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Neuro and Radiant oncology and anesthesia considerations

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Abstract

Radiation therapy is a cornerstone treatment for various types of tumors, including those in the nervous system. It uses high-energy rays or particles to destroy or damage cancer cells while attempting to spare surrounding healthy tissues. Depending on the tumor's location and type, radiation therapy can be broadly applied to larger areas like the brain or precisely targeted at smaller, well-defined tumors using techniques such as stereotactic radiosurgery. Advances in medical technology have made radiation therapy more precise, but some risk to the nervous system remains unavoidable. Head and neck cancer (HNC) is the sixth most common human malignancy with a global incidence of 650,000 cases per year. Radiotherapy (RT) is commonly used as an effective therapy to treat tumours as a definitive or adjuvant treatment. Despite the substantial advances in RT contouring and dosage delivery, patients suffer from various radiation-induced complications. Radiation therapy for nervous system tumors can lead to neurological damage, manifesting as acute, early-delayed, and late-delayed symptoms, with varying degrees of severity and impact on quality of life. The degree of neurological damage depends on factors such as the total radiation dose, the duration of treatment, the dose per session, and individual patient characteristics, including age, genetic predisposition, and overall health. For instance, children are more vulnerable to long-term effects due to the developing nature of their nervous systems, while older adults may face increased risks due to preexisting health conditions. Early-delayed effects typically appear weeks to a few months after the initiation of radiation therapy. These symptoms are generally mild and temporary, including: fatigue; ersisting tiredness, even after rest, can impact daily activities, headaches; recurring headaches may signal ongoing swelling or irritation in the brain, nausea; often linked to the continued healing process or residual swelling. In children undergoing whole-brain radiation, early-delayed symptoms can be more pronounced but often subside over time. Corticosteroids can help manage these symptoms, and physical therapy may be introduced to address any emerging motor coordination issues. Late-delayed effects are the most concerning as they occur months or even years after treatment, potentially causing permanent neurological damage. These effects may include: cognitive decline; issues with memory, attention, and problem-solving abilities, personality changes; mood swings, depression, or reduced emotional resilience, motor coordination problems; difficulty with balance or fine motor tasks, spinal cord damage; radiation near the spine may cause late-delayed myelopathy, resulting in sensory loss, muscle weakness, and Lhermitte sign (a shock-like sensation along the spine when bending the neck forward). Children treated for medulloblastoma or other brain tumors are particularly at risk for these effects due to their higher sensitivity to radiation. Long-term cognitive rehabilitation and regular neurological assessments are essential for managing these complications. Neurologic complications can be seen throughout the course of cancer diagnosis and treatment; some toxicities may not develop for years or even decades after completion of treatment, making diagnosis challenging. However, early recognition is critical as modification of therapeutic regimens can diminish long-term consequences of nervous system injury and improve a patient's quality of life. Neoadjuvant therapy consisting of either chemotherapy, radiotherapy or immunotherapy is associated with toxic effects on different organ systems. Before surgery, a comprehensive neurological examination should be performed and documented in patients suspected of having neurotoxicity. In patients with peripheral neuropathy, attention should be paid to autonomic dysregulation, as this might lead to orthostatic hypotension. The use of regional anaesthesia is not contraindicated, but pre-existing neurological

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abnormalities should be documented. Because there is a wide variety of ICIs, the anaesthetist should pay attention to specific agents and toxicities.

Keywords: Radiation Therapy; Oncology; Chemotherapy; Neoadjuvant Therapy; Toxic Effects

