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Finding the Missing Pieces: Comprehensive Cerebellar Assessments with Cytarabine Administration

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FINDING THE MISSING PIECES: COMPREHENSIVE CEREBELLAR ASSESSMENTS WITH CYTARABINE ADMINISTRATION



CASE STUDY:

Stan (name changed for confidentiality) was a 60 year old male admitted to the hospital with relapsed AML in the summer of 2015 after two years of remission. Stan was first diagnosed three years earlier and subsequently underwent chemotherapy and stem cell transplant with no known neurotoxicity. In 2015, re-induction chemotherapy 7 + 3 with Idarubicin and Cytarabine was completed in the hospital. Prior to treatment, Stan was walking independently with no functional deficits. Current standard of practice at the St. Cloud Hospital for cerebellar monitoring included having the patient sign his/her name daily.

- Day 1 Post Chemo at 0800: Patient reported increased bilateral lower extremity weakness with walking. IV fluids were initiated. No deficits noted in signing of the name.
- Day 1 Post Chemo at 2300: Patient is now unable to void, requiring ongoing straight catheterizations. Stan reports inability to walk, has significant decreased sensations in bilateral lower extremities. Still able to sign his name without deficits noted.
- Day 2 Post Chemo at 0800: Neurology consulted. Stan reports weakness has reached his bilateral upper extremities. MRI of lumbar, thoracic, cervical and head all negative. Findings all suggest acute paraplegia and painful peripheral neuropathy as a result of acute cytarabine neurotoxicity.
- Within several weeks of ongoing therapy, patient had regained all bowel/bladder function and most function and strength in bilateral upper and lower extremities.

DISCUSSION:

- There were several unknown variables to explain why Stan experienced probable neurotoxicity with non-high dose therapy. No data was available regarding therapies received prior to transplant. There is a possibility the patient had exceeded the recommended lifetime dose limit and/or had a previous neurotoxic reaction in the past, making him more susceptible.
- The case was discussed with Kathleen Rieke, MD of Neurology. Dr. Rieke recommends any patients receiving Cytarabine in ANY strength be assessed for neurotoxicity, including assessment of motor strength and function of all four extremities every shift.

WHAT IS CYTARABINE?

Cytarabine (Ara-C) is an anti-metabolite chemotherapy agent used to treat acute leukemia and/or refractory non-hodgkin's lymphoma. The drug is cell-cycle specific and inhibits DNA synthesis thus halting cell division. The dose-limiting toxicity of this drug is NEUROTOXICITY, especially when given in high-dose concentration (Szoch & Kaiser, 2015). This is caused by a widespread loss of Purkinje cells in the cerebellum (Lee & Wen, 2015). With high-dose cytarabine administration, there is a high concentration of drug that crosses the blood-brain barrier in the cerebral spinal fluid with 50% of the chemotherapy still in the plasma concentration (O'Leary, 2004).

WHEN IT BECOMES NEUROTOXIC

- Patient's receiving high-dose cytarabine have a 7-28% incidence of developing neurotoxicity; high doses include $\geq 1\text{-}3\text{g}/\text{m}^2$ (Lee & Wen, 2015).
- 10-25% of patient's develop neurotoxicity when the cumulative dose exceeds 30 grams in a lifetime (Lee & Wen, 2015).
- There is a 60% incidence of cerebellar toxicity recurrence for patient's who showed previous toxicity (O'Leary, 2004).
- Other risk factors include decreased hepatic and/or renal dysfunction and/or age >60 years old (Szoch & Kaiser, 2015).
- Symptoms usually develop 2-8 days after initial dose and may persist 3-10 days after discontinuation of therapy (O'Leary, 2004).
- For those >50 years old, symptoms may persist for more than 30 days even if therapy is stopped (O'Leary, 2004).
- Up to 30% of patients may not regain normal cerebellar function (O'Leary, 2004).
- Symptoms include gait and balance disturbances, alterations in fine motor skills, memory loss, peripheral neuropathy and/or seizures (Lee & Wen, 2015).

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NURSING CONSIDERATIONS

A study conducted at the University of Maryland Greenebaum Cancer Center found that one in four nurses felt there were widespread inconsistencies with cerebellar assessments. One of every two nurses felt the current assessment was incomplete and the patient may be suffering as a result. (Szoch & Kaiser, 2015)

There has to be a better way!

