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Seizure related to paclitaxel and carboplatin infusion in a breast cancer patient

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ABSTRACT

Seizures are a common symptom of brain tumors, whether primary or metastatic. Seizures in patients with breast cancer can sometimes occur for reasons unrelated to the tumor, such as metabolic encephalopathy, cytotoxic chemotherapy, paraneoplastic syndromes, cranial irradiation, and stroke related to cancer. Many chemotherapeutic agents have also been reported to cause seizures (paclitaxel, cisplatin, 5-fluorouracil, methotrexate, and cyclosporine). We present the case of a 45-year-old female who experienced an acute seizure shortly after receiving an infusion of paclitaxel and carboplatin for grade 3 ductal breast cancer. This rare adverse drug reaction should raise awareness among physicians and pharmacists when treating cancer patients.

Keywords: seizure, acute symptomatic, paclitaxel, carboplatin, breast cancer

INTRODUCTION

Breast cancer is the second most common cause of death among women in the United States, with 287,850 new cases in 2022 and 43,250 deaths from breast cancer that year [1]. Breast cancer can metastasize to various organs, such as the bones, lungs, liver, and brain. Approximately 24% of breast cancer cases metastasize to the brain. Despite this, data on the incidence of seizures in breast cancer patients with brain metastases is limited [2]. A review of 106 studies found that 12% of breast cancer patients with brain metastases experienced seizures. Other studies have indicated that chemotherapy agents may have epileptogenic properties, meaning they can trigger seizures, with examples including methotrexate, fludarabine, vincristine, cisplatin, cytarabine, and etoposide, as well as other drugs prescribed for cancer patients (tricyclics, clozapine, bupropion, penicillin, and phenothiazines) [3].

Brain metastasis is a common complication in metastatic breast cancer, particularly in advanced stages (stage IV), where cancer cells from the primary breast tumor spread to other parts of the body via the bloodstream or lymphatic system. It is estimated that 10-16% of patients with advanced breast cancer develop brain metastasis, with the likelihood varying depending on the breast cancer subtype. Breast cancer is a diverse disease, and the specific subtype a patient has significantly influences the risk of developing brain metastasis. Subtypes like triple-negative and HER2-positive breast cancers are more likely to lead to brain metastasis. In contrast, tumors positive for hormone receptors, especially estrogen receptor-positive (ER+), generally have a lower risk of brain metastasis compared to hormone receptor-negative tumors [4].

The mechanism of brain metastasis in breast cancer can involve several pathways, including hematogenous spread, where tumor cells travel through the bloodstream aided by the tumor's vascularity and cell adhesion molecules, as well as lymphatic spread and infiltration through the blood-brain barrier. HER2 is a critical protein that plays a role in cell growth and division. In certain breast cancers, overexpression of HER2 can occur, making these cancer cells more aggressive and increasing their likelihood of metastasizing, including to the brain [5]. HER2-positive breast cancers are known to grow more rapidly and carry a higher risk of brain metastasis. This increased risk is due to the overexpression of HER2, which not only promotes aggressive primary tumor growth but also enhances

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the tumor's ability to invade the bloodstream, making it more likely for cancer cells to reach and metastasize to the brain [6].

The clinical presentation of brain metastasis in breast cancer patients can vary, including seizures, headaches, neurological deficits, cognitive changes, visual disturbances, behavioral and personality changes, nausea, and vomiting. Neurological examinations are essential for evaluating clinical symptoms and neurological function, helping to detect any deficits or abnormalities that may result from brain metastasis [7]. Radiological imaging, including MRI and CT scans, serves as the primary diagnostic method for detecting brain metastasis. On these images, brain metastases typically present as contrast-enhancing masses, a result of the disrupted blood-brain barrier around the metastatic lesion, which allows contrast agents to accumulate in the tumor. Radiological imaging is also vital for distinguishing metastatic brain tumors from primary brain tumors and identifying the presence of multiple metastatic lesions in the brain [8]. Radiological imaging can also detect peritumoral edema, swelling, and inflammation in the brain tissue surrounding a metastatic lesion. This edema typically appears as an area of increased signal intensity on MRI scans. MRI is considered the gold standard for brain imaging, particularly in detecting and characterizing brain metastasis, as it is capable of visualizing small or multiple lesions, determining their precise location, and assessing their relationship with surrounding brain structures. On the other hand, CT scans are useful for identifying large, calcified, or hemorrhagic brain metastases [9].

