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Antibody Myopathy Associated with Anti-Hydroxymethylglutaryl Coenzyme: A Reductase in a Simvastatin User

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Abstract

Autoimmune myopathies result from direct or indirect injury to muscle fibers mediated by the immune system. The term myositis is generally interchangeable with “Idiopathic Inflammatory Myopathy”, which refers to primary autoimmune muscle diseases. These include dermatomyositis, inclusion body myositis, antisynthetase syndrome, and Immune Mediated Necrotizing Myopathy (IMNM). Other known causes of inflammatory myopathies include infections, drugs, mixed connective tissue diseases and cancer. In 2017, the European neuromuscular centre described two subtypes of IMNM, each mediated by a different antibody: Anti-SRP and Anti-3-Hydroxy-3-Methyl Glutaryl Coenzyme A reductase (Anti-HMG-CoA), each presents with a different clinical and histopathological course. The first is associated with a more aggressive disease and a low response to conventional immunotherapy. In this review, however, we will focus on the latter, MNIM related to anti-HMG-CoA.

Keywords

Immune necrotizing; Glutaryl coenzyme; Auto immune diseases; Electro myography; Intravenous immunoglobulin

Abbreviations

CK: Creatin Kinase; MRI: Magnetic Resonance Imaging; Anti- HMG- CoA: Anti Hydroxi methylglutaryl Coenzyme-A Reductase; IMNM: Immunomediated Necrotizing Myopathy; Anti-SRP: Anti-Signal Recognition Particle; ALT: A Lanineamino Transferase; ASt: A Spartateamino Transferase; LHD: Lactatede Hydrogenase; Anti- LKM-1: Anti Liver Kidney Microsome Type 1; Anti- DNA: Anti-Double Stranded DNA; Anti-SCL 70: Anti-Scleroderma-70; Anti- ENA SN RNP: Anti- Extractable Nuclear Antigens Small Nuclear Ribo Nucleo Protein; PAS: Periodic Acid Schiff ; SLCO1B1: Solute Carrier Organic Anion Transporter 1B1; CYP3A4: Cytochrome P450 3A4; MHC-1: Major Histocompatibility Complex 1; IVIg: Intravenous Immunoglobulin; PCSK9: Proprotein Convertase Subtilisin/Kexin Type 9

Introduction

Anti-HMG-CoA related IMNM, whose pathogenesis is not fully understood, was first described in adults with a history of statin exposure [1]. Unlike patients with statin-induced toxic myopathies or intolerance to statin drugs, in whom symptoms improve upon discontinuation of drug, these patients persist with muscle weakness and elevated Creatine Kinase (CK) despite discontinuation of the drug [2].

The typical clinical presentation of statin-related IMNM occurs in adults and is characterized by the development of acute or sub-acute symmetrical proximal muscle weakness accompanied by significant elevation of CK [3]. Distal weakness, extra-muscular symptomatology or smooth muscle involvement is uncommon and occurs in less than 10% of cases [4]. Other rare manifestations include dysphagia,

arthralgias, myalgias and Raynaud's phenomenon. The classic presentation, so it is important to be aware of it and suspect this pathology even though it does not present in a common way [5]. In addition to elevated CK, reflecting cell membrane damage and muscle necrosis, other enzyme markers may be elevated, including aldolase, lactate dehydrogenase, transaminases, aspartate transaminase, alanine transaminase. Enzyme elevation has been linked to anti-HMG-CoA antibody titers [6].

Literature Review

A man with a relevant medical history of diabetes mellitus and dyslipidemia, under treatment with ezetimibe/simvastatin 10/20 mg for one year, presented to the Hospital [7]. He presented with a two month long ailment characterized by intermittent hand oedema and cervical pain exacerbated by movement, as well as proximal and distal muscle weakness in all four limbs, which made it difficult to walk [8]. Subsequently, dysarthria, dysphagia and cervical muscle weakness were added to his symptoms. The physical examination revealed preserved mental functions, unaltered cranial nerves, diminished gag reflex, 2/5 strength in shoulder and pelvic girdle muscles and lower limb distal muscles, meningeal signs were absent, proprioceptive and stereoeptive sensitivity were preserved[9].