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COMPONENTS OF A COMPREHENSIVE ASSESSMENT

- Nurses need to have the means to accurately and consistently assess and document neurological changes noted with Cytarabine administration. The assessment tool must be comprehensive, covering several areas of cerebellum function. Assessments should be completed every shift and/or prior to each dose of cytarabine (Brown & Hall, 2010) (O'Leary, 2004).
- The initial assessment and first dose of High-Dose Cytarabine should be completed during the day time hours to promote patient satisfaction and ensure accuracy of assessment (Szoch & Kaiser, 2015).
- The assessment should be relatively short in time (approximately 5-10 minutes or less); especially with the increased demands placed on hospital-based nursing care. Tool should be easy to understand for nurses at all skill levels and integrated into current charting practice (Brown, 2010).
- *If the patient fails any aspect of the assessment, the upcoming dose should be held and the oncologist notified immediately.* If the patient is to receive medications that may alter gross motor skills, such as narcotics, a cerebellar assessment should be completed prior to administration to ensure accuracy of the assessment (O'Leary, 2004).
- Crucial components of cerebral and cerebellar functional assessments include: (Brown, 2010) (Szoch & Kaiser, 2015)
 - ✚ **Gait and balance:** Watch for signs of arrhythmia or asymmetry. This is best completed by patient walking heel to toe in straight line.
 - ✚ **Handwriting:** Most often monitored by signing his/her name; preference to utilize a skill that usually doesn't change over time.
 - ✚ **Speech Pattern:** Have patient state name, date, time, and situation.
 - ✚ **Body Tremors:** Monitor for tremors while standing or walking.
 - ✚ **Nystagmus:** When present, this will cause involuntary rapid eye movement when attempting to focus on an object.
 - ✚ **Point - to - Point Testing:** Patient's finger directly makes contact with observer's finger and his/her own nose several times as observer moves throughout patient's vision field.
 - ✚ **Rapid alternating hand movements:** Patient will pat hands on thighs in rhythmic motion as fast as possible without losing coordination.
 - ✚ **Romberg Test:** Measures three sensory systems in cerebellum to maintain stability, including vision, proprioception and vestibular sense. To complete successfully, patient will stand with feet together and eyes closed for 5-10 seconds. (Brown, 2010) (Szoch & Kaiser, 2015)

SAMPLES OF ASSESSMENT TOOLS

Functional Test	Baseline	Date	Date	Date	Date	Date	Date
Nystagmus Lateral twitching of patient's eyes 4 or more times when tracking slow-moving objects.							
Finger-nose-finger Patient touches an index finger to your finger (held in front of your face, patient's nose, and back to your finger 5 times).							
Thigh pat Patient pats palms of hands on thigh as quickly as possible for 10 seconds.							
Romberg Patient stands with feet together and closes eyes.							
Tandem gait evaluation Patient walks heel-toe for minimum distance of 10 feet.							
Gait observation Patient walks a minimum of 10 feet, turns, and walks back toward observer.							

(O'Leary, 2004)

Test	Normal	Abnormal
Nystagmus: Involuntary eye movement Ensure baseline documentation	Absent	Present
Speech Pattern	Clear	Prolonged separation of syllables (scanning speech)
Handwriting: Take a blank page or use the template below and add patient ID label. Have patient write a sentence or two which may include information such as person, place, time and situation. Each entry should be dated and timed. This page is to be ultimately scanned as part of the permanent medical record.	Unchanged from baseline	Deviation from baseline
Point-to Point Testing: Patient takes his/her index finger and his/her nose. Move your finger about as this task is performed.	Successful completion	Unsuccessful completion
Rapid Alternating Hand Movements: Patient strikes one hand on the thigh, raises the hand, turns it over, and then strikes it back down as fast as possible. Repeat a few times.	Successful completion	Unsuccessful completion
Gait	Steady, upright	Unsteady, tilted, shuffling walk
Body Tremor When Standing or Walking	Absent	Present
Romberg Test Have patient stand with feet together and eyes closed for 5-10 seconds without support.	Balance maintained	Balance not maintained

(Brown & Hall, 2010)

- Test
- Normal
 - Abnormal
- Nystagmus
- Absent
 - Present
- Speech pattern
- Clear
 - Prolonged separation of syllables
- Handwriting
- Unchanged from previous assessment(s)
 - Deviation from previous assessment(s)
- Point-to-point testing
- Successful completion
 - Unsuccessful completion
- Rapid alternating hand movements
- Successful completion
 - Unsuccessful completion
- Gait
- Steady, upright
 - Unsteady, tilted, shuffling
- Locus of control
- Alert, oriented to person, place, time and situation
 - Not alert or oriented
- Body tremor when standing or walking
- Absent
 - Present
- Romberg test
- Balance maintained
 - Balance not maintained

Figure 1. The Cerebellar Neurologic Assessment

(Brown, 2010)