1. Introduction

Radiation treatment is a form of care for primary brain tumors (benign and malignant) as well as cancer that has metastasized to the brain. Radiation can follow brain surgery, or it can be the primary course of treatment if surgery is not possible. Radiation treatment uses high-energy beams to target and destroy brain tumor cells. It's a painless, non-invasive procedure that targets the DNA of tumor cells, preventing them from growing or spreading. The goal is to shrink the tumor or stop it from growing while protecting as much healthy brain tissue as possible and reducing the long-term effects of treatment. Radiation therapy choices depend on the patient, the type of tumor, the tumor's location, and the size of the tumor. Most patients receive either traditional radiation therapy, which uses X-ray beams (photons) that pass through the tumor and continue beyond it, or proton therapy, which uses proton particles that release their energy directly at the tumor and then stop. Some patients may undergo stereotactic radiosurgery, which is not actual surgery – no incision is needed. However, the treatment delivers targeted, high-dose radiation that acts like the scalpel of a surgeon in the way it destroys the tumor. Chemotherapeutic agents may have different effects on the immune system ranging from stimulatory to immunosuppressive effects. They affect both the innate and adaptive immune system. The innate immune system might be affected through myelosuppression leading to chemotherapy-induced neutropenia (CIN). If neutropenia is severe, the risks of systemic infections and sepsis increase. The incidence of neutropenia with fever (temperature >38.5°C) is around 50% for solid tumours and over 80% for haematological malignancies. The duration of neutropenia varies from a few days to weeks and depends on several factors, including the severity of neutropenia. In the management of CIN, multiple (irradiated) transfusions, myeloid growth factors (granulocyte colony-stimulating factor) to boost neutrophil production and antibiotics may be necessary.1 Pancytopenia, characterised by a reduction in the number of erythrocytes, leucocytes and platelets, may have serious consequences for perioperative care. During the perioperative period, oxygen-carrying capacity is decreased, whilst the risk of haemorrhage and opportunistic infection is increased. Preoperatively, haemoglobin concentration, thrombocyte counts and peripheral blood differentiation should be performed to exclude pancytopenia. In patients with (severe) CIN or pancytopenia, postponement of surgery should be considered until blood values have been recovered sufficiently. Irradiation affects the immune system, which can be observed both inside and outside the tumour. DNA damage-induced cell apoptosis releases alarmins, which activate the innate and adaptive immune system that results in a pro-inflammatory response. This response activates T-cells to induce a systemic antitumour inflammatory response, the abscopal effect. It is unclear whether this proinflammatory environment with activated cytokines, chemokines and other damage-associated molecular patterns (DAMPs) has consequences for the perioperative period. Conversely, irradiation also leads to immunosuppression by inactivating natural killer cells and DCs [1-28].

2. Neuro and Radiation oncology

Radiation therapy is widely used for benign and malignant brain tumours as it is effective and well tolerated. However, damage to the surrounding healthy nervous system tissue leads to a variety of complications both in the short term and long term, ranging from mild and self-limiting to irreversible and fatal. Radiation neurotoxicity is due to a combination of early inflammation and oligodendroglial damage followed later by brain tissue necrosis, white matter damage, accelerated vascular disease and the development of secondary tumours. Irradiation of tissue causes different types of DNA damage through the production of highly reactive free radicals: single-strand break, double-strand break (the major lethal lesion), base damage and DNA crosslinks. A range of DNA damage repair mechanisms operate to help maintain genomic stability. However, some lesions fail to repair adequately, and it is the accumulation of these lesions that may eventually lead to cell death, either by a programmed mechanism such as apoptosis or autophagy or via mitotic catastrophe at a future cell division. If the damage does not cause cell death, it may lead to a late manifestation of radiation such as the development of a secondary tumour, sometimes several years or decades after radiation exposure. Changes in the cellular microenvironment are also a major factor in the determination of cell fate and reduction in neurogenesis. The oxidative stress induced by radiation results in upregulation of proinflammatory pathways and an increase in number of activated microglia, which act as potent inhibitors of neurogenesis. Radiation can also trigger the death of endothelial cells, causing thrombus formation on the exposed matrix and small vessel occlusion. Furthermore, accelerated atherosclerosis and microangiopathy after radiation can lead to vascular insufficiency and infarction. The patient undergoes CT imaging while immobilised in the treatment position, usually via a thermoplastic head shell. Diagnostic MR images obtained previously are coregistered with the planning CT scan and used to delineate the treatment targets and relevant organs at risk. This is known as the gross target volume. Depending on the underlying

