consisting of CPK (MM) and IgA was seen deposited in the motor end plates and membranes of muscle fibers, supporting a possible immune etiology for the disease.

Because the condition is rare, it can often take years before a correct diagnosis is made.

➤ **Treatment** (*The good physician treats the disease; the great physician treats the patient who has the disease*)

The goal of treatment is symptomatic as there is no permanent cure yet.

- 1) Anticonvulsants, including phenytoin and carbamazepine, usually provide significant relief from the stiffness, muscle spasms, and pain
- 2) Plasma exchange
- 3) IVIg
- 4) Botox injections
- 5) Immunosuppressants, such as Prednisone
- 6) Cannabis
- 7) Steroids
- 8) ACTH injections
- 9) Rituximab

Neuromyotonia has been long recognized by several physicians, however its rarity and the variability of its clinical manifestation and ways of presentation is probable the most crucial aspect why it's frequently misdiagnosed or wrongly treated.

I am not, just a bed number (case study):-

If you had told me a couple of years back, I would not be writing this note instead planning into the future. A part of me is surprised, as was all healthy & hearty, not on any peculiar medication & no known allergies except periodic diarrhea since a couple of months. There was no history of alcohol or any other substance abuse & completely believed that *true healthcare reform always starts in one's kitchen*.

As a senior executive in the Investment Banking space based out of Mumbai, my experience journey speaks in itself, from being recognized as the Employee of the Year to having the maximum number of Channel Partners to have recorded, deployment in exotic products to have bagged the maximum number of reality deals in the organization, I am a 38 year individual with parents & a sibling in the family.

One of the evenings in Feb'16 during my walking session, got trapped into a severe pain in the Lumbar region & continuous cramps in right leg. The pain could be described as some sharp object stabbed at the lumbar extending till the femoral region which started alleviating & aggravating.

Next morning was tough as the pain still persisted & was accompanied with enough stiffness which made movement toilsome. Anyhow gathering all my muscle, I presented myself to a conventional Orthopedic who after a thorough investigation put me on drugs.

The post pain realization of diarrhea slowly denting the body had factored in. All of a sudden things took an evil turn & seeing my Gastroenterologist again seemed a wise decision. He asked me to get my CPK levels tested immediately & consult a Neurologist. As the levels were very high, I preferred returning back to my hometown in Kanpur as soon realized that a gig's world's was quickly transforming into serious profiling. It was inconceivable how I was bought directly to be hospitalized from the airport with no guess that my encounter with time had just started.

The essential first step in managing the situation began with a detailed medical evaluation. One after the other, investigations started & the doctors decided to put me on the Steroid therapy for next 5 days as they diagnosed Polymyositis. Post being in the hospital for a week I was advised to take up my further investigations in Bombay Hospital under a team of experts.

In March'16, I got under the lights with general examination which revealed average body built whereas Motor examination reported average muscle status with wasting. Presence of stiffness all over was more in the upper limbs. There was excess weakness with spontaneous gross fasciculations in both arms & in the face over the masseter muscle and around the eye. Coordination was normal and plantar reflex was normal. Nerve conduction study and EMG were done and confirmed the diagnosis showing

neuromyotonic discharge with fibrillation, positive sharp waves and continuous muscle fiber activities. Special blood tests were conducted to detect specific antibodies which were negative.

I was diagnosed with *Isaac Syndrome* even called *Neuromyotonia* in the month of March'16. Some of the other tests showed traces of *Membranous Glomerulonephritis* (is a slowly progressive disease of the kidney. It leads to changes and inflammation of the structures inside the kidney that helps filter wastes and fluids. The inflammation may lead to problems with the functionality).

The team of doctors decided on IVIg therapy injected intravenous, which is the use of a mixture of antibodies to treat a number of health conditions. Considering the tests (EMG, Pet-CT, MRI Lumber Spine, Sonography, Kidney biopsy etc...) & treatment, my stay at the hospital was almost for a month. I was discharged from the hospital in April'16 with some medicines & a suggestion to consult another neurologist in Lucknow, if need be with a recommendation that there is no such thing as a fair flight & all vulnerabilities must be exploited.

