

Low Dose Human Intravenous Immunoglobulin Infusion With Contraception Reversal, Omission Of Water Foods Without Scales, Gills And Consumption Of Essential Fatty Acids Rich Diet, Reverted Neuro Myelitis Optica, Systemic Lupus Erythematosus, Progressive Systemic Sclerosis, Demyelination Encephalopathy

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Abstract: 18 year old male presenting with acute onset of abortive seizures, giddiness, diagnosed by Magnetic Resonance imaging as demyelination encephalopathy, received Intravenous immunoglobulin of 10gms, and he recovered. Consumption of prawns, water living, fish without scales, gills and essential fatty acids deprived diet as sunflower refined oil consumption, were present as etiology.

15 year old female of 30kg weight, presenting with thickened, bound down skin, positive antinuclear antibody, diagnosed as progressive systemic sclerosis, received intravenous immunoglobulin 15 grams, marvelously the skin reverted to pliability, soft beauty was restored. Consumption of prawns, water living, fish without scales, gills and essential fatty acids deprived diet as sunflower refined oil consumption were present as etiology.

24 year old female of 40 Kg weight, presenting with joint pains, positive antinuclear antibody, diagnosed to have systemic lupus erythematosus, received 20 gm of intravenous immunoglobulin and her symptoms and laboratory parameters improved. Consumption of prawns, water living, fish without scales, gills and essential fatty acids deprived diet as sunflower refined oil consumption were present as etiology.

34 year old female on wheel chair, of 80 Kg weight, presented with quadriparesis, dystonia, myoclonus epilepsy, high grade fever secondary to uro sepsis with indwelling catheter for the past 9 months, prior to which she had developed visual problems with weakness, she had been diagnosed to have neuro myelitis optica; past history of consuming oral contraceptives for four months, intramuscular pricking of needles in both arms as part of acu puncture treatment for 15 days prior to the onset of illness, using essential fatty acids deprived diet also were present; she was on treatment with steroids, methotrexate and azothioprine for nine months; she had received three plasmapheresis; since her records showed no auto immune antibody evidence in serum or cerebrospinal fluid analysis, in view of her high sepsis immuno-suppressants were discontinued; recurrent uro sepsis required treatment with sensitive antibiotics; magnetic resonance imaging had shown gross demyelination with thinning of fibers in the cervical cord, multi focal demyelination in cerebral cortex; during the course of illness, she manifested areflexia suggesting poly radiculopathy phenomenon; she received intravenous immunoglobulin 15 gm; slowly with omega three fatty acids supplementation and antituberculous treatment for urinary tract Koch's, she improved steadily and she is able to walk normally without dystonia.

35 year old female diagnosed to have progressive systemic sclerosis with generalized thickening of skin, anti nuclear antibody being positive, with desaturation of SPO₂-86%, mild pulmonary hypertension, on cyclophosphamide, steroids, methotrexate, received immunoglobulin 25gms as 5gm/day over 5 days; there was dramatic improvement in skin changes and saturation to 95%; consumption of fish without scales and gills, sunflower refined oil without fatty acids were present and exposure of germ cells to raw endometrial surface by three days after last menstrual period without abstinence for 7 days after last menstrual period were present as probable etiology.

I. Case Details

18 year old male, an engineering college student presented with giddiness, focal seizures; he had been diagnosed to have demyelination encephalopathy based on magnetic resonance imaging of 15 days duration; he was afebrile; his high density lipo-protein level was 32 mg/dl; he could afford intravenous immunoglobulin of 10gms, with omega 3 fatty acids supplementation, dietary advise to consume essential fatty acids rich diet, specially virgin coconut oil, ground nut oil, palm-olein oil, and gingili oil with their fat content, he improved. He was recommended to avoid consumption of prawns, crabs, fish without scales, gills with toxins in them which can mediate by molecular mimicry, auto immune mediated demyelination and essential fatty acids deprived diet as sunflower oil, refined oil.

