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Treatment of Brain Tumors and Age-Dependent Neurodegenerative Diseases Using Nano Medicine: Advantages and Limits

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Abstract: The blood-brain barrier (BBB), cancers' high invasiveness and variability, the lack of access of tissues for early diagnosis and efficient surgery, and anti-cancer medication resistance all provide challenges to the treatment of central nervous system (CNS) malignancies, especially brain tumours. These challenges can be overcome by developing novel and effective therapeutic strategies, such as immunotherapy, gene therapy and targeted drug delivery systems. Additionally, better diagnostic tools and improved surgery techniques need to be developed to increase the effectiveness of treating CNS malignancies. Nanomedicine-based treatments have the potential to sustain bio-distribution and accumulation of therapeutic agents at the appropriate target location while facilitating drug penetration across the BBB. This would enable more precise delivery of nanomedicines to the tumor site, thus reducing the side effects of chemotherapy and radiation therapy. In addition, nanomedicines are more efficient in crossing the BBB, which makes them an ideal option for CNS malignancy treatment. For an expanding class of anti-cancer drugs, the use of lipid-, polymer-, or metal-based nanocarriers provides a cutting-edge drug delivery strategy. The nanocarrier surface is made to have an active ligand-binding structure that may be altered to target certain cancer cells, such as an antibody or a cancer cell marker. Nanomedicines are used to treat cancer by targeting specific cancer cells with drug-loaded nanocarriers. These nanocarriers have an active surface that binds to a specific target, making it possible to deliver drugs to the right place in the body.Primary CNS lymphomas, neuroblastoma, medulloblastoma, glioblastoma, and ependymoma were recently targeted by easily absorbed nanocarriers.

Keywords: nanomedicine, tumors, central nervous system, blood-brain barrier and nanocarriers

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1. INTRODUCTION

Among the most prevalent, harmful, and challenging illnesses to treat are brain disorders such as brain cancer and deficiencies in the central nervous system's (CNS) ability to operate. Brain disorders can cause a wide range of physical and mental symptoms, from memory loss to motor skill difficulties, and can be incredibly difficult to diagnose and treat due to the complexity of the brain and its many interconnected pathways. The blood-brain barrier, a tightly controlled interface in the body that regulates the passage of chemicals from the blood to the brain, and the fact that the brain is a relatively fragile organ isolated from systemic circulation are the primary causes of this. As a result, it is essential to ensure that any treatments for neurological diseases and disorders are carefully formulated and administered to minimize potential risk. It has been demonstrated that the BBB, a significant physiological barrier, prevents 98% of therapeutic medicines from entering the brain. Neurological diseases and disorders, such as Alzheimer's and Parkinson's, can significantly impact a person's quality of life[1]. These diseases and disorders can cause a wide range of physical and mental impairments, including memory loss, confusion, difficulty speaking, and difficulty with movement. In addition to the BBB, the variability of neurodiseases' tumours and their complex nature, the lack of accessible early detection and efficient treatment of brain diseases is also complicated by surgical intervention. However, there are also treatments available for brain disorders that can be helpful in managing symptoms and improving quality of life. These treatments include medication, therapy, and lifestyle changes. The following advantages are connected to this field's prospects: 1) targeted administration of drugs with the intended pharmacological effects; 2) Improvement pharmacokinetics (increased solubility and bioavailability, enhanced penetration through histo-hematic barriers into organs and tissues, as well as through cell membranes); 3) regulated absorption of the supplied material into the intended organ (brain, nervous tissue); 4) reduced first-pass metabolism-related adverse effects; and 5) development of replacement pharmaceuticals [2-5] The FDA-approved, clinically tested, and this study critically analysed experimentally developed nanotherapeutic medicines for the treatment of brain diseases such brain cancer and neurodegenerative disorders. The study looked at the efficacy of these drugs and their potential to diagnose, treat and prevent brain illnesses, including their ability to cross the blood-brain barrier, their pharmacokinetics and pharmacodynamics, their safety and stability, and their efficacy in animal models. These nanotherapeutic drugs have the potential to revolutionize the treatment of many brain illnesses, and further studies are needed to fully assess their effectiveness and safety. We highlighted the potential applications of nanomedicine for both clinical workers and scientists in the fields of medicinal chemistry and pharmacology in order to highlight the originality of this review. Nanotherapeutics have already been used in the fields of medicinal chemistry to develop new and improved drugs for a variety of diseases[6]. Nanoparticles can be used in drug delivery systems to increase the stability of drugs, and to increase their bioavailability. Nanoparticles can also be used to improve the solubility and bioavailability of drugs, and to reduce their toxicity. Figure 01 represents pictorial representation of Brain disorder.

