Immunotherapy and brain cancer

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Introduction

Immunotherapy is a class of biological treatment, which uses the patient's own immune system to detect and destroy the cancer cells. Immunotherapy uses substances either natural (within the body) or synthetic (made in laboratory) to stimulate or subdue body's own immune system response to fight cancer. Brain is difficult to reach through medication as it is shielded by membrane called Blood Brain Barrier (BBB) from any harmful substances. The BBB is extremely selective semipermeable membrane border of endothelial cells. It prevents any harmful substances from entering into brain through blood stream. It keeps bacteria and other infectious substances from reaching brain, which unfortunately includes helpful cancer treating drugs. Cancer cells have a wicked way of tricking the immune system into thinking they are self and no harm to the body. As the tumour in brain grows in size and the pressure they impose on brain, interfering with healthy normal brain function, causes highly painful and life changing symptoms in patients suffering from brain cancer. Brain and nervous system cancers are two primary cancers that effects in both adults and children.

Types of brain cancers

The types of brain cancer are categorised by the type of cell they originate from. They include;

Astrocytoma: Cancer begins in astrocytes, these are star shaped cells called glial cells or neuroglial cells found in central and peripheral nervous systems.

Glioma: Cancer begins in glial cells present around nerve cells.

Meningioma: Cancer originates in membranes covering brain and spinal cord called meninges.

Medulloblastoma: Cancer begins in posterior fossa (base of skull region).

Neuroblastoma: Cancer forms in neuroblasts in adrenal glands.

Immunotherapy for brain cancer

Currently, FDA has approved three immunotherapy options in treating brain and nervous system cancers.

Checkpoint Inhibitors: Immune checkpoints are the molecules that surround the surface of activated T-cells of the immune systems. The primary purpose of the immune checkpoints is to suppress uncontrolled inflammatory responses. Pembrolizumab (keytruda) is a checkpoint inhibitor targeting PD-1/ PD-L1 pathway. This drug has been approved in treating advanced brain cancers. Pembrolizumab is effectively tolerated in high grade glioma patients, with low response rate and improved progression-free survival even when used in combination with bevacizumab. Durvalumab is a checkpoint inhibitor targeting PD-1/ PD-L1 pathway.

Targeted antibodies: Bevacizumab (Avastin) is a monoclonal antibody (mAB) targeting VEGF/VEGFR pathway and inhibits tumour blood vessels growth. This has been approved in treatment of recurrent glioblastoma. Dinutuximab (Unituxin) is a monoclonal antibody (mAB) targeting VEGF/VEGFR pathway. It has been approved in treatment of paediatric neuroblastoma.

Vaccine: The goal of therapeutic vaccination against brain tumours is to boost patient antitumor immunity by allowing T-cells to recognise tumour associated antigens. This is believed to trigger an immunological response, which would finally result in cancer cells being eradicated. Pembrolizumab (Keytruda®) is a checkpoint inhibitor targeting the PD-1/PD-L1 pathway. It has been approved in treatment with advanced pancreatic.

Combination therapy: In patients with brain malignancies, immunotherapeutic methods have failed to provide effective clinical responses. This is due to brain tumours' various immune evasion mechanisms as well as tumour heterogeneity. When used in combination with other drugs or therapies (radiotherapy or chemotherapy), immune checkpoint inhibitors helps patients with brain

cancer with sporadic improvements in overall survival.

Immunotherapeutic drugs, by itself or in combination with current standard-of-care, can provide a much needed improvement in patient survival while delaying disease progression

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