15 year old female, a school student with 30Kg weight, presented with progressively increasing thickening of skin, of her fore arms, back, legs, for the past 3 months; one episode of tonic clonic seizures also was present; her antinuclear antibodies were positive; being native of coastal area, frequent consumption of prawns, crabs, fish without scales, gills was present as probable etiology, auto immunity being mediated by molecular mimicry of the toxins of prawns, crabs, and fish without scales, gills; she's been fed on essential fatty acids deprived diet such as sunflower oil, refined oil from childhood; she received intravenous immunoglobulin of 15gms given as 5gm/day infusion for three days; it was a pleasant observation, even prior to the third dose of 5gm immunoglobulin infusion, her skin pliability, texture was normalizing; it was a complete recovery.

24 year old female of 40 kg weight presented with poly arthralgia of 6 months duration, diagnosed to have systemic lupus erythematosus with antinuclear antibody being positive; she was on Penidure-benzathine penicillin prophylaxis for rheumatic fever treatment; history of consumption of fish without scales, gills, prawns, was present; essential fatty acids deprived diet of consumption of sunflower refined oil was also present; she was not practicing contraception; probable exposure of germ cells to the raw endometrial surface, during the recommended seven days abstinence after last menstrual period was also considered; she received immunoglobulin infusion of 20gms as 5gm infusion/day over 4 days. Erythrocyte sedimentation rate has reduced, urine sediment normalized, arthralgia improved, no further manifestation of systemic lupus erythematosus have appeared for the past six months.

34 year old female had developed sudden onset of visual impairment, with double vision in the left eye, followed by weakness, was diagnosed to have neuro myelitis optica and was on treatment with azothioprine, steroids, methotrexate, for the past 9 months; she had received three plasmapheresis; her vision had improved; past history of using oral contraceptives, condoms, for four months was present; for fifteen days prior to the onset of symptoms she had undergone acupuncture treatment with perpendicular needle prick in both palms for one hour/day; consumption of sunflower refined oil, prawns, fish without scales, gills was present; when she presented to us she had quadriparesis with dystonia of the left upper limb, cushingoid features with obesity, conscious but had continuous myoclonus epilepsy with high grade fever of 103F, of four days duration; indwelling Foley's catheter was present, turbid urine was draining; her previous records showed absence of antinuclear antibody, cerebrospinal fluid analysis showed increased protein of 115mg/dl, but there were no cells detected or polymerase chain reaction for tuberculosis, herpes were negative; liver enzymes were borderline elevated, high density lipoprotein was only 28mg/dl; Magnetic resonance imaging showed demyelination with thinning of cervical cord, multifocal demyelination in cerebral cortex; urine culture grew *Escherichia coli*.

She received Piperacillin Tazobactam for the urosepsis, levitracetam, clonazepam, phenobarbitone to control her seizures, omega three fatty acids to improve her cholesterol synthesis to enable repair of thinned out axons; myoclonus epilepsy was controlled; all immunosuppressants were discontinued in view of severe sepsis and antinuclear antibody being negative; contraception was advised to be prohibited; essential fatty acids rich diet including virgin olive oil for cooking was advised; ursodeoxycholic acid was prescribed to improve her liver enzymes, an attempt was made to remove her indwelling catheter, due to wheel chair life there was initial reluctance; since she got three times urinary tract infections requiring Piperacillin Tazobactam, catheter removal was planned, during the third episode of severe urosepsis within a period of four months, she developed a transient phase of worsening of weakness with areflexia in all four limbs; hence poly-radiculopathy overlap was considered and intravenous immunoglobulin transfusion of 15gms was given as 5gms /day for three days, as they could not afford more than that; catheter was removed, there was significant residual urine by ultra sonogram with mild hydronephrosis of the right kidney, hence neurogenic bladder was considered and with Bethanechol hydrochloride 2.5mg twice daily she was encouraged to empty her bladder frequently as much as possible; her weakness started to improve; but she developed titubation during fever spikes, due to recurrent urinary tract infections, in an immunosuppressed background, hydronephrosis picture by scan, urinary tract Koch's was considered and she was started on rifampicin, isoniazid, in addition to antibiotics; thereafter there was no uro sepsis, she continued omega 3 fatty acids, virgin olive oil for cooking, contraception and consumption of shell fish, prawns, fish without scales and gills were prohibited since these can initiate, aggravate autoimmune⁷ etiology; there was steady improvement of her weakness, dystonia; oh, it was marvelous to see the reparative capacity of cells, she walks normally, the distorted, left hand, upper limb has become soft and normal by four to six months

35 year old lady weighing 50kg presented with generalized skin thickening, decreased oxygen saturation of 86% by pulse oximetry, mild pulmonary hypertension and was diagnosed to have progressive systemic sclerosis with positive status of anti nuclear antibody, was on cyclophosphamide, steroids, azothioprine, and sildenafil; she received intravenous immunoglobulin 25gms, as 5gm/day over 5 days; her skin changes and saturation improved dramatically.