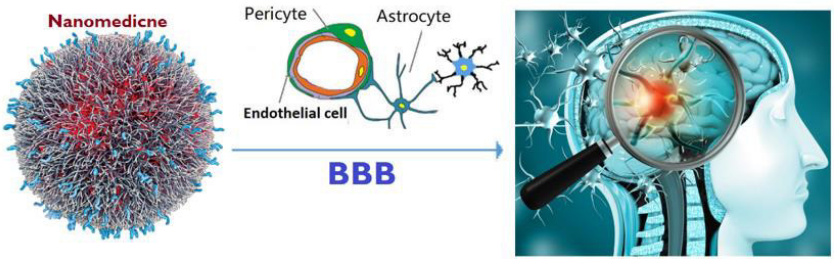

Fig 1: Blood-brain barrier of Brain disorder[7,8]

2. SHARED FEATURES OF THERAPEUTIC SYSTEMS THAT UTILIZE NANOPARTICLES

Nanotechnology, which is utilized extensively in medicine to treat most illnesses, including oncological and neurological disorders, refers to the design of potential pharmaceutical agents with the desired features in the size range of 1-1000 nm[9]. This size range is particularly advantageous in drug delivery, as these particles can easily penetrate cells and target specific sites, while reducing the risk of adverse side effects. Furthermore, nanotechnology has enabled the production of more efficient drugs, with increased potency and improved bioavailability. The tiny size and great target specificity of nanomedicine provide new, powerful approaches to the creation of novel drugs. The nanoscale particles can easily reach their target by bypassing the body's natural barriers, such as the blood-brain barrier. This means that the drugs can be delivered with greater precision and accuracy, reducing the amount of drug needed for treatment, and thus decreasing the risk of side effects. The make-up of the nanoparticles (NPs) utilized in the detection and therapy of brain disorders. Furthermore, the properties of the NPs, such as size, surface charge, and surface coating, need to be carefully tailored to ensure that they reach their desired target effectively and safely. Nanoparticles are typically used for drug delivery systems in the detection and therapy of brain disorders[10]. They offer the advantage of being able to deliver drugs with greater precision and accuracy, reducing the amount of drug needed for treatment, and thus decreasing the risk of side effects.

3. A FUNCTION FOR THE BLOOD BRAIN BARRIER (BBB) IN MEDICATION DELIVERY

The BBB, which restricts the transit of biologically active substances and medications, must be penetrated in order for pharmaceuticals to be developed for the treatment of brain illnesses. The blood-brain barrier (BBB) acts as a protective filter for the brain, preventing many substances from entering the central nervous system. This makes it difficult for drugs to enter the brain, and thus it is necessary to ensure that drugs are designed to be able to penetrate the BBB in order to be effective. To ensure that drugs effectively reach the brain, they

must be designed to penetrate the BBB, as it blocks many substances from entering the central nervous system. The BBB strictly regulates the entrance of substances into the brain which complicates the process of drug delivery. Drug delivery methods for the brain have been discussed on several occasions. The blood-brain barrier (BBB) is a protective membrane which surrounds the brain and helps to keep it safe from external substances and pathogens. Endothelial cells are from the blood vessel wall (BBB[11]. Endothelial cells tightly regulate the passage of substances in and out of the brain, making it difficult for drugs to pass through them. The probability of a drug passing through the blood-brain barrier is estimated to be less than 10%. The blood-brain barrier can be thought of as a protective wall, like a castle wall guarding the brain from harmful substances, with the endothelial cells being the watchful soldiers at the gates. They are highly selective, only allowing in substances that are deemed safe and keeping out those that are not.