tumour histology, the radiotherapist will delineate an appropriate margin around the visible tumour to account for possible microscopic infiltration (Clinical Tumour Volume), and a small additional margin is then added to account for small movements that can occur even within the immobilisation device. This final volume is called the planning target volume. The radiotherapy dosimetrists and physicists create a treatment plan that delivers the prescribed dose homogenously to the planning target volume, while ensuring that the organs at risk do not receive more than the maximum allowed. The relationship between radiation dose and cell survival varies between tissues. Cells may be killed by a single lethal radiation hit or by a succession of sublethal hits. In addition to the overall radiosensitivity of certain tissues, there is also a difference in sensitivity to treatment fraction size. Acute radiation encephalopathy appears within 2 weeks of the start of brain radiation therapy and occasionally a few hours after the first fraction. The most common symptoms are drowsiness, headache, nausea and vomiting together with a worsening of pre-existing neurological deficits. About 6–12 weeks after the end of radiation therapy, patients may experience worsening of pre-existing neurological deficits, leading to the suspicion of tumour progression. Imaging is usually unhelpful as the MRI may show appearances of tumour progression that resolve over the next few months without any specific antitumour intervention. This phenomenon is known as 'pseudoprogression' and occurs in up to 30% of patients with glioblastoma treated with concomitant temozolomide and radiotherapy. An early-delayed subacute brainstem syndrome can occur 1–3 months after radiation therapy for pituitary or head and neck cancer, where the treatment fields overlap the brainstem. Clinical features include ataxia, dysarthria, diplopia and/or nystagmus as well as hearing loss. MR brain scan sometimes shows high signal change within the white matter of the brainstem and the cerebellar peduncles, which may enhance. This condition usually responds to corticosteroids within a few weeks; very rarely it results in coma and death. Radionecrosis is the most common late complication and was first described pathologically in 1948 in a series of patients, one of whom had a recurrent 'rodent ulcer of the scalp' and a normal brain. Radionecrosis most commonly follows focal radiation therapy for a brain metastasis but can also occur in patients who have had radiation therapy for extracranial and extra-axial tumours, in whom normal brain was included within the radiation field. It has been known for many years that radiotherapy can cause delayed cognitive impairment that varies from mild memory loss to a severe dementia. This complication develops more frequently in adult survivors of childhood brain tumours and in patients with low-grade gliomas where the tumour remains in remission for many years. Radiation-induced dementia is characterised by a 'subcortical dementia' pattern associated with diffuse white matter injury, usually starting within 2 years of treatment. Patients may present with a picture similar to normal pressure hydrocephalus and develop progressive memory loss, reduced attention, gait difficulties, urinary incontinence and fatigue. There may be emotional lability and apathy that is difficult to distinguish from depression. Antidepressants are frequently tried but do not improve cognitive function. Eventually, patients may develop akinetic mutism. MR scan of brain shows ventricular enlargement, diffuse confluent subcortical white matter change, with cortical and subcortical atrophy. Radiation can damage the intracranial vasculature leading to ischaemic stroke or haemorrhage. The carotid artery can become stenotic after cervical radiotherapy for lymphomas or head and neck cancers and occasionally can rupture a few weeks after radiation therapy causing death. However, late-delayed complications are more frequent and generally occur many years after treatment (median time about 20 years for extracranial arteries, 7 years for intracranial arteries). Radiation-induced vasculopathy is an accelerated form of atherosclerosis and often occurs in unusual locations. Moyamoya disease is a progressive occlusive cranial vasculopathy characterised by abnormal anastomoses and netlike blood vessels at the apices of the intracranial internal carotid arteries, the proximal anterior cerebral arteries and middle cerebral arteries.26 It results in decreased cerebral blood flow with an increased risk of stroke, transient ischaemic attacks and focal seizures. It often develops in patients who had cranial radiation therapy as young children, particularly those treated for optic chiasm glioma, a condition often associated with neurofibromatosis type 1, which is a risk factor for vasculopathy in itself. The strong association between neurofibromatosis type 1 and moyamoya is one of the reasons why radiation has been replaced with chemotherapy in younger children with optic pathway gliomas. A lower motor neurone syndrome resembling motor neurone disease has been described after radiation therapy to the distal spinal cord and cauda equina, mainly as treatment for testicular cancer and lymphoma. It presents with progressive proximal and/or distal symmetrical leg weakness associated with muscle fasciculation and wasting, but with normal sensation. The most clinically important cranial nerve implicated in delayed radiation toxicity is the optic nerve, which can be damaged many years after treatment for orbital, pituitary or suprasellar tumours. The optic nerve apparatus is regarded as a major organ at risk when planning treatment to nearby targets. Radiation therapy-induced optic neuropathy usually presents with subacute painless visual loss, progressing to monocular or binocular blindness with optic atrophy. Funduscopy of anterior lesions shows papilloedema and peripapillary haemorrhage, sometimes associated with radiation-induced retinal lesions, but is usually normal in posterior lesions. Initial symptoms include distal paraesthesiae and dysaesthesiae, muscle weakness and atrophy confined to specific myotomes, dermatomal sensory loss and early loss of reflexes. The lack of pain and presence of myokymia, when present, strongly suggest the diagnosis and help to differentiate from malignant infiltration of the plexus. There may also be visible skin complications such as radiation dermatitis, painful induration of the axillary region and/or lymphoedema. During the later stages, there is progressive motor loss that can vary from localised muscle weakness to an almost complete paralysis of the limb. There are several types of external beam radiation therapy (EBRT). The goal is to target the tumor and limit damage to nearby