Seizures are common in cancer patients, with brain metastases being the leading cause in adults. These metastases often originate from the skin, breast, lungs, kidneys, and colon, with approximately 70% annually coming from the lungs or breast [10]. The frequency of seizures differs based on the type of brain neoplasm. Cancer patients are at an elevated risk for seizures due to several factors that are not directly related to the tumor, including cytotoxic chemotherapy, metabolic encephalopathy, paraneoplastic syndromes, cranial irradiation, and strokes linked to cancer. Additionally, various chemotherapeutic agents can also trigger seizures [11,12]. Patients with systemic cancer generally have a higher incidence of epilepsy. Seizures are prevalent among cancer patients, affecting up to 60% of those with brain metastasis. This situation necessitates the use of anticonvulsant medications in conjunction with antitumor treatments like chemotherapy. However, combining these therapies can significantly increase the risk of drug interactions, with brain tumor patients experiencing a six-fold higher risk compared to those with systemic cancer. Pharmacokinetic drug interactions can occur due to alterations in the absorption, distribution, metabolism, or elimination of medications. Chemotherapy agents and tyrosine kinase inhibitors can influence the pharmacokinetics of other treatments administered concurrently. Using anticonvulsants (AEDs) in combination with chemotherapy or tyrosine kinase inhibitors involves a risk of drug-drug interactions (DDIs). These drug classes can stimulate enzyme activity, and tyrosine kinase inhibitors may also enhance the toxicity of other drugs by inhibiting enzyme function [13].

Enzyme-inducing anticonvulsants (EIAEDs) can enhance the clearance of chemotherapy drugs that are metabolized concurrently by about two to three times, affecting medications such as cyclophosphamide, irinotecan, paclitaxel, and teniposide. The clearance can increase up to four times faster when combined with tyrosine kinase inhibitors like lapatinib, imatinib, dasatinib, and crizotinib. Moreover, tyrosine kinase inhibitors, especially imatinib and crizotinib, can lead to the inhibition of enzymes that are crucial for the metabolism of other treatments. Many newer anticonvulsants do not affect drug metabolism but can alter enzyme activity through interactions with different medications, such as other anticonvulsants, chemotherapy drugs, and tyrosine kinase inhibitors. Furthermore, glucocorticoids can induce metabolic changes as well. Consequently, these interactions can lead to drug toxicity unless dose adjustments are implemented [13].

Paclitaxel is a chemotherapeutic agent used for various types of cancer. Indications for paclitaxel use include breast cancer, ovarian cancer, bladder cancer, lung cancer, prostate cancer, and various other solid tumors [14]. The therapeutic effects of taxanes (paclitaxel) are due to the blockade of microtubule depolymerization, which leads to the inhibition of cell division. The antiproliferative effects of platinum-based drugs (carboplatin) result from DNA-protein and DNA cross-linking, leading to the blockage of DNA replication and/or repair [15]. Paclitaxel works by inhibiting cancer cells from multiplying into new cells, thereby inhibiting cancer growth. Carboplatin is activated within the cell and forms reactive platinum complexes that cause cross-linking of DNA molecules within the cell. This results in structural changes to the DNA and inhibits DNA synthesis, which can affect cell death, particularly in rapidly dividing cells [16].

Carboplatin, an antineoplastic medication, belongs to the class of platinum-based agents and is categorized as an alkylating agent. It exerts its effects through several mechanisms: (1) by transferring alkyl groups to guanine residues in DNA, leading to DNA fragmentation and the creation of mismatched bases, and (2) by forming interstrand