4. BRAIN CANCER THERAPY WITH CLINICAL AND EXPERIMENTAL NANOMEDICINES

A broad range of illnesses that can affect any region of the body are collectively referred to as cancer. The word "cancer" is utilized to signify any tumour or cancerous development brought on by an abnormal and uncontrolled cell division that has the potential to distributed to several bodily regions. All oncological illnesses are characterised by unchecked cell growth and proliferation, this leads to the formation of isolated cell groupings known as tumours or malignant neoplasms. Tumors created by cancer may progress to many bodily regions and design metastases, making it a particularly concerning and dangerous illness. A number in those cells might be discovered in the lymph or blood move and disperse to other organs and bodily tissues. Tumors can invade and damage adjacent tissues and organs, in addition spread across the body to other areas the bloodstream or lymphatic system. It is known as metastasis, and that's the primary factor in cancer death[12]. Metastasis occurs when the initial tumor's cells dissociate, travelling via means of blood or lymph to other bodily regions. It is the essential reason why cancer is so difficult to treat, as the cells are capable grow cancers new in different components of the organ. To make matters worse, metastasis can happen quickly and unexpectedly, making it even harder to combat and cure cancer.

5. GLIOBLASTOMA

Glioblastoma location is due to the fact that astrocytomas are typically found in the white matter of the brain, which is located near the junction of the frontal, temporal, and parietal lobes. This makes it difficult to surgically remove the tumor without damaging surrounding tissues. Therefore, these tumors often require a multidisciplinary approach that combines surgery, radiation, and chemotherapy to ensure maximum efficacy while limiting the risk of tissue damage. This is because the blood vessels as in region pass through a narrow corridor which allows for easy access to the tumor. Additionally, the dense and intricate network of cells in this area make it difficult for the tumor to spread. Consequently, this makes the glioblastoma particularly challenging to treat, as it is deeply rooted within the brain and is surrounded by delicate and important structures. The glioblastoma is most commonly found in the cerebrum, which is the largest major section of the brain. Many hemorrhages, necrosis, and tiny blood arteries with a small membrane prominent endothelial growth are features of this tumor. Many haemorrhages, necrosis, and tiny blood arteries with a small membrane prominent endothelial growth are features of this tumor, making it particularly challenging to treat as these blood vessels are difficult to access and penetrate[13]. For example, the locations with relation to the brain tumour can make surgical removal more difficult, as certain regions are not easily accessible .Temozolomide (TMZ) is the gold typical initial line and the sole one first-line medication authorised in order to treat glioblastoma (grade IV glioma) (3-methyl-4-oxoimidazo) TMZ works by inhibiting DNA replication and repair in tumor cells, making them more susceptible to radiation and chemotherapy treatments[14]. In certain cases, the tumor may be too large or too deeply situated in the brain for surgery to be a viable option, and TMZ Perhaps the the only treatment option available.

6. EPENDYMOMA

Ependymomas usually cause symptoms such as headaches, seizures, blurred vision, and neurological deficits. It can also cause hydrocephalus, which is an increased pressure in the brain due to a build-up of cerebrospinal fluid. The spinal cord and other regions of the central nervous system might get infected by the tumour, and may cause symptoms such as headaches, seizures, and paralysis. It can also lead to hydrocephalus and other neurological complications. This is due to its ability to deliver high doses of radiation to the tumor while minimizing the radiation dose to healthy surrounding tissue, allowing for more effective targeting of the tumor. Additionally, radiation therapy has been shown to possess high rate of success in treating ependymoma. Radiation therapy is used because it can target the tumor cells more precisely than traditional treatments, reducing the risk of damaging healthy cells. In addition, fewer side effects than surgery or chemotherapy, reducing the risk of further complications. Additionally, surgery is often used to reduce the size of the tumor and improve symptoms, and chemotherapy is occasionally used for cases that are more aggressive or not responding to radiation[15]. To eradicate cancer cells, radiation treatment is employed, reduce the size of the tumor, and prevent recurrence of the tumor after surgery. It is also utilized to alleviate pain such as headaches, seizures, and paralysis caused by the tumor. However, despite recent advancements in radiation therapy technology, the percentage of people who survive with such conditions is still low, largely because unfavourable repercussions have started to appear. For instance, radiation therapy can increase the risk of a secondary cancer or other long-term side effects such as skin damage, infertility, and organ damage. Therefore, it is important to closely monitor the treatment process and seek medical advice to reduce the potential risks associated with radiation therapy and to improve patient outcomes.