Initial blood tests revealed elevated transaminases: ALT 621 U/L, LDH 1448 U/L, ASt 506 U/L, and CK 62,334 U/L. There were no reports of elevated azoosides or electrolyte disturbances [10]. An MRI scan was requested, which showed a fatty infiltration of posterior muscle planes in both pelvic limbs and oedema in the right buttock. With a suspected myopathy, an electromyography of the four limbs was requested [11]. The results reported a polyneuropathic pattern and revealed that the pelvic limbs were the most compromised. Therefore, the following myositis-specific antibodies laboratory tests were requested: anti- LKM-1, anti-smooth muscle, anti-DNA, anti-Jo, anti-La, anti-SCL 70, anti-ENA Sm RNP, all of which were negative.

A gastrocnemius muscle biopsy was also carried out, showing non-specific focal regenerative changes. Other typical markers of inflammatory myopathies such as macrophage infiltration or infiltration of other inflammatory cells, Pas, Gomori's trichrome and Masson's trichrome stainings were all negative. Fibrosis, collagen deposits, cytoplasmic bodies, inclusion bodies and tubular aggregates were also absent. Given the patient's clinical presentation and the results of paraclinical studies, we requested antibodies against HMG-CoA, which were found to be 9 times above the normal upper limit, therefore confirming the diagnosis of IMNM.

During hospitalization, he was managed with high-volume crystalloid solutions despite the fact that acute renal injury was never demonstrated. His statin was discontinued and immunosuppression with prednisone at 1 mg/kg/day was started as soon as the inflammatory myopathy was suspected. The patient showed partial clinical improvement and progressive decrease in CK and transaminases, until ASt 353 U/L, ALT 482 U/L, DHL 1079 U/L, CK 9115 U/L were obtained, which led to his hospital discharge, continuing with the same treatment scheme at home. Two weeks later, he presented again with difficulty walking and oedema in the pelvic limbs, as well as an increase in CK to 19,939 U/L. At this point it was decided to re-admit him for immunosuppressive adjustment with intravenous immunoglobulin 10 g/day for 5 days. The response to treatment was adequate, with a progressive decrease in CK to 10,500 U/L, as well as improvement in muscle strength and ability to walk.

Discussion

Like other autoimmune diseases, the interaction between immunological and environmental factors can predispose the patient to this condition. The presence of the HLA-DRB1 * 11:01 allele has been described as an immunogenic risk factor for developing anti-HMG-CoA myopathy. A polymorphism in the SLCO1B1 gene on chromosome has been identified as an important genetic risk factor. Other described risk factors are the use of drugs metabolized by CYP3A4 as these increase serum statin levels, alcoholism, hypothyroidism, renal failure, liver failure, and familial or personal history of statin intolerance. It has also been observed more frequently in women. Different drugs have been linked with the occurrence of muscular symptoms. Statins are commonly associated with manifestations ranging from mild asymptomatic CK elevation, myalgias, to life-threatening rhabdomyolysis. Less frequently;

autoimmune syndromes such as immune-mediated necrotizing myopathy with autoantibodies against hydroxymethylglutaryl coenzyme A reductase (anti-HMG-CoA) have been described. Several studies have reported a 37.5% to 94% association between these antibodies and statin exposure. There are antibodies were found in statin-naïve patients who had been exposed to certain foods. The duration of statin exposure prior to the clinical presentation varies from 2 months to 10 years.

