Neurotoxicity in Cancer Care: A Case-Based Approach

Oncology nurses are in a unique position to identify the signs and symptoms of cancer treatment-related neurotoxicities. Refresh your knowledge of cognitive deficits, peripheral system disorders, and central system disorders. By examining cases, you’ll enhance your ability to assess and manage short- and long-term dysfunctions.

Target Audience: Registered Nurses, Advanced Practice Nurses

Level of Content: Intermediate

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Full Disclosure: Nothing to Disclose

Objectives:
At the end of this session, participants will be able to:
1. Distinguish between treatment-related neurotoxicity and neurologic cancer symptoms.
2. Identify the pathological mechanisms of treatment-related neurotoxicity.
4. Delineate evidence-based interventions for symptom management and quality of life (QOL) in the care of patients with cancer and treatment-related neurotoxicity.
Neurotoxicity: A Case-Based Approach

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Objectives

• Distinguish between treatment toxicity and neurologic cancer symptoms.
• Identify pathological mechanisms of treatment-related neurotoxicity.
• Discuss potential short and long term neurologic sequela of oncologic treatment.
• Delineate evidence based interventions for symptom management and quality of life (QOL) in the care of cancer patient with treatment related neurotoxicity

Why is this Important?

• Disease symptomology vs. treatment toxicity
• Advances in systemic cancers therapies
• Increased survival
• Potential impact on quality of life
• Provides opportunities for additional research

Cancer Treatment-Related Neurotoxicity

• Central Nervous System
  • Surgery
    • Traumatic
    • Ischemic
  • Radiation
    • Acute
    • Early Delayed
    • Late Delayed
  • Chemotherapy
    • Encephalopathy
    • Intracranial hemorrhage
    • Posterior reversible leukoencephalopathy
  • Myelopathy
  • Paraneoplastic disorders

• Peripheral Nervous System
  • Radiculopathy
  • Plexopathy
  • Myelopathy
  • Neuropathy
  • Myopathy
  • Paraneoplastic disorders

Case Study

• JD is a 61 year old male with a history of smoking, asthma and a history of seizures that started in 2005. CT scan at that time showed an abnormality in right posterior temporal lobe. Started on Dilantin and Decadron
• Seen in 2007 with generalized seizures with an aura of a headache sensation.
• CT scan done revealed an enhancing mass with edema in the right posterior temporal lobe. A CT of the chest also showed a lesion in the right hilar region.

Case Study cont’

• JD was diagnosed with NSCLC with brain metastasis.
• On 6/07 had SRS for the right parietal-temporal lesion. Currently being treated with Gemcitabine and Carboplatin. On Keppra for seizure management
• Seen in 8/07, No evidence of brain disease evident with regular follow ups
• Seen 4/08 with reports of new morning headaches relieved with Acetaminophen
• MRI showed an enhancing abnormality at the surgical resection site. Compared to previous study, the area grew 38% (unidimensional) or 63% (two dimensional measurement)
Case Study cont’d

- May 2008 – still reports seizure. Approx. 10 days ago, had an episode of slurred speech, disorientation and asymmetrical smile. In the emergency room, received increased doses of dexamethasone and Keppra®. In addition, his wife reports his auditory hallucinations
- PET showed mild hyper-metabolism in the area of metastasis and surgery. In addition, hyper-metabolism at the right medial temporal lobe is noted.
- He experiences significant changes in mood and depression with elevations in dexamethasone doses

Diagnostic Options

- Surgery
- Ictal activity vs. encephalitis (inflammatory or infectious)
- Repeat MRI and Brain PET

Radiation Necrosis

- Occurs in cerebral hemispheres and spinal cord
- Brain tolerance dose (45-50Gy), increased risk with higher doses (Ruben, et al, 2006)
- High dose of 78-94 Gy associated with 17% risk of RN (Bauman, et al, 1996)
- Incidence has increased despite improved safety and delivery of radiation treatment
- Increased risk within the first 2 years
- Hyper-fractionation and use of radioprotective agents can minimize risk (Nieder, et. al, 2002)