II. Discussion

Systemic lupus erythematosus is an auto immune¹ disease in which organs and cells undergo damage initially mediated by tissue binding auto antibodies and immune complexes. In most patients auto antibodies are present for a few years before the first clinical symptoms appear; clinical manifestations are heterogeneous; 90% of patients at diagnosis are females belonging to the child bearing years; people of all genders, ages and ethnic groups are susceptible.

Systemic sclerosis is a connective tissue disorder of unknown etiology; heterogeneous clinical manifestations, chronic and often progressive course; diffuse cutaneous form of systemic sclerosis is characterized by thickening of the skin and distinctive involvement of multiple internal organs, most notably the lungs, gastro intestinal tract, heart and kidneys; systemic sclerosis is an acquired sporadic disease with a world wide distribution and affecting all races. Female preponderance specially during child bearing age, declining after menopause is noted, concordance for antinuclear antibody is greater; patients with systemic sclerosis have increased serum antibody to human cytomegalovirus, suggesting a possible link by `molecular mimicry` between systemic sclerosis and cytomegalovirus infections.

A comprehensive view of the pathogenesis of systemic² sclerosis must incorporate the three cardinal features of the disease 1] vasculopathy 2] cellular and humoral auto immunity 3] progressive visceral and vascular fibrosis in multiple organs.

Pathologic criteria of demyelinating³ diseases are destruction of myelin sheaths of nerve fibers with relative sparing of the other elements of nervous tissue.i.e. axons, nerve cells and supporting structures; lack of Wallerian or secondary degeneration of fiber tracts, infiltration of inflammatory cells in a peri-vascular and particularly para venous distribution. Auto antibodies have been found directed against myelin, oligodendrocyte, glyco protein and myelin basic protein; subsets of T cells are activated to activate B cells; inflammatory process erodes blood brain barrier and destroy oligodendroglia and axons.

Neuro myelitis optica is an aggressive⁴ inflammatory disorder, consisting of acute attacks of myelitis and optic neuritis which can be bilateral or unilateral; myelitis is severe, transverse and longitudinally extensive involving 3 or more contiguous vertebral segments and these symptoms are more common in multiple sclerosis which occurs in Asia; majority of these cases are associated with an antibody to a water channel, aquaporin 4, which is found in cells near the ventricular system of the brain; MRI scans are either normal or have high signal lesions restricted to the region of the ventricular system; spinal MRI scans show lesions which are typically longer than the segments involved in multiple sclerosis; clinical deficits tend to recover less well than those of multiple sclerosis and the disease may be more aggressive with more frequent relapses; treatment with immunosuppressive agents such as azothioprine, steroids or cyclophosphamide and or plasmapheresis seems to be more effective than in multiple sclerosis.

Contraception results in smashed fragmentation of Germ Cells, to acentric fragments,⁵ ring chromosomes, chromatid breaks, being identified by immune surveillance as foreign, leading to auto immunity; associated reduced endogenous estrogen or androgen, results in defaulted cell cycle, cell metabolism of differentiation, growth, controlled multiplication, degeneration, apoptosis, regeneration, genomic⁶ repertoire, leading to impaired immunity; auto-immunity is also produced by consumption of fish without scales and gills due to its toxins mediated cytotoxicity, by molecular mimicry, in non contraceptive users also. Abstinence for 7 days after last⁷ menstrual periods prevents germ cell's exposure to raw endometrial surface; abstinence for 45 days after male baby delivery, 90 days after girl baby delivery prevents germ cells exposure to raw placental detached surface and reduces auto immunity.

Contraceptive users demonstrated 15 fold increase in auto-immune diseases among 20-35 years [p <0.0005]; 40 fold increase in auto-immune diseases among 35-50 years [p <0.0005]; 5 fold increase in autoimmune diseases were seen with consumption of fish without scales and gills in non contraceptive users also. Endogenous estrogen was reduced below normal in 61% of patients using contraception [p <0.0005].