The electromyography pattern shows an irritative myopathy. Findings include low-amplitude, short-duration potentials, positive sharp waves, fibrillatory potentials and repetitive myotonic or pseudomyotonic discharges. The gold standard imaging study is a Magnetic Resonance Imaging (MRI). Common findings are oedema and muscle atrophy with fatty substitution mainly in the lateral rotators, glutes and the medial and posterior compartments of the pelvic limbs with preserved muscle architecture. The intensity of the signal is generally proportional to the swelling and the severity of said swelling. However, since these findings are non-specific, the main utility of MRI is in to select the areas for performing a biopsy and for disease monitoring.

Findings from the muscle biopsy in IMNM, unlike in other inflammatory myopathies, where cellular infiltrates composed mainly of CD8+ T lymphocytes and macrophages are usually observed, show muscle fibers in different stages of scattered necrosis with little or no lymphocytic infiltration. Diffusely distributed regenerating fibers and increased expression of Major Histocompatibility Complex 1 (MHC-1) in the sarcolemma are also characteristically observed. The histopathological findings described are variable and may not be universally present.

Corticosteroids are commonly the first line of treatment in inflammatory myopathies with doses equivalent to 0.5-1 mg/kg/day of prednisone. Most patients with statin-associated immune-mediated necrotizing myopathy require different lines of immunosuppressive therapy. Methotrexate, azathioprine, mycophenolate mofetil and plasmapheresis have been used with variable results. Recent evidence supports the use of IV immunoglobulin (IVIg) in IMNM, even as monotherapy, although the classic scheme combines methotrexate or azathioprine with corticosteroids. The intravenous immunoglobulin was started early in combination with steroids given the relapse in symptoms and severity of the disease. This was done with the patient responding adequately to treatment. Rituximab use has also been described in patients with anti-SRP-positive IMNM refractory to conventional immunotherapy. Withdrawal of immunosuppression is possible after showing improvement with the treatment for 6 months to 1 year [11]. In patients at high cardiovascular risk, who require lipid-lowering management after statin withdrawal, PCSK9 inhibitors have been used safely.

Despite their low frequency, it is important to identify typical and atypical clinical manifestations related to statin use due to their variability and severity, with consequent repercussions on the initiation of timely and appropriate treatment, with rare symptomatology such as distal weakness, dysarthria and dysphagia; it also differs from most cases in that significant CK elevation often implies acute renal damage, which was never present in our patient.

Anti-HMG-CoA-related IMNM belongs to the group of idiopathic inflammatory myopathies, in which, although clinical symptomatology and serology support the identification of the specific type of myopathy, the gold standard for identification continues to be the muscle biopsy. This allows differentiation from other autoimmune myopathies such as polymyositis, dermatomyositis, and inclusion body myositis, non-specific and anti-synthetase syndrome. Magnetic resonance imaging should always precede the muscle biopsy in order to decide the site from which the biopsy will be taken.

Conclusion

In this clinical context, management includes, in addition to drug withdrawal, immunosuppression, which must be maintained for a long period of time to avoid relapses. Although corticosteroids are considered the first line of treatment, they are generally insufficient, so the following lines will be adapted on an individual basis. In this, the patient showed improvement with the administration of intravenous immunoglobulin, a drug that has been used as monotherapy. We used intravenous

immunoglobulin early in the relapse upon worsening of symptoms, with which we obtained excellent clinical and paraclinical response.

Author's Contributions

MACC compiled and interpreted the patient data, was a major contributor in writing the manuscript. BPA compiled patient data, collected data for use in academic research. SIM was in charge of clinical and paraclinical neurological review. RVL reviewed the proposed diagnostic pathways. DRH guided diagnostic path. All authors read and approved the final manuscript.

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None

Conflict of Interest

The authors declare that there was no conflict of interests.