Diagnosis

- Radiographic identification is limited
- Metabolic imaging and perfusion scans may aid in discrimination
- Tumor recurrence in conjunction with radiation necrosis delays correct identification
- Histo-pathological diagnosis

Clinical Manifestations

- Asymptomatic
- Increased intracranial pressure
- Cognitive dysfunction
- Focal neurological deficits (Giglio & Gilbert, 2003; Meyers, et al, 2000)

Pathophysiology

- Vascular Injury
- Glial Injury
- Neuronal Injury
- Enzymatic Disturbances
- Inflammatory Response
Treatment Options

- Corticosteroid therapy
- Surgery
- Hyperbaric Oxygen Therapy
- Bevacizumab

Hyperbaric Oxygen (HBO) Therapy

- Chuba et al. (1997) – 10 children with brain necrosis. All patients initially improved. Four died from disease and 5 of the remaining 6 sustained improvement
- Feldmeier and Hampson (2002) – systematic review supported the beneficial use of HBO in different types of radiation injuries
- Cihan et. al (2009) – Pt with PCNSL developed radiation necrosis who failed steroid therapy and refused surgery. HBO resulted in clinical and radiographic improvement

HBO Therapy

Regimen
- 20-30 sessions at 2.2.24 atm (Cihan, et al, 2009)
- 60 sessions (3 months), the 50 sessions (2.5 months) (Na et al, 2014)

Advantages (Na et al, 2014)
- reduction in steroid dose
- Symptom and imaging improvement
- Used to treat symptom recurrence

Side Effects

- Ear pain
- Sinusitis (Chuba et al, 1997)
- Lower seizure threshold (Feldmeier, 2002)
- Tumor progression (Chuba et al, 1997)

Radiation Necrosis

- Vascular Injury
  - VEGF Expression

Bevacizumab

- Monoclonal antibody against VEGF
- Used to treat a variety of cancers
- Side effects include hypertension, increased risk of thromboembolic events, hemorrhage and hypersensitivity
- Dosage: 5-10 mg/kg every two weeks (up to 4 cycles)
The Future...

- From human embryonic stem cells, isolated oligodendrocytes progenitors were transplanted
- Repair major white matter tracts resulting in structural and functional repair
- Behavioral testing showed complete recovery of cognitive function
- Additional transplantation in the cerebellum resulted in recovery of motor deficits

Nursing Management

- Assess neurological baseline to detect changes
- Monitor for complications from treatment
- Implement home services as needed
- Evaluate compliance with medications and treatment plan
- Educate patient and caregiver regarding self-care strategies

Case Study

- SA, a 50 year old female with recently diagnosed right temporal glioblastoma multiforme (Stage IV astrocytoma) in October 2014
- Resection done at another institution and her perioperative course was complicated with psychosis and encephalopathy. She was also placed on suicide watch during this period.
- Postoperative course complicated by increased intracranial pressure secondary to hydrocephalus and VP shunt was placed.
- Patient expresses anger about illness. Husband indicates that his wife's personality is different, she is impulsive and her language is "colorful."
- Presents for treatment options. Currently she experiences left sided weakness and neglect

Case Study cont'

- Medication List
  - Seroquel 25mg oral at bedtime
  - Pantoprazole 40mg oral daily
  - Dexamethasone 4mg oral 3 x day
  - Colace 100mg oral 2 x day
  - Flax seed

Case Study cont'

- Due to increased cerebral edema caused by the residual tumor, SA was started on Standard therapy for GBM (radiation and Temozolomide)
- Dexamethasone tapered and Seroquel changed to Zyprexa with periodic dose adjustments.
- Decrease in agitation noted with steroid taper, however, persistent insomnia
- Presents with 4-5 days of headache, one episode of chills, decreased appetite and interaction

Corticosteroids

- Biological mediators
- Two Main Groups
  - Glucocorticoids (Cortisol)
  - Mineralocorticoids (Aldosterone)
- Synthetic corticosteroids
  - Common usage in the oncology population
Uses

- Prevent or treat chemotherapy induced nausea and vomiting
- Target lymphomas in the CNS
- Treat cerebral edema

Peritumoral Edema

Steroids

- Mechanism of action

Dexamethasone

- Most common
- Improvement of symptoms related to increased ICP (Posner, 1995)
- ↓ mineralocorticoid effect
- Dosing
- Works effectively but...