7. NEUROBLASTOMA

Neuroblastoma(NB) is an aggressive cancer type, with a tendency to quickly spread to distant sites, including the bone marrow and lymph nodes. Although NB can occur in any age group, most frequently in young children, with the majority of cases occurring in children under ten years of age. Neuroblastoma commonly affects babies and young children, and is the most common solid tumor found outside the brain in infants[16]. A malignancy that targets the peripheral nerve system is called neuroblastoma and is increasingly typical in infants, as their still-developing bodies are more vulnerable. It

can happen in any bodily component, but most commonly affects the abdomen, chest, or neck. According to the current state of the tumour, radiation therapy, immunotherapy, chemotherapy and surgery are some of the NB therapies that may be employed. In order to combat NB, healthcare professionals must develop a successful therapy plan, tailored to the individual patient and the severity of their disease. Neuroblastoma (NB) is a cancerous tumor that develops from immature nerve cells. Although medical advances in paediatric oncology, particularly in regard to treatment of neuroblastoma, the side effects of current treatment that adversely affect kids' lifestyle quality necessitate fresh methods used in the area. To provide the greatest care outcomes for patients with NB, healthcare professionals must actively seek and utilize the latest research and advancing technologies in paediatric oncology, aiming to create a personalized and comprehensive treatment plan that minimizes long-term side effects. Treatment plans should be based on the patient's age, cancer stage, tumor biology and overall health, and account for any potential long-term side effects. It should also take into consideration the psychological effects on the patient and their family, and provide the necessary support to improve the patient's quality of life. Psychological effects can include fear, anxiety, depression, and feelings of helplessness. These can have a tremendous impact on the patient's physical and emotional well-being, and can lead to decreased self-esteem and a feeling of isolation.

8. MEDULLOBLASTOMA

The most frequent malignant embryonic brain tumor is medulloblastoma (MB). MB is a type of tumor that develops in the cerebellum, which is the part of the brain responsible for movement and coordination. It is among the most prevalent kind of malignant brain tumour in kids and has the possibility of expanding to certain other body regions. Treatment for MB includes surgery to eradicate the tumor, radiation therapy, and chemotherapy[17]. In some cases, a combination of these treatments is necessary to provide the best outcome. Based on the MB categorization on two factors: (1) histological characteristics that distinguish between desmoplastic, classical, and large-cell medulloblastoma; and (2) molecular profiling, which divides MB into four subgroups: WNT (Wingless), Sonic hedgehog (SHH), group 3, and group 4, each of which has a significantly different clinical course and prognosis. The clinical course of medulloblastoma (MB) is determined by its classification, which is founded on its histological characteristics and molecular profiling. The MB classification helps to identify the best treatment option and prognosis for a patient, as each subgroup of MB has a significantly various clinical outcomes and prognosis.