healthy brain cells. To limit the harm, your healthcare provider may use special types of EBRT such as: 3-D conformal therapy (3D-CRT). For this treatment, a computer uses imaging scans to match the radiation beams to the shape of the tumor from different angles. These may be CT or MRI scans; Intensity modulated radiation therapy (IMRT). This is a lot like 3D-CRT. It lets the healthcare provider control the intensity or strength of the radiation beams pointed at different parts of the tumor; Conformal proton beam therapy. This is like IMRT. But it uses energy beams of charged particles called protons instead of X-rays. Protons stop more quickly than X-rays after hitting a target. This may lead to less damage to the tissues the beams pass through to reach the tumor; Stereotactic radiosurgery (SRS). This method can be used on small tumors. Though it's called surgery, there's no cutting. A high-energy dose of radiation is sent to the tumor from many angles. It may be given as a single dose. Or it may be given as several doses over a few days. There are 2 main types of SRS; Gamma knife radiation. This uses radiation beams called gamma rays. The rays are sent from a machine and focused at the tumor from hundreds of angles at the same time. Treatment is usually done in 1 session; Linear accelerator based. Instead of sending many beams at once, this machine moves around the head to send radiation to the tumor from different angles. Treatment is usually done in 1 to 5 sessions. Imaging tests will be done to see if the cancer has spread to other parts of your brain or spinal cord. If the cancer has spread, you may have radiation to your whole brain and spinal cord. Brachytherapy, for this treatment, the radiation is placed very close to or inside the tumor. This is done during surgery. The radiation the implants give off travels a very short distance. This helps limit the effect on nearby healthy tissue. Liquid Radiation After Brain Tumor Surgery, another radiation treatment is the GliaSite radiation therapy system (RTS) developed at Johns Hopkins. It delivers radiation from within the hole created by the surgical removal of a malignant brain tumor. GliaSite RTS is used for newly diagnosed, metastatic and recurrent brain tumors. A few days after surgical removal of the tumor, liquid radiation is delivered to the edges of the tumor hole through a catheter (a thin, hollow tube). The liquid radiation targets places in and around the tumor site where cancer cells may remain. It delivers a precise amount of radiation for a few days. Then the catheter is removed. Although the physical and biologic principles of radiation therapy have remained relatively unchanged, a technologic renaissance has led to continuous and ever-changing growth in the field of radiation oncology. As a result, medical devices, techniques, and indications have changed considerably during the past 20–30 years. The resultant improved ability to delineate normal from abnormal tissue has enabled radiation oncologists to achieve more precise targeting and helped to mitigate treatment-related complications. Nevertheless, posttreatment complications still occur and can pose a diagnostic challenge for radiologists. These complications can be divided into acute, early-delayed, and late-delayed complications on the basis of the time that they manifest after radiation therapy and include leukoencephalopathy, vascular complications, and secondary neoplasms. Radiation necrosis (RN) is a delayed complication of cranial radiotherapy and is characterized by progressive tissue injury, inflammation, and vascular compromise. Although advances in stereotactic radiosurgery and fractionated radiotherapy have improved tumor control, RN remains a significant source of morbidity that can mimic tumor recurrence both clinically and on imaging. Relevant mechanisms include endothelial injury, disruption of the blood–brain barrier, and glial-driven edema and necrosis. Advanced imaging techniques, including MR spectroscopy, diffusion-weighted imaging (DWI), and MR perfusion, can aid in distinguishing RN from recurrent tumor, though each has limitations. DWI demonstrates elevated apparent diffusion coefficient (ADC) values in RN due to necrosis, gliosis, and vessel dilation, in contrast to the dense cellularity of recurrent tumors, with an ADC ratio cutoff of >1.30 exhibiting 86.7% diagnostic accuracy in differentiating RN from tumor progression. Alternatively, PET imagining can be utilized to detect hypometabolic tissue, a hallmark characteristic of RN. In clinical practice, the main challenge is often distinguishing tumor progression from radiation necrosis and pseudoprogression, as all three can have similar imaging and clinical features after radiation therapy. This diagnostic uncertainty significantly affects treatment decisions, since strategies vary greatly between true progression and treatment-related effects. The clinical presentation of RN is variable and ranges from focal neurological deficits to generalized symptoms such as cognitive decline, headache, and seizures. Cardiotoxicity from chemotherapy occurs frequently and may evolve over a number of years. Although the pathophysiological mechanism is not fully understood, chemotherapeutic agents damage the myocytes in the heart, and as the heart has limited capacity to repair damage, these effects are prolonged, often presenting as left ventricular (LV) dysfunction, arrhythmias and heart failure. Chemotherapeutic agents and associated toxic effects on different organ systems AKI, acute kidney injury; ARDS, acute respiratory distress syndrome; DI, diabetes insipidus; LVEF, left ventricular ejection fraction; SIADH, syndrome of inappropriate antidiuretic hormone secretion. Pulmonary toxicity can be induced by chemotherapy agents, of which bleomycin toxicity is the most commonly known. Life-threatening interstitial pulmonary fibrosis may develop in 5–16% of patients given bleomycin in concentrations >400 IU m−2.8 Lung injury typically develops within 6 months after the start of bleomycin treatment and is associated with life-long risks of pulmonary toxicity, especially when high inspired oxygen concentrations are used.Chemotherapeutic agents are often eliminated by the kidneys, and this can therefore lead to chemotherapy-induced acute kidney injury (AKI). Acute kidney injury can present with proximal tubular injury characterised by proteinuria, phosphate wasting, Fanconi syndrome (hypophosphataemia, hypokalaemia, glycosuria and proteinuria) and magnesium wasting. Chemotherapeutic agents are mostly metabolised by the liver, and this is affected in patients with pre-existing liver disease. In most patients, hepatotoxicity is asymptomatic and is limited to increases in liver enzymes, but in severe cases, inflammatory hepatitis, cholestasis, steatosis and end-stage liver disease may occur.