I couldn't lie to myself, & started to laugh on the ambulance not realizing that feeling better was just a temporary phenomenon. Soon my health proved a tragic experience wrapped in bonkers, making me crawl through broken glass & within 3 months timeframe I was on my way to Lucknow. As it's always said that no medicine or doctor has a strike rate of 100%, I could experience it happening in my case. The medicines denied integrating with my system. Diarrhea which was on a break for a while again took its full swing. Pain, Sugar, BP & all the other symptoms returned & my hopes of recovery showed signs of a day dream with open eyes.

Unexpectedly I was getting weaker. The situation remained the same for some time where I slept for almost 14 hrs a day due to weakness & persisting pain in spite of being on heavy medications with pain killers, immunosuppressive agents, blood pressure, intestine related medicines, diabetes, probiotics & steroids became a part of my daily food platter. The daily intake of medicines went as high as 38 with enough food restrictions due to shooting sugar levels, fluctuating blood pressure & diarrhea. I was recommended to be on complete bed rest till things started to improve a bit when we decided to see Dr. Panagariya & his team in Jaipur @ Aug'16.

In Nov'16, I was again admitted for IVIg therapy, in Jaipur hospital which I did not respond to & had to be stopped midway.

I was asked to go to Mumbai again, this time to see a different set of specialists to know a little better, the difference between stories & realities. The trip came across as Phishing in my own backyard due to the suggestions varying rational expectations.

I was given some medicines with immunosuppressants & ask to continue it for some good two months.

In March'17 as the overall health stats didn't show favorable improvement, I was asked to take weekly shots of ACTH injection (It may work directly on the brain in addition to stimulating the adrenal glands. It may also be used in treatment of various other childhood seizures when other treatments have failed). I started to revamp though for couple of days there was a weird feeling in the brain.

When it's wise to have an alternative health, as a mainstream (May'17): - A crucial part of my treatment agenda was Naturopath as I am always on a look out for therapies which could help me from a longer term perspective without much of side effects . Came across this center in Hyderabad & decided to try it for a week. Post my visit there & meeting the doctors, the need of staying back for longer was felt which lasted for a month. Due to change in my daily diet chart, the stomach did settle to a lot extend. I realized that they added a lot of Coconut in their food curries which has *anti-inflammatory qualities* without making any change in my allopath medicines. Setting strict expectation with one's palate is the key & crucial step to lifestyle modification.

The Indian state of mind & nature sense (July'17): - Naturopath treatment was impressive so I decided to make a second visit @ Rishikesh, this time with a pinch of spiritual touch. My stay lasted there for almost a month with corrections in food habits, meditation & body posture corrections. We all have the capacity and strength to expand our conscious mind with interior research. An amalgamation of naturopath treatment with a spiritual touch can deliver extraordinary results if followed diligently and inculcated as a routine change.

As medicines & treatments have limitations, the health keeps showing signs of deterioration periodically. It was time for a checkup with my monthly health stats. My doctor made some changes in the medicines & asked me to wait patiently for results to unwind. Pain killers which were on sabbatical became a daily phenomenon again. I was admitted to Medanta Medicity @ Gurgaon for Plasmaferis in Dec'17. Though I was taking the procedure light, it proved me wrong, each passing day. The central line which was inserted around the pelvic region, created issues with its inlet & was a nightmare till the last day of completion.

Post discharge it took me good 20 days to get a bit normal as there was enough weakness & usual pain at the back & thigh area, all medications being like before. The journey continuous..... I am focusing on the journey, not the destination. Therefore if you can't go back to your mother's womb, you'd better learn to be uncomfortable & fight back. To do otherwise is to settle.

➤ **Medical Streams (tried & tested)**

Have tried the following streams of medicine: - (They that will not apply new remedies must expect new evils)

- 1) Allopathic (Mankind has survived all catastrophes. It will also survive modern medicine – Gerhard Kocher)
- 2) Naturopath (The art of medicine consists in amusing the patient while nature cures the disease)
- 3) Homeopath (Extreme remedies are very appropriate for extreme diseases)
- 4) Yoga (Yoga teaches us to cure what need not be endured and endure what cannot be cured — founder of Iyengar Yoga, and considered one of the foremost yoga teachers in the world)

- 5) Meditation practices (Natural forces within us are the true healers of disease)
- 6) Music therapies (One good thing about music, when it hits you, you feel no pain, Bob Marley)