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Epidemiological COVID-19 data for the Region of Eastern Rodopi, Bulgaria

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Abstract

The Epidemiological COVID-19 of rtPCR diagnostic tests for people with travel arrangements and border-crossings movement and the importance of restrictive measures, diagnostic testing and limited travels in order to contain the pandemic of COVID-19 during the summer months of 2020. The rtPCR test results were prerequisite for any planned trip and border crossings, therefore the collected data is cumulative and statistics incredibly helpful and necessary. Our Molecular Diagnostics Unit is licensed within the territory of Bulgaria. Our methods were strict protocols from the guidelines of National Center for Infectious and Parasitic Diseases-Bulgaria, the kits we use are all CE, the overall concept in sync with the global regulations as from the CDC and the WHO. We demonstrate an increase of the numbers of infected randomly tested travelers during the summer months and thereafter, giving a glimpse of the magnitude of the pandemic that followed after. We show a total increase of infection from 12.5% in July to almost 56% for the month of November.

Keywords: COVID-19; SARS-CoV-2; Global pandemic; Border-crossings restrictions.

Introduction

In the beginning of the year 2020 the news of the new and deadly disease broke. We only had limited information of this brand new virus from the family of the Coronaviruses; some vague specifics we had yet to discover. Swiftly it became evident, the entire world would be affected and will partake in the fight against it, as well as describing the symptoms, the major manifestations, treating patients, testing, preventing and contributing to the global knowledge in the prevention and cure[1]. We established our COVID unit testing lab within the Microbiology and Virology Division in the main County Hospital in the town of Kardzhali, Eastern Rodopi, Bulgaria[2]. Upon the beginning of our new line of work, we immediately started testing a huge amount of inpatients and outpatients as we did our best to provide prompt service, deliver results the same day, report to physicians and local health authorities for the appropriate measures and prescription of quarantine to whoever tested positive[3]. We have been working according to mandatory regulations for border crossings globally and locally and provided standard testing plus verified result certification.

Objectives

The tested patients for the months of the pandemic produced data from July to November 2020 we report, as we believe might be an important piece of evidence toward the global understanding of the spread, contagious power, significance, morbidity and mortality. We believe our data is very important for the region we live in, not only with regards to treating patients, controlling the spread and guiding the health authorities measures locally, as well as contributing to the bigger picture of understanding this new and deadly disease globally (Figure 1).

A statistical of hypothetical development of the pandemic. According to the authors in the viral article "The Hummer and the Dance" Strong coronavirus measures today should only last a few weeks,

there shouldn't be a big peak of infections afterwards, and it can all be done for a reasonable cost to society, saving millions of lives along the way. If we don't take these measures, tens of millions will be infected, many will die, along with anybody else that requires intensive care, because the healthcare system will have collapsed.

Methodology

We base our statistical data on the results we collect directly from testing patients in our hospital on a daily basis. Our testing methods are the rtPCR for COVID19 according to the global standards of the WHO and the CDC guideline. Our methodology utilizes isolation of RNA from patient's samples prior to the rtPCR protocol. The isolation is being done manually [4]. The rtPCR was run in the Applied Bio systems StepOne Real-Time PCR System. Our supporting methods of testing are the rapid tests with whole blood or plasma, as well as the nasopharyngeal antigen testing via swabs [5]. The reagents we use are supplied from different sources, governmental, official central supply, local grants or purchases. All of our reagents and kits are CE.

Results

For the testing we collected data from Key dates, which include the date of onset of disease, date of admission to hospital, date of confirmation of infection, and dates of travel [6]. Demographic information about the age and sex of patients/cases. Geographic information, at the highest resolution available down to the district level [7]. We excluded information that was at the building level so that cases could not be identified. Geographic information was subdivided into administrative units. All the information collected with the results was entered into the national system for COVID for Bulgaria within the same day. Summaries of the data are shown in Figure 2. According to the data there is an increase in the patients tested positive from the beginning of the summer through July until November. During the summer months the travel across borders was achieved only with evidence of a negative PCR test (Figure 3). We recorded mainly negative and healthy individuals traveling through earlier on, but with the shift of the seasons, the patients with positive tests increased. We have no data for the objectives and the purpose of people's travelling reasons and the need to cross borders, but we speculate the summer months were for family annual vacation, as well as business related and the need to travel back home for people with seasonal jobs throughout Europe (Table 1).