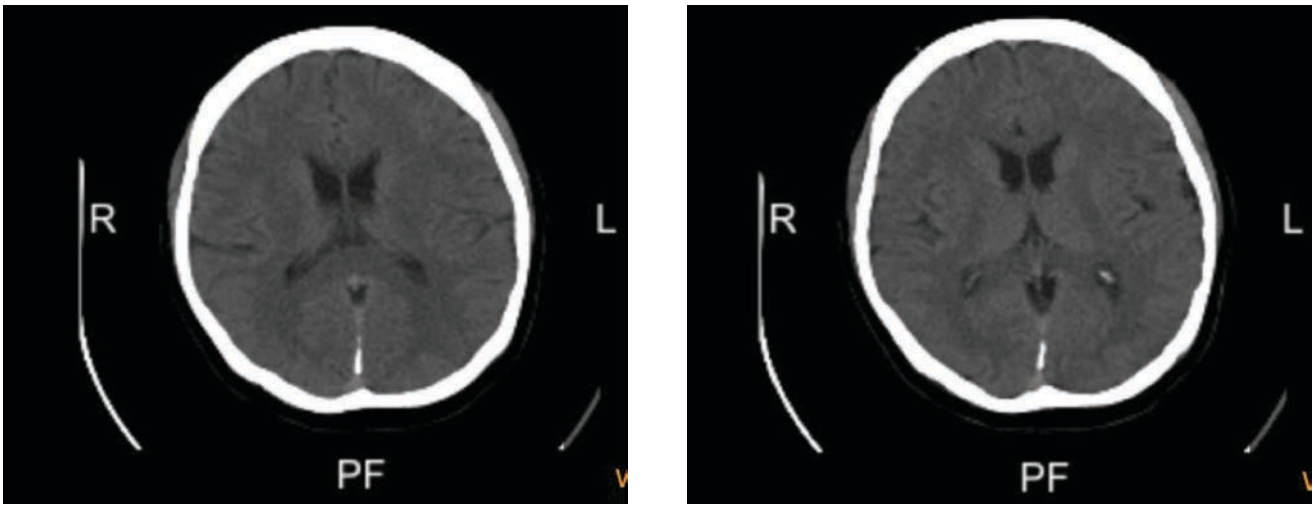

FIGURE 1. The brain CT scan of the patient ruled out brain metastases

or intrastrand cross-links, which cause DNA damage and hinder the separation of strands during DNA synthesis or transcription [17]. Carboplatin and paclitaxel may both induce nerve toxicity as a side effect, often manifesting as axonal sensory peripheral neuropathy. Although neurotoxicity affecting the central nervous system, like acute seizures, is uncommon, there have been past reports linking these drugs to seizures, cortical blindness, aphasia, hemiparesis, and coma [18].

We report the case of a 45-year-old woman diagnosed with ductal breast carcinoma who experienced a seizure shortly after receiving an infusion of paclitaxel and carboplatin. Her laboratory tests returned normal results, and a CT scan of the brain showed no signs of primary metastasis or meningeal carcinomatosis. She had no symptoms of infection, a history of seizures, fever, or medications that might predispose her to such an event. After eliminating other potential causes, the seizure was most likely attributed to the chemotherapy, with carboplatin and paclitaxel being the probable agents due to their temporal association with the adverse event.

CASE PRESENTATION

A 45-year-old woman, who had received her first chemotherapy after a mastectomy for ductal carcinoma of the breast, was referred to the emergency department following a general tonic-clonic seizure that occurred 10 minutes after receiving an infusion of paclitaxel (210 mg) and carboplatin (300 mg). Her premedication regimen included ondansetron (8 mg), one ampule of ranitidine, and one ampule of dexamethasone (4 mg). During the seizure, she exhibited up-rolling of the eyeballs and tongue biting. She was sedated with intravenous diazepam and started on phenytoin.

After the seizure, the patient showed signs of confusion, drowsiness, and slurred speech. A neurology examination confirmed a diagnosis of simple partial seizure with secondary generalization. Electroencephalography (EEG) revealed abnormal activity, including sharp waves and a slowing pattern. A computed tomography (CT) scan of the brain showed no focal lesions. Laboratory tests, including complete blood counts, renal function tests, blood glucose levels, liver function tests, and serum electrolytes (calcium, chloride, potassium, sodium, and magnesium), were all within normal limits. Additionally, the chest X-ray, electrocardiography, and two-dimensional echocardiogram were normal. The patient's blood pressure remained stable before, during, and after chemotherapy. There were no complaints of fever or signs of sepsis.