Cancer immunotherapies manipulate the host's immune system to recognise and reactivate the antitumour immune response. Different types of immunotherapies include interferon; immune checkpoint inhibitors (ICIs); and, more recently, chimeric antigen receptor T-cells. These genetically manipulated T-lymphocytes express T-cell receptors that can recognise tumour-specific antigens. Immune-related adverse reactions of immunotherapies relevant to perioperative care include endocrine, cardiac and pulmonary toxicities. Toxic effects of immunotherapy on the cardiovascular system are rare, of which myocarditis is the most common (incidence of 1.14%). Clinical presentation ranges from non-specific (fatigue) to severe (dyspnoea and chest pain) symptoms. Finally, corticosteroids such as dexamethasone are traditionally first-line treatment due to their ability to reduce local edema and stabilize vascular permeability to reduce blood–brain barrier leakage. However, prolonged use is limited by adverse effects such as hypertension and immunosuppression, which can severely impact an individual's quality of life, particularly in patients who are undergoing adjuvant chemo- or immunotherapies. A short, tapered course of the lowest dose that provides symptomatic relief is recommended to avoid rebound edema. Bevacizumab, a monoclonal anti-VEGF antibody, targets the VEGF-mediated vascular permeability that underlies RN. Its convenient administration, long half-life, and minimal side effects make it a reliable treatment option. Notably, repeated courses of bevacizumab show high efficacy, with recurrent symptom relief in 90% of patients treated with subsequent cycles. Surgical Resection of necrotic tissue is typically recommended for patients with significant mass effect, increased intracranial pressure, refractory neurological symptoms, or progression despite conservative management. Rates of success are high, with over half (54%) of patients reducing or discontinuing steroids postoperatively and up to 83% of patients reporting clinical improvement. Laser interstitial thermal therapy (LITT) is a minimally invasive alternative that allows for targeted ablation of necrotic brain tissue while enabling concurrent stereotactic biopsy for accurate diagnosis. Early studies report neurological improvements and reduced seizure frequency in 50–70% of patients and improved functional status reported in 70–80% of cases, suggesting that LITT may eventually challenge current first-line medical therapies [29-80].