9. PRIMARY CNS LYMPHOMA

Primary lymphomas are a subtype of malignant neoplasms with distinctive features, an aggressive history, and ineffective therapy outcomes. Despite advances in treatment, primary lymphomas are still associated with poor prognoses[18]. Primary lymphomas are often difficult to diagnose due to the lack of definitive symptoms and the absence of early warning signs. Additionally, they are often resistant to traditional treatments such as chemotherapy and radiation, making them hard to handle. Chemotherapy is often ineffective in treating primary lymphomas typically greater drug's inability to penetrate the tumor cells. Additionally, the drugs used in chemotherapy can cause serious side effects, such as nausea, hair loss, and fatigue, which can further complicate the patient's treatment. They make approximately 2.4–3% of all brain tumors and 4-6% of extranodal lymphomas. The forms are often found in the brain's paraventricular white matter (60%) and corpus callosum (5-18%), respectively. Most primary lymphomas in the brain are found in the cerebrum, while others are found in the spinal cord, lymph nodes, and other parts of the body. Between 25 and 50 percent of tumors have several localizations. Primary lymphomas of the brain are often difficult to diagnose and can cause severe neurological symptoms. As such, early diagnosis and treatment are key for successful outcomes. However, some primary lymphomas of the brain can be benign and not cause any neurological symptoms. In these cases, treatment may not be necessary. In the treatment of neurodegenerative illnesses, clinical and experimental medicine is used. These diseases affect millions of people worldwide and can cause severe disability, decreased quality of life, and even death. They are also some of the costliest diseases to diagnose and treat, with many treatments still in the experimental stages. These illnesses can be especially difficult to deal with due to their highly progressive nature, which means that they can cause a rapid deterioration in quality of life. Additionally, due to their complexity, these illnesses are often difficult to treat effectively. These illnesses include neurological disorders such as Alzheimer's, Parkinson's, ALS, and multiple sclerosis. The UN reports that nearly 1 in 6 people in the world suffer from neurological disorders. These neurological disorders cause immense suffering and disability, making it paramount to invest in better treatments and cures. These neurological disorders can have devastating impacts on individuals, families, and communities. They can ruin lives, cause financial instability, and even lead to premature death. Investing in better treatments and cures is a necessary step to reducing suffering and disability, and helping those affected by these disorders to lead healthy, productive lives.

9.1. Alzheimer's disease

As a result, it is important to understand the underlying mechanisms of AD and to develop effective interventions in order to reduce its impact on our society. AD is characterized by a gradual decline in cognitive and behavioral functions. It is caused by a build-up of proteins in the brain called amyloid-beta and tau, which form plaques and tangles that damage the neurons and eventually lead to the death of brain cells. To further minimize the effects of AD, research is being conducted to find ways to reduce the production and accumulation of the amyloid-beta and tau proteins and protect neurons from damage. Hopefully, through sustained effort, we can find a way to effectively manage this devastating condition. This results in a decrease in the number of neurons, resulting in a decline in the communication between them, which affects memory, language, decision-making, and other cognitive functions. For example, a recent study has identified a gene that could be a potential target to reduce the production of the amyloid-beta protein, which is thought to be a major contributor to the development of Alzheimer's disease. The buildup of amyloid-beta and tau also affects the operation of the neurotransmitters, leading to further decline in cognitive and behavioral functions. Neurotransmitters are chemical messengers in the brain that help regulate communication between neurons. They are responsible for normal brain functioning, including learning, memory, and mood. When these neurotransmitters become disrupted due to the buildup of amyloid-beta and tau, it can lead to a decline in cognitive

and behavioral functions. There are several risk factors for dementia that have been discovered to far, but age is always considered to be the most significant one. Alzheimer's disease is a severe protein-conformational illness that is mostly brought on by the improper processing and polymerization of usually soluble proteins. Alzheimer's disease is the most common cause of dementia, and is characterized by the build-up of amyloid-beta and tau proteins in the brain, which disrupts the normal functioning of neurotransmitters.

9.2. Parkinson's disease

The frequency of Parkinson's disease (PD), the second most prevalent progressive neurodegenerative illness, has significantly increased during the previous three decades. This trend is expected to continue, making it imperative to research the underlying causes of PD and develop treatments that are more effective. This could be due to a combination of factors, such as increased life expectancy, improved diagnosis and awareness, and environmental exposures. More research is needed to identify the exact cause. Parkinson's disease is fundamentally a neurodegenerative condition characterised by the early loss of dopaminergic neurons in the substantia nigra pars compacta (SNpc). Yet the specific process of how this occurs is still unknown, suggesting that further studies are needed to gain a better understanding of the pathology of Parkinson's disease. To help bridge this gap in knowledge, researchers are now exploring the role of other neuronal networks in the pathology of Parkinson's disease, with the hope of uncovering the most effective approach to treating this neurodegenerative condition. Further research could reveal the precise mechanism of how Parkinson's disease occurs, leading to a greater understanding of how to effectively treat this complex neurodegenerative condition. The most common symptoms of Parkinson's disease include tremors, muscle stiffness, slowness of movement, and impaired balance and coordination.