➤ **My Experience, the hard way (important section)**

- 1) Disease: - Dis – Ease. Body & Mind needs to be at ease & common synergy
- 2) Closely monitor your blood & other body stats regularly without fail
- 3) Most Critical: - A good doctor and team
- 4) Adopting to new aspects of treatment can contribute to healing: - Yoga, Meditation, Walking, Calmness of mind & body, Being positive
- 5) Important: - Make proper synopsis before consulting any doctor (he needs to know it all, from medicines to various treatments to other doctors consulted to medical tests)
- 6) Changes in lifestyle can work wonders (eating, sleeping, drinking habits)
- 7) While on medicines, close monitoring of sugar & BP levels, eyes, stomach, kidney is must
- 8) We should keep in mind that Allopath has symptomatic drugs which are not the cure; therefore trying alternate streams of medicines can be helpful from a longer term perspective
- 9) One's body can stand almost anything. It's the mind that needs to be convinced: - It is the key ingredient to recovery
- 10) Keep involved: - for mind distraction
- 11) Surroundings matters: - keep it positive (The need is to do more even with less)
- 12) The self-management plan should be reviewed from time to time to ensure the advice remains current
- 13) A dose of care can cure the impossible
- 14) Right body postures can help reduce pain
- 15) Read about your own condition & keep informed
- 16) The holy trinity between the doctor, you & the treatment becomes a dangerous Bermuda triangle when there is communication gap
- 17) Avoid & try reducing dosage of pain killers from the physical longevity prerogative: - try SRP (systematic reduction plan)

18) Careful watch on any infection, body scratches, pain, and uneasiness should be discussed with doctor

19) People on steroids & suffering from high sugar levels should maintain a *strict diet chart*

20) *Enough water in-take with medicines*: - Swallowing medicines without enough water may prevent the medicine from acting properly and may even lead to undesired side effects in some cases. One example is the class of drugs known as nonsteroidal anti-inflammatory agents

21) *Eat less Sugar, you are sweet enough already*: - For me the following helped in controlling my sweetness –

i) Bitter Gourd juice

ii) Indian Gooseberry juice

iii) Jamun fruit grounded seed – one spoon empty stomach

22) Gluten free food might relieve symptoms

23) *Family, a nature's masterpiece*: - One of my biggest strengths & support function in this tedious war field was my Family. I never realized when it became 'Our' journey from 'My' journey.

There is no such thing as a perfect family; for life time partnership each member has to become, in a special way, the servant of the other. I am blessed to have profound vital forces safeguarding me & we are still holding on to our roots. Even if I try penning down their support & be thankful to my parents & siblings, it will be a manual, even before I realize.

24) *Health cover*: - One of the most important aspects of my treatment as it provided me with financial security to peace of mind to coverage of specific medication & ailments to cashless hospitalization benefits.

25) *Try Diving down not drowning down health care cost*: - We can't shy away from the fact that world's most expensive drugs fall under the umbrella of ultra-rare diseases. However all patients like us have legitimate expectation of treatment whether the condition is common or rare.

At times, being smart, is even to know when to play dumb. Whenever, I sensed the treatment could cost a bomb, I connected with genuine distributors candidly rather than being on retailer's disposal or hinged onto the hospitals to walk me through.

➤ **Medical Terminologies, be acquainted**

- 1) **Antibody**: - A protein molecule made by the immune system in response to a foreign invader (antigen), like bacteria or a virus. The antibody binds itself to the antigen and either kills it or marks it for attack by other cells.

- 2) Autoimmune disease: - An illness that results when the immune system mistakenly attacks healthy tissues.
- 3) Biopsy: - A procedure in which a sample of cells or tissues is taken for laboratory examination.
- 4) Chronic disease: - An illness that lasts for a long time, often a lifetime.
- 5) Glaucoma: - Abnormally high fluid pressure in the eye that can lead to vision loss or blindness.
- 6) Immunoglobulin: - An antibody that plays a critical role in mucosal immunity.
- 7) Immunosuppressant: - A medication that suppresses the immune response and can be used to treat autoimmune disease.
- 8) Immunosuppressed: - having a weakened immune system.
- 9) Myokymia: small muscle contractions that can occur in any muscle group.
- 10) Myositis: An inflammation or swelling of the muscles often caused by injury, infection, or an autoimmune disorder.
- 11) Steroids: - A family of substances that share a similar chemical structure, including certain hormones (e.g., testosterone) and various drugs. "Steroids" is often used as a shortened form of Corticosteroids.
- 12) Syndrome:- A medical condition characterized by a collection of symptoms (what the patient feels) and signs (what a doctor can observe or measure)