3. Anaesthesia considerations

The intersection of neuro-oncology, radiant oncology (radiation therapy), and anaesthesia involves a critical, multidisciplinary approach to managing patients with brain and spinal cord tumors. Anesthesiologists play a vital role not only during surgery but also in facilitating radiation procedures, managing unique risks, and potentially impacting long-term cancer outcomes. Pre-operative assessment for pre-existing neurological deficits or side effects from prior treatments like chemotherapy-induced neurotoxicity. Intra-operative monitoring and management of potential complications that can arise during brain surgery. Perioperative management, as surgical stress can influence immune response, a factor that some studies suggest might affect cancer recurrence. Anesthetic choice: Research is ongoing to determine if specific agents (e.g., intravenous propofol vs. volatile anesthetics) or techniques (e.g., regional anesthesia) have better oncological outcomes by modulating the immune system less. Radiation therapy uses high-energy beams to shrink tumors and eliminate cancer cells. While often a painless procedure, patient immobilization is critical for accurate treatment delivery, which presents unique challenges, especially in specific populations. Pediatric patients or those with cognitive/behavioral challenges often require sedation or general anaesthesia for repeated radiation sessions to ensure motionlessness. Logistical challenges often involve providing anaesthesia in "remote locations" outside the main operating room, requiring specialized equipment and experienced personnel. Airway management can become complex for patients who have received radiation to the head and neck, as the tissue properties can change, leading to difficult intubations. Neurocognitive outcomes are a major area of study; anesthesiologists and oncologists collaborate to minimize radiation-induced cognitive impairment, considering the cumulative effect of both radiation and anesthetic exposures on the developing brain, especially in children. The convergence of these fields highlights the necessity of a multidisciplinary team (neuro-oncologists, radiation oncologists, anesthesiologists, etc.) to optimize patient care and outcomes. This collaboration involves: Tailored treatment plans that account for the unique vulnerabilities of each patient, weighing the benefits of aggressive treatment against potential long-term side effects. Ongoing research into the interactions between cancer treatments and anaesthetic drugs to improve therapeutic effects and quality of life [81-89].

4. Discussion

When treated with radiotherapy and chemotherapy, pediatricians with brain tumors experience potential neurologic complications, especially if done frequently under anesthesia. Some complications are neurocognitive changes, leukoencephalopathy; acute neuroendocrine dysfunction arising from irradiation of the hypothalamus or pituitary (chronic dysfunction is associated with younger age at the commencement of treatment); brain lesions due to raised intracranial pressure, and Para-neoplastic syndromes like Eaton–Lambert may occur. Thus, understanding these complications is very important for radiation therapy and anesthesia teams. The aim of anesthesia in pediatrics with brain tumors is to provide adequate analgesia, sedation, and anxiolytics, control unwanted motor activities while

performing a diagnostic or therapeutic procedure to enable a rapid return to the baseline level of consciousness, and to reduce risks of adverse events related to anesthesia

A significant number of patients with a solid tumour have to undergo neoadjuvant therapy comprising either chemotherapy, radiotherapy and immunotherapy (alone or in combination) before surgical resection of the tumour. Neoadjuvant therapy offers the ability to treat both the primary tumour and possible distant metastasis. These treatment modalities not only target rapidly dividing cancerous cells, but also non-malignant cells and thereby induce toxicity. Toxicity leads to serious adverse effects that can worsen a patient's health and is therefore relevant to the anaesthetist. Moreover, patients with liquid tumours, such as leukaemia or lymphomas, may present for surgery, for placement of vascular access or to treat complications of the treatment.