Case Study cont’

- During SA’s course of treatment and need for steroids, there were multiple attempts to taper her steroids in response to her behavioral side effects

Neuropsychiatric Effects of Steroids

- Reported in the literature in the 1950’s
- Incidence 2%-60%
- “Steroid Psychosis” – vague terminology
- Mainstay usage in the neuro-oncology population
- Clinical manifestations varied

Pathophysiology of Neuropsychiatric Effects

- Precise mechanism not fully understood
- Effect on the hippocampus
- Direct effects on neuronal membranes
- General brain tissue changes during corticosteroid use

Risk Factors

- Corticosteroid dose - > 40mg/day Prednisone
- Blood Brain Barrier Damage
- Hypoalbuminemia
- Gender
- Psychiatric History
- Age
- Cytochrome P450 inhibition
- History of previous neuropsychiatric reaction to corticosteroids
- Longer acting corticosteroids
**Treatment**

- Decreasing corticosteroid dose
  - Clinical efficacy
- Lithium
  - No solid evidence
  - Use caution with co-administration of steroids
  - Renal impairment
- Neuroleptics
  - Olanzapine (Zyprexa®)
    - Risk of weight gain and diabetes
    - Monitor for extrapyramidal reactions
  - Chlorpromazine (Thorazine®)
    - Monitor for extrapyramidal reactions
    - Sedation

**Future Considerations**

- Need for randomized controlled trials
- Increased knowledge on mechanism of neuropsychiatric effects
- In most studies, patient were receiving prednisone
- Research specifically on oncologic populations

**Chemotherapy-Induced PN**

- Overall incidence approx. 40% although depends on:
  - chemotherapy regime,
  - duration of exposure and
  - assessment methods (Hershman, et.al, 2014)

**Chemotherapy-Related Neuropathy**

- Chemotherapy related neuropathy:
  - peripheral neuropathy - CIPN
  - other neuropathies
- Radiation induced neuropathy:
  - Pts with CRC or GYN cancer with involvement of sacral plexus or upper airway cancer with radiation to the brachial plexus are at increased risk to developing radiating neuropathic pain (Paice, 2009)
- Surgery induced neuropathy:
  - Phantom pain s/p amputations
  - Post mastectomy &
  - Post thoracotomy syndromes

**Case Study**

KR is a 56yr old male
- dx with CRC with liver mets
- underwent surgery for colon resection and implantation HAI pump and mediport
- Obese, previous 1ppd smoker x 12 yrs, quit 8 years ago, admits to 3-4 etoh drinks daily
- meds- atorvastatin, MVI, FeSO4, colace
- labs- CBC with slight anemia hgb 11.4,
  - BMP wnl, serum glu wnl, chol 290,
Risk Factors Pre-Treatment

- Diabetes
- Alcoholism/chronic alcohol use
- Nutritional (vitamin) deficiencies
- Peripheral vascular disease/atherosclerotic ischemic disease
- Age?
- Altered labs:
  - Low magnesium
  - Low albumin
  - Anemia
- HIV (r/to viral involvement or to HAART therapy)
- Amyloidosis
- Genetic polymorphisms

Case Study cont’

Planned treatment course: adjuvant modified FOLFOX6, with FUDR HAI

- Oxaliplatin 85mg/m² over 2 hrs
- leucovorin 400mg/m² over 2 hrs
- 5-fluorouracil 1000mg/m² daily x days CI via mediport