At the time of discharge, she was fully alert, seizure-free, and independent. Two weeks later, she reported no neurological complaints. She continued receiving phenytoin injections for three days without any further seizure episodes. Upon discharge, she was prescribed oral phenytoin and levetiracetam.

DISCUSSION

Seizures in cancer patients can arise from primary and metastatic brain tumors, paraneoplastic syndromes, or treatment-related factors such as radiation therapy, chemotherapy, and medications (antibiotics, narcotics). Although seizures occur in less than 1% of patients treated with systemic chemotherapy, chemotherapy agents, especially platinum-based drugs, are known to cause significant adverse effects on the nervous system [19]. Platinum-based agents are considered first-line cytotoxic treatments for various cancers, but they are also associated with neurotoxicity [19]. These drugs are linked to peripheral sensory neuropathy due to their ability to penetrate the dorsal root ganglia and peripheral nerves more readily than the brain, which has limited per-

meability due to the blood-brain barrier. Common toxic effects of platinum-based drugs include hypokalemia, hypocalcemia, and hypomagnesemia [20].

Several reports have documented neurological toxicity associated with paclitaxel and carboplatin, including cases of transient cortical blindness, seizures, and posterior reversible encephalopathy syndrome (PRES) [20,21]. On CT scans, PRES is characterized by subcortical vasogenic edema and notable white matter lesions in the parieto-occipital areas. Although the clinical signs and symptoms are non-specific, common manifestations of PRES include headaches, seizures, altered mental status, and visual disturbances, often accompanied by hypertension

Chemotherapy agents linked to PRES include taxanes, immunosuppressants, folate antagonists, angiogenesis inhibitors, anthracyclines, platinum derivatives, vinca alkaloids, and antimetabolites. In PRES, a rapid increase in hypertension exceeds the limits of cerebral blood flow autoregulation, resulting in hyperperfusion that disrupts the blood-brain barrier and allows plasma and macromolecules to leak into the interstitial space [22].

A case of reversible posterior leukoencephalopathy syndrome (RPLS) was reported in a lung cancer patient from Japan, suspected to be linked to vascular endothelial toxicity resulting from a carboplatin and paclitaxel regimen. RPLS is characterized by symptoms such as headaches, altered consciousness, seizures, visual disturbances, and cerebral edema, particularly affecting the posterior regions of both cerebral hemispheres, especially the parieto-occipital areas. This syndrome frequently occurs as a complication of chemotherapy due to its toxic effects on the central nervous system (CNS). Seizures may present at the onset of neurological symptoms and can start focal. The mechanism behind RPLS involves cerebral vasogenic edema, and brain capillary leak syndrome, along with compromised vascular autoregulation. Additionally, the cytotoxic effects of immunosuppressive and chemotherapeutic drugs on the vascular endothelium can contribute to the disruption of the blood-brain barrier. Platinum-based agents have occasionally been linked to CNS toxicity [23].

Encephalopathy, both acute and late-onset, has been observed with paclitaxel, although some cases involved underlying brain metastasis, prior radiotherapy to the brain, disruption of the blood-blain barrier, or brain surgery. Seizures shortly after paclitaxel infusion initiation have been reported, with one case describing hypersensitivity symptoms like chest tightness and flushing followed bye a generalized tonic-clonic seizure within 5 minutes of infusion. However, in our patient, the paclitaxel infusion proceeded without incident. Cremophor, a solvent used in paclitaxel formulations, is also a known neurotoxic agent with procoagulant effects, potentially contributing to thrombotic-embolic events. Cremophor is a formulation ingredient containing surfactants used for various poorly water-soluble drugs, including paclitaxel [23]. Paclitaxel, a potent antimitotic agent, stabilizes and prevents microtubule depolymerization by targeting tubulin. It has broad antitumor activity with side effects including myelosuppression and peripheral neurotoxicity, but central nervous system (CNS) toxicity following IV administration is rarely reported [24].