Cholesterol deprived diet results in decreased endogenous hormones synthesis since low density lipoprotein is converted to endogenous estrogen, steroid hormones; with resultant 50% increase in degenerative diseases. The concept is germ cells traverse the lumen of genital tract lined by mucosa, physiologically; raw bloody, incompletely regenerated⁷ endometrial surface exposure to germ cells, also can initiate auto antibodies, i.e. 7 days abstinence after last menstrual period {3 days shedding+4 days regrowth of endometrium}, 45 days abstinence after boy baby delivery, 90 days abstinence after girl baby delivery(raw detached placental surface is double for girl baby with xx, more estrogen synthesis which is 2-3 steps later in synthesis than androgen, hence longer duration of lochia i.e. 22 days for male baby delivery, 45 days for girl baby delivery, so double the time of abstinence allowing time for the shed endometrium to re grow) if not observed by fathers, life partners, then raw endometrial surface exposure to germ cells can initiate auto immune processes or auto reactive cells endangering mother's life peripartum by e.g. Vasculitis and can be transmitted in low titer exposures to the next child born, leading to collagen vascular diseases in the child by teen age, since the immune multiplication increases with age. Shell fish, fish without scales, gills, on ingestion [their cells with their proteins-(flesh)

initiate] auto antibodies either by molecular mimicry or hapten mediated mechanisms by their toxins or proteins ; consumption of fish without scales, gills is seen to be associated with pancreatic cancers, painful diverticulitis requiring hemicolectomy, angioneurotic edema, myoclonus, demyelination with transverse myelopathies, poly radiculopathies, nephritis, urticaria, gastro enteritis, gastrointestinal neoplasm. When a mother wears copper-T or uses some contraception in between pregnancies, auto antibodies developed by smashed fragmentation of germ cells are transmitted to the progeny through the placenta and the child born after contraception, as they grow in age they increasingly manifest auto immune diseases as the autoimmunity multiplies with age; in addition, placenta accrete like complications can develop during pregnancy following contraception, secondary to chronic endometriosis, fibrosis of endometrium. A teen ager without practicing contraception (generally in our country, premarital sex is still prohibited) can develop auto immune diseases by this above portrayed mechanism-interim contraception between pregnancies by the parents and trans placental transmission or by consuming fish without scales, gills. Contraception reversal ⁸ leads to halt of germ cells destruction, restoration of endogenous estrogen or androgen, cell cycle, cell metabolism, auto immune diseases regress-79.9% and does not progress to multisystem involvement or end stage diseases Figure 1.