As our data builds further and we collect more evidence, we can report solid evidence for one very good reason for the spread of the COVID infection in regions near border crossings. For the Greek authorities to grant entrance to the citizens with Greek passports the rtPCR negative results were prerequisite. We also observe percentages of positive not by peaks, but rather steady increase in numbers. The increase of positive tests further gave an increase of morbidity and mortality (not presented), lots of patients with a need of hospitalization, exceeding the available hospital beds, exhausting the hospital resources and staff. The increase in infected people exposed many doctors and healthcare workers to an immense risk on the job, a rather grave situation, just like anywhere else in the world.

Discussion

As we believe our data has been collected daily and reported to local and national authorities, we continue to study the trends and nuances of the mass number of tested individuals. Although we separate and count the foreign passports in our database, we firmly believe the reason for testing is for travel across borders. We cannot tell though what percentage of the Bulgarian passport-holder healthy individuals, subjected to testing, had the intention of traveling and therefore we can only speculate, based on the data we present. However non-exact and biased the results, we think the trend shows clearly enough the evidence of spread due to people travel and movement, regardless of mechanisms of spread-via infected patients or simply mechanically disseminating the virus particles. Furthermore, the actual rtPCR protocol as such, there is a considerable amount of wait before the results become available, so simply we have no control over the patients physical contacts during that time; the time they spend at the local grocery store or a restaurant, the lingering at the actual hospital and the like. Based on our evidence, we can make a suggestion that we observe a higher percentage of infected,

tested positive and ultimately sick patients in the larger cities near border crossings, where the testing for SARS-Cov2 is being done.

Conclusion

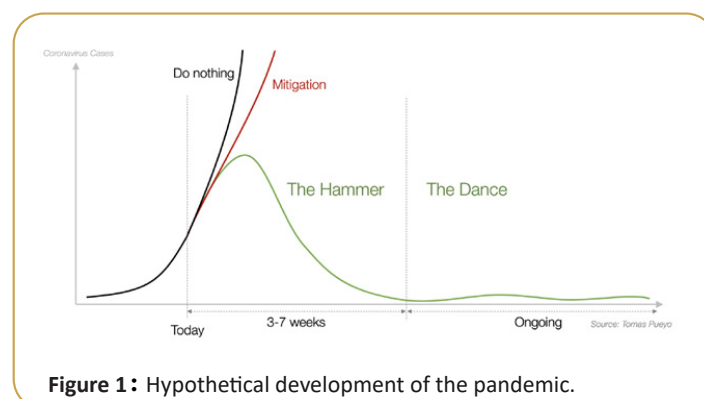
As we experienced several complete lockdowns, followed by slight removal of restrictions we can only hope we follow the scheme outlined by the hammer and the dance. Our greatest hope is that with more and more medicinal products now available, more and more people take the advantage and can hope to be slowly moving back to normalcy. The current report represents retrospective data and suggests the possibilities, available to nations and applicable locally and of immense importance near border-crossing regions in a situation of pandemic with such magnitude and without the immediate access to vaccines and reliable treatments for brand new infectious outbreaks.

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Table 1: The important aspects of epidemiological data.

Month	Total number of patients tested	Total number of positive patients	Number of patients with foreign passports	Patients with foreign passports tested negative	Patients with foreign passports tested positive
July	1015	127	15	15	0
August	1044	101	70	70	0
September	900	153	91	81	10
October	1405	546	92	73	19
November	947	527	51	28	23