Clinical observations have shown that paclitaxel can mitigate the antiplatelet toxicity of carboplatin when the two drugs are combined, although the antitumor activity and white blood cell toxicity are additive. This effect is due to the interaction between the two drugs at the platelet precursor level [25]. The pairing of carboplatin and paclitaxel shows antagonistic interactions when tumor cells are treated with carboplatin before paclitaxel or when both drugs are given at the same time. However, minimal antagonism is observed when paclitaxel is given before carboplatin. Administering paclitaxel (Taxol) alongside carboplatin has shown advantages; a 1996 study indicated that this combination is more effective for treating advanced-stage ovarian cancer while presenting lower toxicity compared to the Taxol and cisplatin combination. The cisplatin-Taxol group experienced significantly higher rates of gastrointestinal, renal, metabolic toxicities, and leukopenia compared to those treated with the carboplatin-Taxol combination. Toxic side effects, such as nausea and weight loss, were also less frequent with carboplatin-Taxol. Additionally, carboplatin-Taxol can be safely and effectively administered over a 3-hour infusion period, whereas cisplatin-Taxol requires a 24-hour infusion, necessitating hospitalization [26].

However, paclitaxel must be administered before carboplatin because if carboplatin is given first, paclitaxel (Taxol) will not exert its effects on cancer cells. Research indicates that previous or simultaneous treatment with carboplatin can hinder Taxol-induced degradation of I-kappa, B-alpha, and phosphorylation of BCL-2. Additional analysis indicated that carboplatin notably disrupts the cytotoxic effects of paclitaxel on mitotic arrest and apoptotic cell death, unless paclitaxel is given before carboplatin. Additional studies have shown that the interaction between paclitaxel and carboplatin is heavily dependent on the sequence of administration, with the most effective results occurring when paclitaxel is given first, followed by carboplatin [26].

An algorithm for diagnosing chemotherapy-induced seizures was established using the WHO-UMC causality assessment system, considering: (1) onset of encephalopathy shortly after chemotherapy infusion; (2) exclusion of other physical or metabolic fac-

tors that could trigger seizures; (3) absence of concurrent administration of other drugs or analgesics; and (4) response to withdrawal [26,27]. Platinum-based chemotherapeutic agents are considered a first-line cytotoxic treatment option for various cancers, including lung, colorectal, ovarian, bladder, testicular, and breast cancers. Due to their cytotoxic nature, these agents are not free from side effects, one of which is electrolyte disturbances, particularly hypomagnesemia. This is most commonly seen with cisplatin (10%-90%) and with carboplatin at around 10%. The neurological consequences of hypomagnesemia may encompass seizures, vertigo, ataxia, nystagmus, athetosis, and choreiform movements. Additionally, nephrotoxicity is a recognized adverse effect of platinum-based agents, with a reduction in magnesium levels considered an early sign of cisplatin-induced kidney damage, while a rise in creatinine levels typically indicates a later stage of injury [27].

It is proposed that platinum agents are filtered through the glomerulus, with cisplatin being significantly more filtered than carboplatin or oxaliplatin, which are mainly attached to plasma proteins. These agents subsequently access renal tubular cells through organic cation transporters, resulting in nephrotoxicity and disrupting magnesium reabsorption in the ascending loop of Henle and the distal tubules. Furthermore, proton pump inhibitors (PPIs) are known to induce hypomagnesemia that does not respond to oral magnesium supplementation and can also trigger tonic-clonic seizures. It is suspected that PPIs increase luminal pH in the intestine, which diminishes the affinity of magnesium influx channels (Transient Receptor Potential Melastatin 6, TRPM6/7) for magnesium absorption [27]. Peripheral neuropathy is the most frequent neurological side effect of cancer therapy and often serves as a limiting factor for dosing, especially in older adults. Numerous conventional chemotherapy agents are known to cause this condition. Neuropathies induced by these drugs can be worsened by pre-existing or newly developed peripheral neuropathy due to non-cancer-related factors, such as diabetes or alcohol use. Additionally, the risk may increase when neurotoxic drugs are used sequentially or in combination, such as vinorelbine following platinum-based therapy. To prevent chemotherapy-induced peripheral neuropathy without reducing the effectiveness of treatment, several neuroprotective strategies have been proposed, including calcium and magnesium supplementation and the use of agents like glutathione, glutamine, acetyl-L-carnitine, and erythropoietin. Limited evidence suggests that glutamine may help prevent neuropathy associated with paclitaxel and oxaliplatin [28].

