Managing Long Term Side Effects of Chemotherapy: The Road to Recovery

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Plan of Action

- Chemotherapy related cognitive dysfunction
- Peripheral neuropathy
- Weight gain
- Early menopause
Chemo Brain

- A problem with many names
  - chemotherapy related cognitive dysfunction
  - mild cognitive impairment (MCI)
  - chemo fog / chemo brain
- Impaired memory and difficulty with concentration
- Incidence varies widely from study to study (16-65%)
Chemo Fog – Common Symptoms

- Has this ever happened to you?
  - Forget things that you usually have no trouble recalling (memory lapses)
  - Difficulty concentrating
  - Difficulty remembering details like names, dates, etc
  - Difficulty with multi-tasking
  - Taking longer to do things
  - Unable to find the right words to finish a sentence

- But what causes chemo fog?
  - Can chemo get inside the brain?
Blood Brain Barrier

- Consists of a network of tightly sealed cells in the brain
- Capillaries in brain pump foreign molecules away from the brain while allowing others (glucose, insulin) in
- Not well understood HOW chemotherapy results in ‘chemo fog’
What causes chemo brain?

- Exact mechanism unclear
- Potential causes:
  - Chemotherapy direct effect
  - Decreased estrogen levels
  - Cytokines (small messenger chemicals in the bloodstream)
    - IL-2, IL-1, TNF-alpha, IL-6,
  - Depression, fatigue, anxiety
  - Clotting in small blood vessels in brain
  - Genetics
  - Other medications might contribute to slower cognitive function (pain medications, steroids, anti-nauseants, etc)
Other Contributing Factors

- Medications
- Patient age
- Stress
- Anemia
- Sleep problems
- Depression
- Tiredness (fatigue)
- Hormone changes or hormone treatments
- Other illnesses, such as diabetes or high blood pressure
- Anxiety or other emotional distress
What we know about chemo fog

- It appears to be a real phenomenon
- For most people, chemo brain develops during chemotherapy (as early as first or second cycle) and seems to improve over time after stopping treatment
- Seems to resolve in most patients when re-tested at 1 and 2 years, however, in some patients, cognitive dysfunction persisted even at 10 years following chemotherapy
- Not yet known which chemotherapy drugs are more likely to lead to chemo fog although 1 study suggested that anthracyclines are not as bad as CMF chemotherapy
- Patients notice very subtle changes compared to their friends/family who may not notice this as much
Are there studies on chemo fog?

- Inagaki et al (2007) found that breast cancer patients exposed to adjuvant chemotherapy had small volumes of grey and white matter on functional MRI of the brain.
- 106 breast cancer patients – 55 had chemo/51 did not.
- At 1 year following chemotherapy, prefrontal gyrus (decision-making), parahippocampal (STM to LTM) and cingulate gyrus (emotions, learning and memory) were smaller at 1 year.
- However, at 3 years, this difference disappeared between the 2 groups.
- Changes in brain correlated with worsening attention/concentration and memory.
Ongoing studies in chemo fog

- Functional MRI and PET scan imaging of brain pre and post chemotherapy
- Studies looking at effects of
  - EPO-alpha
  - Methylphenidate
  - Cognitive rehabilitation
    - Stress management and developing compensatory strategies
What can I do to manage chemo brain?

- Day-to-day coping
- Get a good night sleep
- Exercise and eat healthy
- Set up and follow routines. Try to keep the same daily schedule.
  - Use a detailed daily planner.
  - Serious planner users keep track of their appointments and schedules, “to do” lists, important dates, websites, phone numbers and addresses.
- Track your memory problems. Keep a diary of when you notice problems and the events that are going on at the time
- Try not to focus so much on how much these symptoms bother you.
- Exercise your brain (sudoku, crossword puzzles, etc)
Peripheral Neuropathy
Anatomy 101 - Nervous System

- Central nervous system
  - Brain and spinal cord
- Peripheral nervous system
  - Peripheral nerve fibers bring sensory information from environment into the central nervous system
- Some chemotherapy drugs can damage cells that make myelin sheath for nerve cells
Peripheral neuropathy

What are the symptoms?
- Numbness and tingling (pins and needles) in the fingers/toes (stocking/glove)
- Initially starts off as numbness, but can progress to a ‘burning’ feeling
- Can become quite painful as condition progresses and nerves become more damaged
- If neuropathy continues to worsen, can lead to motor dysfunction
  - Problems buttoning up shirt
  - Can’t pick up a coin off the table
Peripheral neuropathy

- Most commonly seen following administration of chemotherapy drugs:
  - Paclitaxel (Taxol) (dose dense AC/T)
  - Docetaxel (Taxotere) (TC, FEC/D)
  - Cisplatin or carboplatin (TCH)
- More pronounced in patients with pre-existing conditions:
  - Longstanding diabetes
  - Alcoholism or nutritional deficiencies (vitamin B12)
  - Carpal tunnel syndrome
Severity of Peripheral Neuropathy

- Grade O – no symptoms (normal)
- Grade I – numbness/tingling not interfering with day to day function
- Grade II – numbness interfering with function but not interfering with activities of daily living
- Grade III – numbness/tingling interfering with activities of daily living
- Grade IV – permanent sensory loss interfering with function (motor)
How common is it?