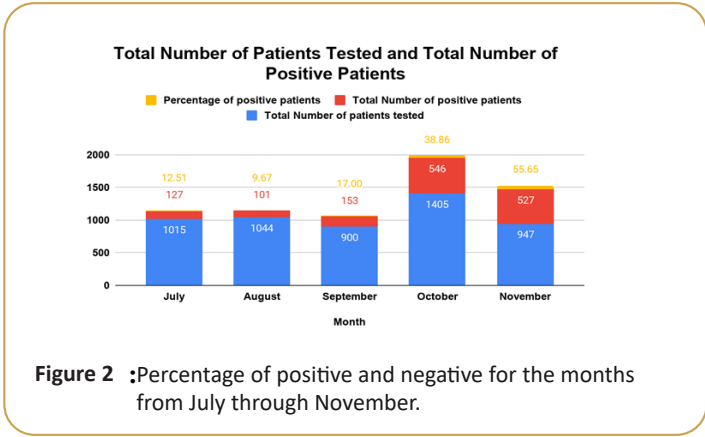


Figure 2 :Percentage of positive and negative for the months from July through November.

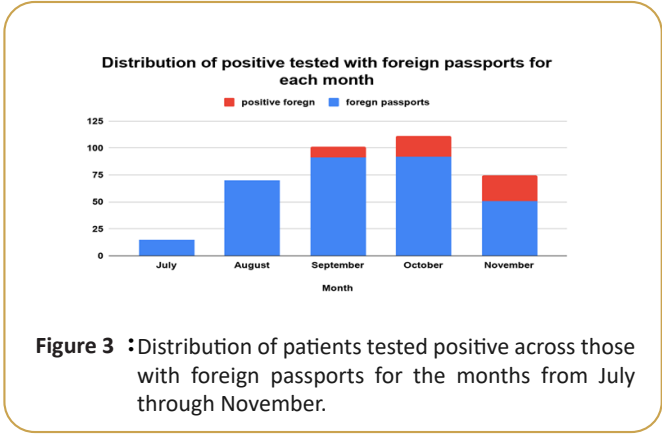


Figure 3 :Distribution of patients tested positive across those with foreign passports for the months from July through November.

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Causes and Management of Amblyopia

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Description

Amblyopia is a condition where the eyes do not develop vision properly in childhood. It is sometimes also known as Lazy Eye. Amblyopia is a mutual problem mainly seen in new born babies and young children. It is essential to recognize and treat amblyopia as early as possible. Otherwise, a child suffering with amblyopia will not grow normally with healthy vision. Amblyopia can develop from other eye to another eye and cause vision problems. There are some disorders that may leads to amblyopia in a child. There is Strabismus when the eyes point in two different directions, Refractive errors that eye can "turn off," and vision will not develop properly. Cloudiness in the normally clear parts of the eye where the eyes normally clear lens is cloudy. Droopy eyelid can leads to blockage of vision in a child's developing eye and lead to amblyopia. The patients will face following symptoms and possible eye problems Eye injuries, sudden changes to-or loss of-vision, eye pain, Poor depth perception, Squinting or shutting an eye, Head tilting, Abnormal results of vision screening tests, Eyes that appear to not work together. The Amblyopia can be diagnosed by conducting an eye exam, checking for eye health, a wandering eye, a difference in vision between the eyes or poor vision in both eyes. Eye drops are mostly used to expand the eyes. By using the eye drops it may cause blurred vision that lasts for some hours or a day. Amblyopia generally develops in childhood, usually between ages 5 to 9 years. Recognizing and treating it before age 7 years may cure the condition. Amblyopia can be diagnosed by patient's first eye examination, so that it can be treated in a general optometric practice to dramatically lead to improve quality of life in the developing child and a decrease in vision can be avoided.

Management of amblyopia

Amblyopia can be treated by using atropine eye drops, treating amblyopia can be divided into 3 categories there are paralytic agents (botulinum toxin) for extra ocular muscles to affect eye movements. Autonomic agents (atropine, miotics) for manipulate the refractive status of the eye. Treatment includes drops, eye patches, glasses or contact lenses and sometimes it leads to surgery. Managements for amblyopia include patching, eye drops, and optical penalization of the non-amblyopic eye. The most communal reason of Amblyopia is an imbalance in the muscles that present in the eyes. This difference can cause the eyes to cross in or turn out, and stops them from working together. Difference in sharpness of vision between the eyes is also known as refractive amblyopia. Levodopa pharmacologic treatment has been studied and has shown transitory improvement in vision in amblyopic eyes. However, the precise role of such pharmacologic drugs is unknown. According to the Pediatric Eye Disease Investigator Group, levodopa is ineffective as an adjuvant treatment for amblyopia. Levodopa is not being utilized in clinical trials. Atropine penalization (either as ointment or drops) is an alternate means of obscuring eyesight in patients who refuse patching. It should only be used once a day on patients in their favoured eye.