Seizures are associated with various intravenous chemotherapeutic agents. For some drugs, like high-dose busulfan, the risk is significant enough to warrant prophylactic use of anti-epileptic medications during administration. Seizures may present in a non-convulsive form, appearing as encephalopathy, with non-convulsive status epilepticus confirmed by electroencephalogram (EEG). These seizures can be directly linked to the chemotherapeutic agents or arise due to therapy-induced environmental changes. Immunomodulatory drugs such as interferon and interleukin-2 (IL-2) are also known to trigger seizure activity. Additionally, the cytokine storm resulting from CAR T-cell therapy frequently causes seizures, which are often challenging to manage. Preventative anti-epileptic medications may help reduce the risk of seizures, but when they do occur, controlling them typically requires a combination of multiple anti-epileptic drugs and steroids [28]. Many commonly used chemotherapy drugs, such as platinum-based agents (oxaliplatin, cisplatin, carboplatin), taxanes (paclitaxel, docetaxel), vinca alkaloids, proteasome inhibitors, and thalidomide analogues, can cause direct neurotoxicity and chemotherapy-induced peripheral neuropathy (CIPN). The mechanisms by which these antitumor drugs induce neurotoxicity and peripheral neuropathy include the following: 1) Bortezomib inhibits the 26S proteasome. 2) Taxanes stabilize tubulin proteins, preventing anaphase from occurring. 3) Vinca alkaloids destabilize microtubules, impairing mitotic spindle formation. 4) Platinum-based compounds form intra-strand and cross-strand DNA links. 5) 5-Fluorouracil (5-FU) binds to thymidylate synthase (TS). Both platinum-based compounds and 5-FU disrupt DNA synthesis, contributing to their antitumor effects but also leading to neurotoxic side effects [29].

All platinum-based agents preferentially bind to guanosine and adenosine, forming intrastrand and interstrand crosslinks. Since these drugs do not cross the blood-brain barrier (BBB), their effects are primarily localized to peripheral structures such as the dorsal root ganglia (DRG), which regulate somatic and visceral sensitivity, and the area postrema (AP), which mediates nausea and vomiting. Platinum compounds can also bind to mitochondrial DNA, which lacks repair systems, leading to increased reactive oxygen species (ROS) and oxidative stress. Taxanes, due to their chemical similarity, share a dose-dependent mechanism of action. At high concentrations, paclitaxel binds to the beta-tubulin subunit, enhancing microtubule polymerization and promoting the formation of abnormal mitotic spindles, which inhibit mitosis and trigger apoptosis. At lower concentrations, paclitaxel acts as a microtubule-stabilizing agent, blocking depolymerization and preventing anaphase, thereby activating apoptotic pathways. Although paclitaxel does not directly damage mitochondrial DNA, mitochondria are implicated in its

toxicity. Swollen and vacuolated mitochondria have been observed in sensory nerves, both myelinated and unmyelinated. Similar to platinum agents, taxane-induced mitochondrial dysfunction leads to calcium efflux from mitochondria and the endoplasmic reticulum, resulting in axonal degeneration and DRG cell apoptosis. Because the dynamic assembly of microtubules is essential for the formation of the mitotic spindle during cell division, the stabilization of microtubules induced by taxanes disrupts interphase processes, ultimately leading to cell death [29].

The exact mechanism behind taxane-induced chemotherapy-induced peripheral neuropathy (CIPN) is not fully understood. However, microtubule stabilization may contribute to neuropathy by disrupting axonal transport. Mitochondrial damage has also been implicated in the development of axonal dysfunction, leading to CIPN. In untreated nerve fibers, mitochondria appear enlarged or swollen, often with vacuolation. A key pathway for CIPN induction involves the binding of taxanes to cytosolic neuronal calcium sensor 1 (NCS1), a calcium-binding protein that also interacts with vinca alkaloids. This binding alters intracellular calcium signaling, triggering the activation of calpain, a calcium-dependent enzyme that disrupts mitochondrial function. Activated calpain degrades several proteins, including NCS1, which contributes to neuronal dysfunction. Paclitaxel is mainly absorbed by the liver through the organic anion transporting polypeptide B2 transporter (OATP1B2), which has recently been identified as a mediator of taxane-induced neurotoxicity. This discovery suggests a novel pathway for paclitaxel-induced neuropathy. Inhibiting OATP1B2 pharmacologically or genetically knocking it out in mice offers protection against allodynia, thermal hyperalgesia, and changes in digital maximal action potential amplitudes. Interestingly, the calcium release via the NCS1-dependent pathway can be inhibited by lithium, while the OATP1B2 transport system's function is non-competitively inhibited by the tyrosine kinase inhibitor nilotinib. In both cases, the inhibition of these pathways does not compromise the chemotherapeutic efficacy of paclitaxel [30].