➤ **Social Networking**

Contact via Facebook: - Isaac's Syndrome, Neuromyotonia, Cramp Fasciculation Syndrome, Peripheral N

- 1) Though it's a closed group but one can connect with the admin to join
- 2) People suffering from this disease worldwide exchange ideas & share their stories

➤ **Doctors, contributed to my journey**

1) Dr. Ashok Panagariya (Neurologist):- 7, Raj Niketan, Moti Doongri Road, Jaipur, Rajasthan 302004. Phone: - 0141 262 0585. He is my main doctor.

2) Dr. Bhawana Sharma (Neurologist):- 381, New Sanganer Road, Laxman Path, Vivek Vihar, Jaipur, Rajasthan 302019 Phone:- 0141 229 0496

3) Dr. Nirmal Pandey (Neurologist, Kanpur):- He was among the few who diagnosed & started the right treatment

4) Dr. Khadilkar (Neurologist, Bombay Hospital)

5) Dr. Saumil Shah (Gastrologist, Mumbai)

6) Dr. Sanjeev Amen (Rheumatologist, Mumbai)

7) Dr. Laxman Pillai (Naturopathy, Nature Cure Hospital, Hyderabad)

➤ **Though, I have not connected with them but they are worth a mention:-**

1) National Organization for Rare Disorders (NORD)

55 Kenosia Avenue

Danbury, CT 06810

orphan@rarediseases.org

<http://rarediseases.org> Tel: 203-744-0100; Voice Mail: 800-999-NORD (6673) Fax: 203-798-2291

2) For additional information about the NINDS research programs, contact the Neurological Resources Unit and the Institute's Information Network (BRAIN) at:

BRAIN

PO Box 5801

Bethesda, MD 20824

(800) 352-9424

<http://www.ninds.nih.gov>

3) Mr. Sarosh Irani (Researcher):- saroshrirani@gmail.com

4) Ms. Angela Vincent (Researcher):- angela.vincent@ndcn.ox.ac.uk

➤ **Known to Few**

New research in this specialty: - Legalization of Cannabis in India. Cannabis, also known as marijuana among other names, is a psychoactive drug from the Cannabis plant intended for medical or recreational use.

1) International Association for Cannabinoid Medicines:-http://www.cannabis-med.org/english/bulletin/ww_en_db_cannabis_artikel.php?id=337

2) Even the Members of Parliament are supporting the medicinal use of cannabis:-
<https://www.gqindia.com/content/marijuana-legalisation-india/>

➤ **A Word of Caution:-An appeal**

Diagnosis of a rare disease is one of the biggest challenges, not just India but the World is facing.

There are about 7000+ rare diseases worldwide. As the world is getting smaller & a global battlefield, we as clans have not even scratched the morass surface & the impact is unofficially catching up. My idea here believes in discretion & having a dialogue to unify a fractured & polarizing world when it comes to this subject matter.

Few words of Solutions

- 1) Awareness campaigns are steroids
- 2) Bridging gap in doctor-patient ratio
- 3) Building long-term social and physical infrastructure
- 4) Involvement of corporates and NGOs in providing medical advice using telemedicine
- 5) Try catering to challenges in administration, delivery & cost
- 6) Managing the basic ethics of service & nobility in healthcare professions which are rapidly evaporating
- 7) Perpetual shortage of quality medicine & healthcare providers is rife. The conditions are worse in backward & tribal areas
- 8) Accommodating concerns about overblown spends on prescription drugs that treat rare diseases
- 9) Tight Government intervention
- 10) As Brigham Young once said “you educate a man; you educate a man. You educate a women; you educate a generation”. It’s an extraordinary wise statement

On that note would like to suggest that - Thinking of disease constantly will intensify it. Feel always 'I am healthily in body and mind'. As Charlie Chaplin once said “to truly laugh, you must be able to take your pain, and play with it”. Easy said than done but making an initiative would help.

Rgds

Mudit Dalmia