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Diagnosis and Epidemiology of Lymphoma Disease

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Description

Lymphomas are divided into two categories, Hodgkin's lymphomas and Non-Hodgkin's lymphomas. A fatal diagnosis has become a curable condition. Most non-Hodgkin lymphomas are B-cell lymphomas and grow rapidly (high grade) or slowly (low grade). There are more than a dozen types of B-cell non-Hodgkin lymphoma. The rest are T-cell lymphomas, named for another cancerous white blood cell or lymphocyte. A lymph node biopsy is done to diagnose lymphoma. Then, additional tests will be done to determine the stage (extent) of the lymphoma, including blood tests, bone marrow biopsies, and imaging tests such as CT scan or a positron emission tomography scan. Imaging tests show if the lymphoma has spread to other parts of the body, such as the spleen and lungs. The doctor will then make treatment decisions, which will consider your age, general health, and the stage and type of lymphoma. It is one of the most curable types of cancer. Drug therapies and improved treatments for different forms of lymphoma continue to evolve as researchers better understand how these cancers progress. Standard treatment for advanced asymptomatic follicular lymphoma, mantle cell lymphoma, and early, unfavorable Hodgkin's disease (refers to patients with clinical stage I or II disease and one or more risk factors). The efficacy of an innovative investigational drug that has the potential to become a new treatment option for patients with relapsed or refractory disease for whom there are currently no treatment options available.

Epidemiology of lymphobia disease

The standard of care for patients with asymptomatic advanced follicular lymphoma has been a vigilant approach in which chemotherapy is delayed until the cancer progresses, as this type of cancer often grows slowly before becoming symptomatic. It based on research showing that treating these asymptomatic patients with chemotherapy immediately after diagnosis has no overall survival benefit. Patients avoiding the debilitating side effects of chemotherapy at a time when they feel comfortable. Follicular lymphoma progresses when a type of white blood cell called a "B" cell becomes cancerous. Rituximab is a monoclonal antibody that selectively breaks down cancer B cells and has a more beneficial side effect than chemotherapy. It determines whether treating follicular lymphoma patients with the drug immediately after diagnosis would further delay the time before chemotherapy is needed. Relative risks of lymphoma were classified for three different levels of total disease activity, low, medium, or high, depending on the duration of the disease and the number of swollen and tender joints. Lymphoma was also compared to treatments in broad categories like any DMARDs, any NSAIDs, aspirin, oral steroids, injected steroids, and cytotoxic drugs. In addition, the lymphoma samples were reclassified and analyzed for the Epstein Barr virus (EBV). The risk of lymphoma was particularly low in patients who received frequent corticosteroid injections into swollen joints, and suggesting that strong anti-inflammatory drugs may play a role in protecting against lymphoma. Of all the medical treatments examined, it may increase risk of Azathioprine-only (AZA)-associated lymphoma, which is not considered a traditional DMARD for RA and is rarely used in current treatment. Lymphoma is a type of cancer that affects the blood and begins in the lymph nodes. B cells are the immune cells of the human body that are responsible for producing antibodies to fight infection and ensure long-term

immunity. The B-cell includes both Hodgkin's lymphomas and most non-Hodgkin's lymphomas. The main theory used to explain how lymphoma developed was the malfunction of a mechanism (somatic hyper mutation) used by B cells to modify the genes that code for antibodies. This mechanism is necessary to produce highly specific antibodies, but it also inadvertently changes other genes, leading to lymphoma. Most leukemia's and lymphomas are sporadic, and the specific etiology remains unclear. It malignancies often develop in association with genetic abnormalities, immunosuppression, and exposure to risk factors such as ionizing radiation, cancer-causing chemicals, and oncogenic viruses. The prognosis varies by subtype, with lower chances of survival for adult acute leukemia and more favorable outcomes for Hodgkin lymphoma.