- Dose dense AC/T
  - 4% grade III neuropathy after chemo
- Symptoms usually reach their peak at about 4 months post-chemotherapy
- Neuropathy often improves over the next 6 months, but in some cases, may be irreversible
What can you do about it?

1) Tell your doctor (especially before and during chemotherapy)
   - Dose may be reduced if neuropathy clinically significant to avoid permanent dysfunction
2) Rule out other causes of neuropathy
3) Do any medical therapies work?
   - Cold gloves? – case report
   - Glutamine? - not currently recommended
   - Amifostine? – not recommended until further data avail
4) Avoid alcohol
Treatment of Peripheral Neuropathy

- Analgesics
  - Tylenol, anti-inflammatories (ibuprofen)
- Tricyclic antidepressants (TCA’s)
  - Amitriptyline, nortriptyline
- Anticonvulsants
  - Gabapentin, lyrica
- Treats symptoms, but does not reverse underlying damage to nerves
Practical Suggestions if You Have Peripheral Neuropathy

- Protect areas where sensation is decreased (example; do not walk around without foot wear). Wear thick socks and soft soled shoes.
- Extreme temperature changes may worsen symptoms.
- Wear warm clothing in cold weather. Protect feet and hands from extreme cold.
- Use care when washing dishes or taking a bath or shower; do not let the water get too hot.
- Use potholders when cooking.
- Use gloves when washing dishes, gardening.
- Inspect skin for cuts, abrasions, burns daily, especially arms, legs, toes and fingers.
Weight Gain
Weight gain

- Really??! Weight gain? I thought I would lose weight on chemo!
- Can be very distressing for many patients
- Average weight gain is 5-8 pounds although this depends on several factors:
  - Medications (e.g. steroids for nausea)
  - Nausea (crave comfort foods)
  - Menopausal status
  - Level of activity
  - Diet
Change in body composition

- Most women tend to gain more fat and lose lean muscle mass during chemotherapy.
- Going from pre to postmenopausal can drive this further as estrogen levels decrease leading to more fat accumulation.
- Most women tend to be less active during chemotherapy (muscle aches and pains).
- Some fluid retention with steroids and chemotherapy.
Weight gain and cancer recurrence

- If I lose the extra weight I gained from chemotherapy, can I decrease my chances of recurrence?
Helpful Hints

- During chemo
  - Don’t change your diet radically during chemotherapy

- After chemo
  - Eat a balanced diet (plenty of fruits, vegetables, and whole grains)
  - Avoid white bread, white flour, refined sugar
  - Get physically active (20 min per day) to maintain your muscle bulk and tone and cardiovascular health
  - Ask to see a dietician
  - Support groups (you are not alone in this)
Early Menopause
Early menopause

- Premenopausal women who undergo chemotherapy are at risk for early menopause
- Chemotherapy affects rapidly dividing cells, including ovaries
- Ovaries may not return to normal function
- This can lead to premature menopause and the symptoms associated with reduced levels of estrogen
Hot flashes

- Aside from chemotherapy resulting premature menopause and hot flashes, medications may exacerbate this
  - Tamoxifen
  - Aromatase Inhibitors (letrozole, anastrazole, exemestane)
- Lifestyle modification
- Medications (venlafaxine or other SNRI’s, gabapentin, clonidine)
Vaginal dryness

- Can be a particularly troublesome symptom following premature menopause
- Vaginal lubricants such as replens
- Try to avoid topical estrogens such as estrin or estrogen creams given potential risk of systemic absorption
- Discuss with your oncologist
- Referral to Advanced Practice Nurse at JCC
Recap

- Chemobrain is a real phenomenon – remember the helpful tips to keep your mind sharp!
- Peripheral neuropathy can be a problematic symptom months after chemotherapy is complete – several agents used to treat symptoms
- Weight gain – possible benefits of diet, exercise on reducing risk of breast cancer recurrence
- Early menopause symptoms may be distressing and referral to JCC postmenopausal symptom management clinic may be helpful resource
Thank you for your attention!