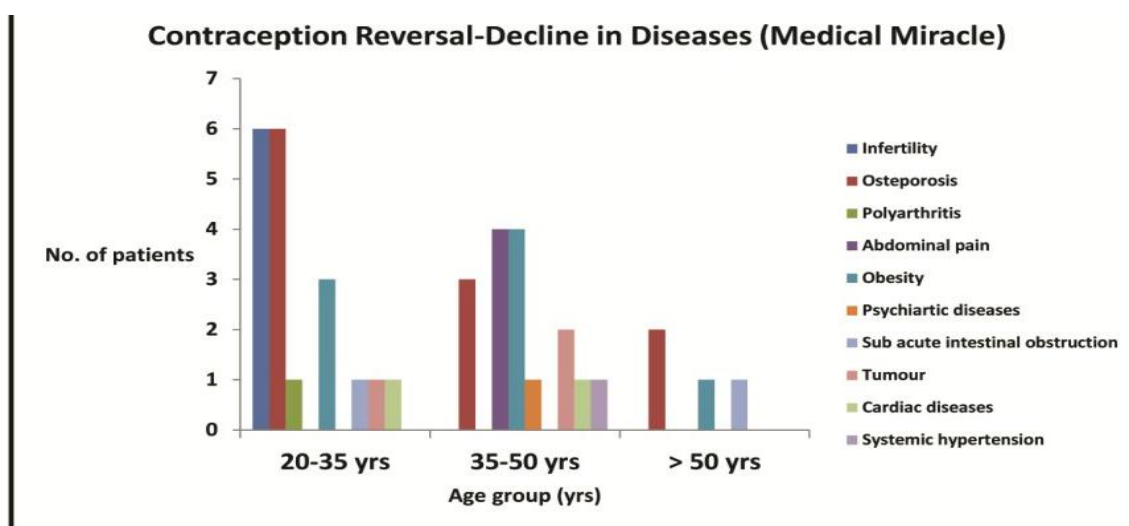


Figure-1-Contraception reversal , decline in diseases Reference 8

Low density lipoproteins are used in synthesis of cell membranes, steroid hormones including estrogen, androgen, catecholamine, other steroids, bile acids, epidermal growth factor and become high density lipo protein; cell death, turnover releases cholesterol from membranes adsorbed onto high density ⁹ lipoprotein and esterifies with long chain fatty acid by an enzyme-lecithin cholesterol acyl transferase, new cholesterol esters are transferred from High density lipo protein to low density lipoprotein by transfer protein, completing the cycle of LDL-HDL-LDL at the tissue. Remarkable cell membranes consist of glyco sphingo lipids, sphingomyelin ¹⁰ and cholesterol Central nervous system has 10 billion neurons, 10-50 times this number of glial cells, all in constant metabolism made up of sphingo lipids, phospholipids, protein lipid complex; transport speed at 400mm/d, little less than electricity, mediated by myelin produced by Schwann cells, wrapping 100 times their¹¹ membranes around the axons, oligodendrocyte also sending multiple processes to form myelin in neighboring axons (with cholesterol free diet ¹²demyelination, neuronal dysfunction results) In the above patients contraception was discouraged, to protect germ cells from fragmenting paving the disastrous path for auto immunity; essential fatty acids rich diet contained in virgin oil was recommended to hasten repair of demyelination by providing fatty acids in the diet to enable body to synthesize cholesterol to be incorporated in cell membranes, specially neuronal tissue; fish without scales and gills, prawns, crabs consumption was discouraged to avoid auto immunity by molecular mimicry mechanism, mediated by their toxins. Abstinence for 7 days after last menstrual period, 45 days after male baby delivery, 90 days after girl baby delivery, to prevent germ cells exposure to raw endometrial surface, to initiate auto immunity was informed and recommended

Immunoglobulin could be infused at low dose approximately 0.5gm/Kg body weight for the total dose; for the patients with neuro myelitis optica and demyelination encephalopathy, still lower doses could only be given, since the cost could not be afforded by them; depends upon the amount of antibodies which need to be blocked by immunoglobulin in the disease status, we may not require to give 0.4gm/kg/day of immunoglobulin × 5days as in the case of Guillaine Barre syndrome or poly-radiculopathy, for every auto immune disease; also the insult initiating the auto immunity should be recognized, considered and reverted as discussed in the text

such as contraception, abortion reversal including tubal recanalization, thankfully these patients had not undergone tubectomy requiring reversal; avoiding fish without scales, gills, consuming virgin oil with fat, observing abstinence to be informed to people, to halt the triggers to produce auto immunity; otherwise immunoglobulins blockade will not be effective as long as the etiology is unattended to.

III. Conclusion

Low dose intravenous immunoglobulin infusion of $< \sim 0.5 \text{ gm/Kg}$ body weight in total, was sufficient to revert neuro myelitis optica, progressive systemic sclerosis, systemic lupus erythematosus, remarkably, when combined with reversing the probable etiology such as contraception, avoiding consumption of prawns, shell fish, fish without scales and gills, recommending essential fatty acids rich diet including virgin oil, and observing abstinence for 7 days after last menstrual period, 45 days after male baby delivery, 90 days after girl baby delivery to avoid exposure of germ cells to raw endometrial surface.

As long as the insult/ etiology of auto immune diseases is not addressed, the disease will progress and the immunoglobulin may be required in large amounts, such as permanent sterilization wherein tubal recanalization is mandatory to end production of auto immune antibodies; any amount of immune suppressants alone or immunoglobulin or monoclonal antibodies may not suffice; how essential are global national policies to revert global contraception, abortion specially including Fallopian tubal recanalization requiring invasive surgical correction; how essential are global policies to be framed to halt contraception, abortion globally specially permanent sterilization, wherein patients are at the mercy of policies, medical forum to recanalize.

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