Toxic effects of neoadjuvant therapy can occur in different organ systems and may affect cardiac, pulmonary, renal, hepatic, bone marrow and immunological functions. Together with the patient's comorbidities and reduced nutritional status, a careful preoperative assessment is essential

Neurotoxicity is a common adverse effect with many chemotherapeutic agents and is an important limiting factor in chemotherapy regimens. The development of neurotoxicity is dependent on cumulative dose and dose intensities, but is also more frequently seen in patients with diabetes mellitus, increased age, hereditary neuropathies or earlier treatment with neurotoxic chemotherapy. Chemotherapy may cause both peripheral and central neurotoxicity.

Neuropathic sequelae following irradiation in the head and neck area include sensorineural hearing loss, alterations in taste and smell functions along with brachial plexopathy, and cranial nerves palsies.

Peripheral neurotoxicity affects predominantly sensory neurones and leads to peripheral neuropathy. Symptoms usually start during antineoplastic treatment and stabilise after treatment is completed. Central neurotoxicity may lead to a wide range of neurological disorders, such as encephalopathy, acute cerebellar syndrome, posterior reversible encephalopathy syndrome, aseptic meningitis, cognitive deficits, hemiparesis and progressive dementia.

Prehabilitation aims to improve a patient's functional status before surgery and enhance postoperative recovery. Studies suggest that prehabilitation improves physical performance and quality of life, and decreases postoperative complications and hospital length of stay. Different forms of prehabilitation have been introduced over the past decade, but a multimodal, individualised approach focusing on nutritional, psychological and physical assessments and intervention seems to provide the best results.

Higher cumulative anesthesia exposure and duration may be associated with neurocognitive impairment and neuroimaging abnormalities in long-term survivors of childhood acute lymphoblastic leukemia, beyond the known outcomes associated with neurotoxic chemotherapies. Anesthesia exposures should be limited in pediatric populations with chronic health conditions who undergo multiple medical procedures.

5. Conclusion

Radiotherapy is undoubtedly one of the major contributors to managing HNC. Nevertheless, even with the most advanced radiation techniques, damage to neighbouring healthy tissues is inevitable. In this regard, radiation-induced neuropathy in HNC showed to be a multifactorial pathological process that takes many shapes depending on the treatment modality, anatomical location and patients' physiological conditions. Cancer mortality in pediatrics aged from 1 to 14 years is the most common cause of non-accidental death in the USA. More than 1,500 pediatrics per year are diagnosed with cancer in the United Kingdom. The American Childhood Cancer Organization (ACCO) has reported that leukemia (30%), brain and CNS tumors (26%), and lymphomas (8%) were the three most common types of cancer in children. Radiotherapy is the process of using high and homogeneous doses of ionizing radiation to treat various malignant diseases. Radiotherapy aims to render the highest possible radiation dose to the tumor while sparing as much of the normal healthy tissue as possible. Radiotherapy may be used as a multi-purpose therapy, adjuvant or neoadjuvant therapy, curative (prevention of organ failure), or palliative purposes. Thus, for providing safe anesthesia, considering the tumor effect on body organs and neurologic complications caused by it can be a great help to reduce anesthesia complications in pediatrics under radiotherapy. As part of the preoperative assessment, the anaesthetist should note the patient's neoadjuvant therapy and possible toxic effects reported. Physical examination should include an accurate evaluation of cardiopulmonary status, combined with ECG, pulse, baseline Spo2, arterial pressure and laboratory tests.

Compliance with ethical standards

Disclosure of conflict of interest

No conflict of interest to be disclosed.

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