Floxuridine (FUDR, 5-fluorodeoxyuridine) 0.12mg/kg daily x 14 days via HAI

Common Chemotherapeutics Causing Peripheral Neuropathy

- platinums:
  - cisplatin, carboplatin and oxaliplatin
- vinca alkaloids:
  - vincristine, vinblastine, vinorelbine
- taxanes:
  - paclitaxel, docetaxel
- bortezomib
- thalidomide, lenolidamide
- ixabepilone
- eribulin

Platinum Compounds

Cisplatin:
- related to the total cumulative dose and to the dose-intensity of treatment
- onset is expected after 250–350 mg/m² -sooner if h/o neuropathy, or with combination therapy (Albers, et al, 2014)
- at a cumulative dose of 500–600 mg/m², almost all pts have objective evidence of PN, being severely disabling in at least 10% of patients (Argyirou, et al, 2012)

Carboplatin:
- neurotoxicity is thought to be considerably less than cisplatin

Oxaliplatin

- neurotoxicity is major dose-limiting AE
- induces two types of PN: acute and chronic.
  - Acute syndrome:
    - distal or perioral paresthesias and pharyngolaryngeal dysesthesias,
    - appear soon after admin, usu transient and completely reversible within hours or days
    - may increase in both duration and severity with repeated administration (Pavorto, et al 2006)
    - incidence rates, ranging from 65% to 98%
    - Cold temperature represents the main risk factor

Oxaliplatin

The chronic form of PN:
- sensory, axonal neuronopathy
- incidence is related to various risk factors: treatment schedule, single dose per course, cumulative dose, time of infusion and pre-existing peripheral neuropathy
- highly likely when cumulative doses 800 mg/m²
- symptoms are partly reversible in about 80% of patients; completely resolve 6–8 months after discontinuation treatment in about 40% of patients (Argyirou, et al, 2008)
Vinca Alkaloids

- **Vincristine**
  - Considered the most neurotoxic drug; Severity is dose-related.
  - $\equiv 2mg/m^2$ many report mild distal paresthesias
  - $\equiv 4mg/m^2$ most have reduction or loss of ankle reflexes
  - $\equiv 8mg/m^2$ can develop motor weakness or gait impairment
  - Can affect cranial nerves leading to vocal cord paralysis, jaw pain or optic neuropathy (rare)
  - Causes constipation, ileus and erectile dysfunction
  - Hepatic insufficiency is risk factor for more severe PN
  - Type 1 Charcot-Marie-Tooth hereditary neuropathy (often previously unrecognized)
  - Risk for developing rapidly progressive, severe PN with low cumulative doses

- **Vinblastine**
  - PN is similar, but less severe
  - Can affect cranial nerves as well

- **Vinorelbine**
  - Dose dependent
  - Usually reversible after drug discontinuation

Bortezomib

- **PN occurs in up to 1/2 of the patients**
  - Symptoms may start at 1.3mg/m²; cumulative dosing is associated with an increased incidence
- **Generally occurs during the first several cycles**
  - Improves or resolves over several months following discontinuation
- **Pts with recurrent MM may develop more severe bortezomib-induced PN than those with newly diagnosed disease.**
- **Severe neurotoxicity (grade 3&4) may occur in up to 30% of patients with recurrent MM**

Vinorelbine

- **dose dependent**
- **usually reversible after drug discontinuation**

Paclitaxel

- **Incidence and severity is r/to cumulative dose $\geq 1100mg/m^2$**
- **at 250mg/m^2 q 3 week - grades 3 & 4 PN in occurs 20-35% pts**
- **conflicting studies that weekly regimes (80mg/m^2) are associated with increased neuropathy** (Seidman, et al 2008; Smith, et al, 2009)
- **3hr infusion found more neurotoxic than 24 hr** (Smith, et al, 1990)
- **symptoms usu improve / resolve within 3–6 mos after d/c of treatment, however, severe symptoms may persist longer**

Docetaxel

- **grade 3 & 4 occurs in <10% pts**
- **usually with cum doses > 600mg/m²**
- **has been associated with Trousseau sign**