Anticonvulsant drugs selectively bind to the alpha-2-gamma subunit of the voltage-gated calcium channel (VGCC), reducing the postsynaptic levels of glutamate and other excitatory neurotransmitters. Gabapentin has traditionally been the primary anticonvulsant used, but pregabalin, a successor of gabapentin with the same mechanism of action, is now also used clinically. These drugs not only affect VGCCs but also interact with other targets, including NMDA receptors, transient receptor potential channels, protein kinase C, and inflammatory cytokines, all of which play important roles in pain and thermal sensation. In a randomized controlled trial involving patients with cancer-induced neuropathic pain, pregabalin was found to be more effective than both gabapentin and amitriptyline, with the added benefit of requiring a lower dose of co-administered opioids. Adding lithium to taxane treatment was shown to prevent the initial rise in intracellular calcium, thereby avoiding calcium overload in mitochondria and calpain activation, which helps preserve cell function [30]. The use of manual therapies and physical modalities offers benefits in treating common cancer symptoms such as fatigue, pain, chemotherapy-induced nausea and vomiting, polyneuropathy, and lymphedema. Modalities like heat, ultrasound, cryotherapy, and manual therapy are frequently used as adjuncts to manage cancer-related pain, control tissue inflammation, and promote muscle relaxation. Additionally, several studies involving electrical stimulation have suggested that this modality may help limit cancer growth [31]. Most cancer chemotherapeutic agents interfere with the absorption of antiepileptic drugs by damaging the intestinal mucosa, which leads to reduced serum levels of antiepileptic drugs and potentially diminishes their effectiveness. Conversely, the chronic administration of hepatic enzyme-inducing antiepileptic drugs, such as phenytoin, phenobarbital, carbamazepine, and, to a lesser extent, oxcarbazepine and topiramate, can lower the serum levels of several cancer chemotherapeutic drugs [32].

The patient had no risk factors and history of seizures either before or during chemotherapy. In addition, the patient had been informed about seizures as a rare side effect of chemotherapy agents. In our patient, other causes of encephalopathy were ruled out by neuroimaging and blood serum examination. The strongest evidence for our hypothesis is provided by the fact that a seizure occurred shortly after the infusion without any other possible causes. Carboplatin appears to be the more likely culprit based on the temporal relationship between its administration and the seizure. However, we cannot completely dismiss paclitaxel as a potential contributing factor [33].

CONCLUSION

Seizures can occur as a rare side effect of chemotherapy, particularly with drugs like carboplatin and paclitaxel. These seizures may manifest as encephalopathy or non-convulsive status epilepticus, often confirmed through EEG. While the exact mechanisms of drug-induced neurotoxicity remain complex, they involve interactions with microtubules, mitochondrial dysfunction, and altered calcium signaling. Chemotherapy-induced peripheral neuropathy (CIPN) is also a common complication, linked to microtubule stabilization and mitochondrial damage. Although anticonvulsant and supportive treatments can help manage these effects,

the risk of seizures may be influenced by the specific chemotherapy agents used and their interactions with other medications. In the case presented, the temporal relationship between carboplatin administration and the seizure strongly suggests it as the cause, though paclitaxel remains a potential contributing factor. Platinum-based agents like carboplatin and paclitaxel can induce neurotoxicity and electrolyte disturbances such as hypomagnesemia, which may contribute to seizures. An algorithm based on WHO-UMC causality assessment criteria helps diagnose chemotherapy-induced seizures. While seizures triggered by chemotherapeutic agents are uncommon and can be caused by various factors, it's crucial for physicians and pharmacists to be aware of this potential adverse drug reaction.

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