Conclusion

The prevention efforts against these malignancies, there is a great need to ensure fair access to diagnostic and treatment services worldwide. About half of the blood cancers that occur each year are lymphomas or cancers of the lymphatic system. This lymph node system in the neck, armpits, mole, chest, and abdomen removes excess fluid from your body and produces immune cells. Abnormal lymphocytes, a type of white blood cell that fights infection, turn into lymphoma cells that multiply and accumulate in the lymph nodes. Over time, these cancer cells affect your immune system.

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Role of Stem Cell Therapies in Alzheimer's Disease

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Description

Stem cell therapy is an exclusive method for treating Alzheimer's disease. It involves the systemic manner of Mesenchyme stem cells into the body. When it was taken in large quantities, these brain stem cells can cause inflammation inside the body and heal it. Stem cells can grow into brain cells, which cure and restore the brain damage diseases caused by neurological conditions, such as dementia. Alzheimer's disease, is an advanced neurodegenerative disease, it is the most common form of dementia. So far, there is no permanent and effective cure for Alzheimer's diseases. In recent studies, stem cell therapy is one of the major treatments using for Alzheimer's disease patients. There are many numbers of stem cell therapies used for the treatment of Alzheimer's disease, brain-derived Neural Stem Cells (NSCs), Induced Pluripotent Stem Cells (IPSCs) and Embryonic Stem Cells (ESCs). Stem cell therapy is also known as recovering medicine, it helps in the repair of diseased, injured or dysfunctional tissue using stem cells and their derivatives. It is the next stage in organ transplantation and using cells instead of donor organs. Stem cells produce new cells for the body as it generates, and replace damaged or lost cells. They have two exclusive properties that help them to generate new cells. They can continuously divide and proliferate to create new cells. As they divide, they transform into other specialized cells, and replacing damaged cells.

Therapies in alzheimer's disease

There are different types of stem cells that can be used for various purposes Induced Pluripotent Stem Cells (IPSCs). Non-embryonic stem cells which are also known as adult stem cells, embryonic stem cells. Embryonic stem cells come from human embryos that are three to five days old, Cord blood stem cells and amniotic fluid stem cells. There are mainly two kinds of stem cells which mainly transplants allogeneic and autologous. In the process of allogeneic transplant, the stem cells are taken from a different person. In the process of autologous transplant stem cells are collected from the patient's blood and then again reintroduced after treatment to get free of the tumorous cells. Stem cells are mainly used for blood disease treatments, cell deficiency therapy, brain disease treatment, cardiovascular disease treatment, tissue regeneration. Tissue rejuvenation is probably the most significant use of stem cells. The classifications of stem cells based on cell type are neural stem cells which are responsible for the production of all nerve cell types during development. They are self- renovating pluripotent cells that produce astrocytes, oligodendrocytes, or neurons. Mesenchymal stem cells which have three main roles in Alzheimer's Disease treatment there are reduction of A β plaque burden through internalization and A β degradation of endosomal-lysosomal pathway oligomers, immune regulation, neurotrophic or regenerative potential. Embryonic stem cells there can differentiate into NPCs in vitro, hence serving as therapeutics when transplanted into animal models of Alzheimer's disease. Induced pluripotent stem cells which helps to regulate endogenous neurogenesis, replace lost neurons, or reverse pathological changes through Induced Pluripotent Stem Cells (IPSCs) have demonstrated early effectiveness. Hence now a days Stem cells is mainly using for the treatment of Alzheimer's disease.

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