Thalidomide, Lenalidomide

**Thalidomide**

- Causes a mainly sensory polyneuropathy, occurs in approximately $1/4$ of treated patients, forces dose reduction or d/c of drug in at least $10\%$ of pts.
- Conflicting evidence as to whether the incidence and severity of thalidomide neuropathy are more closely linked to the cumulative dose or to the duration of exposure (Argyriou, 2012)
- Neuropathy may temporarily worsen then usu improves after drug d/c

**Lenalidomide**

- A derivative of thalidomide
- Lower incidence of PN

Assorted Others

- **Ixabepilone**
  - Overall sensory neuropathy was reported in up to $71\%$ of exposed pts with severe (grade 3&4) between $6\%$ and $21\%$ (Argyriou, et al, 2012)

- **Eribulin**
  - Both sensory and motor neuropathy was seen, approx $35\%$ develop CIPN, severe (grade3&4) in $8\%$; Nearly $1/5th$ of neuropathy do not recover
  - PN was most common AE leading toward drug discontinuation (Miltenberg & Boogerd, 2014)

Symptoms of PN

- **Vary in severity**
  - From mild, numbness & tingling
  - To severe spontaneous painful burning
- **Constant or intermittent**
- **Ascending distal paresthesia and dysesthesia**
  - Paresthesia are usually symmetrical and affect the longest sensory nerves to the extremities in a stocking and glove-like distribution
- **All peripheral nerve types (sensory, motor, autonomic) can be affected**
  - Large myelinated sensory nerve fibers are most vulnerable (Smith, 2013)
- **Symptoms of autonomic neuropathy: constipation, erectile dysfunction, bladder retention, orthostatic hypotension may also be present**
- **Can see impaired balance from diminished plantar sensation & resultant altered proprioception** (Smith, 2013)
- **Alodynia, perioral and cold paresthesias**
- **Lhermittes sign**
**Case Study**

KR tolerated 3 cycles of modified FOLFOX well. He c/o grade 1 diarrhea which responded well to Imodium and dietary changes. He also c/o sustained numbness around his mouth and cold dysgeusia lasting 6-8 days after treatment. He notes tingling in his fingertips and his toes, not interfering with functioning.

**Oxaliplatin- Related Risk Factors**

- High cumulative doses of oxaliplatin are strongly associated with occurrence of chronic peripheral nerve damage (Beijers, Mols & Vreugdenhil, 2014)
- Sustained thermal hyperalgesia after the 3rd oxaliplatin cycle has been identified as an early predictor of chronic PN (Attal et al., 2009)
- Combinatory therapies with other neurotoxic agents increases risk (Argyriou, et al., 2012)

**Assessment**

- Grading scales:
  - FACT GOG-NTX
  - Shortened TNS
  - FACT-Taxane
  - PNS
  - CTCAE

**Pharmacologic Treatment**

- The best available data support a moderate recommendation for treatment with duloxetine (Lunn, Hughes & Willferm, 2014)
- Agents may be offered on the basis of data supporting their utility in other neuropathic pain conditions (Hershman, et al., 2014)
  - anticonvulsants (gabapentin, pregabalin)
  - tricyclic antidepressants (nortriptyline, amitriptyline)
  - compounded topical gel containing baclofen, amitriptyline HCL, and ketamine
  - opioids-oxycontin (Nagashima, et al., 2014)
- Chemotherapy dose/ schedule modifications

**Prevention**

ASCO: "There are no established agents recommended for prevention" (Hershman, et al., 2014)

ONS, PEP: "At present, no interventions for prevention of CIPN can be recommended for practice" (Visovsky, et al, 2009)

Cochrane Review: "In summary, the present studies are limited by the small number of participants receiving any particular agent, a lack of objective measures of neuropathy, and differing results among similar trials, which make it impossible to conclude that any of the neuroprotective agents tested prevent or limit neurotoxicity of platinum drugs" (Albers, 2014)
Case Study cont’