9.3. Amyotrophic lateral sclerosis

Amyotrophic lateral sclerosis (ALS) is a common neurological disorder affecting individuals around the age of 65, with a survival rate of 2 to 5 years from the beginning of the disease. Due to the absence of a reliable remedy, it is essential to focus on preventive measures to reduce the risk of developing ALS. ALS affects the nerve cells in the brain and spinal cord, causing them to slowly break down over time. This leads to a progressive loss of muscle control, making it difficult for those affected to function normally and eventually completely paralyzing them. Apart from weakness, muscular atrophy, and stiffness, ALS in the cerebral cortex, brain stem, and spinal cord are upper and lower motor neurons. As the motor neurons break down, it affects the ability of the brain to send signals to the muscles, leading to a gradual loss of muscle function and eventually complete paralysis. Over time, ALS also affects a person's cognitive abilities, leading to difficulty with speaking, swallowing, and breathing. Muscular atrophy is a common symptom of ALS, and it is caused by the death of motor neurons, which control the muscle fibers. This causes the muscles to weaken and shrink, leading to a decrease in motor function and eventually muscle paralysis. 90–95% of ALS cases are sporadic, while 5–10% of all patients have the familial type of the disease. The death of motor neurons leads to a decrease in the amount of electrical signals being sent to the muscles, which causes them to weaken and eventually stop working. This lack of electrical signals leads to the muscles shrinking and wasting away over time, resulting in paralysis. In familial cases, there is a genetic mutation that is passed down from the parents which causes the motor neurons to die prematurely. For instance, familial ALS is caused by a genetic mutation that is passed down from parent to child, whereas sporadic ALS does not have a known cause.

9.4. Constraints of nanotechnology

Many laboratory and clinical investigations have established the value of NPs as a diagnostic and clinical tool. NPs are cost-effective, have a high degree of accuracy, and can provide rapid results. In addition, they can detect diseases in the early stages, allowing for earlier diagnosis and treatment. NPs have the potential to revolutionize healthcare, as they offer a level of precision and accuracy that is unparalleled. The capacity to tailor the structure of NPs to a particular job, ailment, and organ allows for the resolution of many issues that emerge with conventional medications, such as solubility and stability issues. Nanoparticles are incredibly tiny and can penetrate cells more easily than conventional drugs, allowing them to target specific areas of the body that need treatment[19]. This improved accuracy and precision means that the right amount of medication can be delivered in the right place at the right time, resulting in fewer side effects and better outcomes. As a result, nanoparticles have the potential to revolutionize the medical treatment of diseases and conditions. By combining macromolecules, medications, and imaging agents, this method makes it feasible to create useful NPs that aid in both drug administration and diagnostics. Nanoparticles can be used to deliver medications to specific areas of the body, allowing for more accurate and precise application of drugs than traditional methods[20] . Some of the most common uses for nanoparticles in medicine include imaging (luminescent nanoprobes for optical imaging and magnetic nanoparticles for MRI), targeted drug delivery, and diagnostics.

10. CONCLUSION

It is crucial to look for innovative therapies and radical fixes for the issues brought on by different neurological ailments, such as malignant brain pathologies and neurodegenerative disorders. Neurological ailments can cause severe physical and cognitive impairments, including difficulty with movement, memory loss, and changes in behavior. Such ailments can be debilitating and can severely impact a person's quality of life. Many CNS problems cannot be effectively treated with currently available medications. As a result, it is important to create new treatments that can help alleviate the suffering of those living with neurological disorders. Significant factors include the BBB, the complex character of neurological and oncological illnesses, the inaccessibility of Brain tissues for early detection, and successful surgical intervention. To tackle these issues and drive advancements in neurology and oncology, it is essential to develop innovative treatments and explore novel methods of diagnosis and surgery.

11. AUTHOR CONTRIBUTION STATEMENT

All authors have reviewed and approved the manuscript before submission.

12. CONFLICT OF INTEREST

Conflict of interest declared none.

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