- For his PN, K.R was prescribed pregabalin (lyrica mg.....
- Despite this, he continued with peri-oral numbness, and although his tingling was improved, he developed difficulty with buttoning his shirt buttons
- His oxaliplatin dose was decreased 20%

Non-Pharmacologic Treatment

- ONS PEP: “Currently, the only interventions that can be recommended for nursing practice are education and support to preserve client safety” (Visovosky, et.al, 2009)
- Occupational and rehabilitation referrals
  - Large handles eating utensils, walkers, canes, foot braces
  - Exercise, pool therapy
  - Heat, cold or massage therapy
- Cognitive & Behavioral modification (guided imagery, relaxation techniques for pain control)

Non-Pharmacologic Treatment

- Education
  - Report S&S ASAP
  - Reduce water heater temp
  - Remove clutter, scatter rugs
  - Wear shoes with soles
  - Avoid walking in poorly lit areas
  - Wear gloves when gardening, dishwashing
  - Avoidance of cold liquids, use scarves/gloves
- Support groups

Case Study

M.J is 44 yr old female seen in f/u 6months after completing tx for breast ca
- underwent lumpectomy with radiation and 8 cycles CMF, now maintained on tamoxifen
- married, 3 children, ages 14, 15 & 19
- works 12 hrs/ week at local gift shop
- WBC 6.4, plt 390, hgb 9.4, comp WNL, no menses since starting chemotherapy
  c/o fatigue, “I’m always scattered” losing her car keys regularly, forgot to pick up her husband at the airport
  “I think I still have chemo brain”

Chemo Brain/Chemo Fog

- a neurotoxicity... form of cognitive dysfunction
- an adverse effect of cancer and cancer treatment
- a spectrum of cognitive deficiencies: memory, processing speed, and executive function seem to be most vulnerable
- can interfere with patients’ ability to resume their pre-cancer lifestyle & negatively impact QOL, ability to perform ADLs, affect work performance, caring for and socially interacting with family members (Janeltsis, et.al, 2011)

Symptoms of Chemo Brain

- fatigue
- lack of focus
- mental confusion
- inability to concentrate
- inability to organize daily activities
- loss of memory and memory lapses
- decreased mental clarity
- trouble concentrating and maintaining attention
- trouble remembering details, names and common words
- trouble multi-tasking and finishing certain tasks
- trouble learning new skills and slower thinking and processing (Talker, 2014)
Research Proving Connection

  - Randomized mice to IP mts/5FU or saline: chemo mice performed worse on cognitive tests
- Breast ca: Jansen, et al. 2008
  - pts who rec’d adjuvant chemo reported more cognitive problems than pts who did not have adjuvant therapy
  - pts who received adjuvant therapy were significantly more likely to be classified as cognitively impaired on standardized tests
  - emotional well-being (determined by a standardized measure of QOL), did not differ according to receipt of adjuvant chemotherapy
  - the risk of cognitive impairment is substantially increased for high-dose chemotherapy pts compared to pts in the standard-dose chemo and control groups
- Other cancers: CRC, Breast, Prostate, Ovarian

Research Imaging Studies

- Brown, et al. 1998- Breast ca pts demonstrated MRI white matter abnormalities in women undergoing high dose chemo with auto transplant
- Saykin, Athles & McDonald, 2003- 12 long term breast ca and lymphoma survivors-MRIs revealed significant abnormalities in white & gray matter compared to age matched healthy controls
- Silverman, et al. 2006- PET scans- 16 breast ca pts who rec’d chemo 5-10 yrs previous (some with tamoxifen too) demonstrated significant functional changes (decreased metabolism in the frontal cortex, cerebellum, and basal ganglia) Pts treated with tamoxifen + chemotherapy had decreased metabolism in basal ganglia compared with women treated with chemotherapy alone
- Abraham, et al. 2008- 10 patients with breast ca measured white matter integrity and concluded that adjuvant chemotherapy for breast cancer affects normal-appearing white matter in the genu of the corpus callosum and that this is related to the cognitive deficits graphomotor speed experienced by patients
- Deprez et al. 2012 studied 16 breast ca pts with matched controls- revealed sig decrease in frontal, parietal & occipital white matter tract integrity correlating with decreased attention, pros & memory
- Lagos & colleagues (ASCO abstract) studied PET scans of 128 pts with breast ca; analysis revealed a statistically significant link between reductions in regional brain metabolism and symptoms of chemo brain (Bradbrook, 2103)

Research Pre-Existing Cognitive Impairment

- Wefel, et al. 2004- 18 breast ca pts: before the start of systemic therapy, 33% of women in the current cohort exhibited cognitive impairment.
- Athles, et al. 2008- Stage 1-3 breast ca pts were more likely to be classified as having lower than expected cognitive performance prior to adjuvant treatment as compared to stage 0 pts and healthy controls.
- Jansen, et al. 2011- 71 breast ca pts- cognitive impairment was found in 23% of women prior to chemotherapy -anxiety, depression, fatigue, hemoglobin levels, menopausal status, and patient’s perception of cognitive function were added to the model to determine any association with the cognitive measures.
- Lange, et al. 2014- prospective study of 123 elderly EBC patients (70 ± 4 years) 41% presented objective CD, (> expected in healthy pop. norms)

Rename Chemo Brain?

- Dysfunction can be related to factors such as:
  - anesthesis/surgery
  - individual vulnerability
  - tx induced menopause/ hormonal therapy
  - depression
  - stress
  - fatigue
  - cancer itself
    - hyo ca is independently associated with likelihood of self reported memory problems (Jean-Pierre et al. 2012)
    - Cognitive changes noted with other non-malignant dx

Possible Etiology of Dysfunction

- direct neurotoxic effects:
  - disruption of blood-brain barrier, possible chemical toxicity
  - injury to cerebral parenchyma, neurons, oligodendrocytes (synthesize myelin) & microglia
  - defects in neural repair and altered neurotransmitter levels
  - immune dysregulation and/or release of cytokines (inflammatory factors)
  - reduced metabolism and oxidative stress
  - vascular injury and blood clotting in small central CNS vessel

Case Study

M.J reports she doesn’t understand why she is so scatterbrained.

Her friend Diane had the same breast cancer treatment as MJ and she does not have these issues- and she is 8 years older
Other Risk Factors

- specific regimes/ drugs
- metabolic disorders
- infection/sepsis
- medications
- comorbid conditions- vascular disease
- depression/anxiety
- sleep disorders
- nutritional deficits
- education/ intelligence level
- genetics polymorphisms

Assessment

- Imaging?
- Standardized tools?
- Neuropsychological battery?
- Assess for confounding factors/medications/substances
- PE- evaluate for focal neuro deficits
- Elicit from patient:
  - dysfunction specifics:
    - level of alertness, attention span, capacity to concentrate
    - onset and trajectory over time
  - track memory problems

Interventions

- Attempt to modify confounding factors
- Consider referral for specialized neuropsychiatric evaluation
- Occupational therapy may be appropriate
- Cognitive training-ONS: “likely to be effective” (Von AH, Jansen & Allen, 2014)
- Consider use of psychostimulants (methylphenidate or modafinil) NCCN: “as last line of therapy in survivors for whom other interventions have been insufficient” (Barranger, et al, 2014)
- Physical activity
- Education
  - cancer-associated cognitive dysfunction is NOT a progressive neurologic disorder

Practical Measures

- Organizational strategies:
  - Use memory aids/ outlook reminders, notebook or planners
  - Making and using a list
  - Set up and maintain routines
    - Place for commonly lost objects
    - Sleep / Activity routine
  - Avoid multi-tasking
  - Decrease workload- allow for downtime
  - Encourage relaxation/ use of stress management skills
  - Limit alcohol and other substances that alter cognition
  - Encourage allowing help