Cancer Effects on Fertility

FERTILITY PRESERVATION

-OOCYTE CRYOPRESERVATION
-EMBRYO CRYOPRESERVATION
-OVARIAN TISSUE CRYOPRESERVATION
-GNRH TREATMENT

Menopause and menopausal symptoms

- Hormonal and Non-hormonal therapy
- Discuss the concept of “personalized medicine”

Most Common Malignancies in Women of Reproductive Age

- Hodgkins/NonHodgkins Lymphoma
- Leukemia
- Thyroid Cancer
- Breast
- Melanoma
- Gynecologic Malignancy-cervical, ovarian and endometrial

Treatments

- Surgical
- Chemotherapy
- Radiation
- Combination of any/all of the above
- Immunotherapy

Factors influencing fertility after Treatment

- Timing and extent of surgical intervention
- Age at the time of diagnosis
- AMH-antimullerian hormone
- Type and duration of chemotherapy
- Radiation-is always gonadotoxic
- There is no way to predict with any certainty if a patient will maintain reproductive function after treatment

Preservation Options

- Embryo cryopreservation
- Oocyte/Egg Cryopreservation
- Ovarian tissue Cryopreservation

Embryo Cryopreservation

- Partner or Donor Sperm
- We need 2 weeks for the process
- Prior to freezing the embryos can be tested for cancer causing genes
- Can be frozen indefinitely
- It is more successful to freeze embryos than to freeze eggs-this is probably because we have a lot more experience freezing embryos than eggs

Oocyte /Egg Cryopreservation

- Best if there is no partner or unstable relationship
- This still takes 2 weeks to accomplish
- They would still need In Vitro Fertilization once the eggs are thawed. Freezing process hardens the Zona or “egg shell”. Requires ICSI to fertilize.
- Success requires more oocytes-I tell people that they will need 15-20 eggs per 1 live birth
- Remember this is an insurance policy. The vast majority of patients will never use their eggs.

Ovarian Tissue Cryopreservation

- Much more common in Europe
- Ovarian cortex is frozen
- Usually 1 ovary is removed and sliced into thin strips
- Tissue is replaced via laparoscope in peritoneal pockets
- Usually survives 2 years and then is repeated
- There are no reported pregnancies in patients >38
- Very few pregnancies between 35-38
- Only option for urgent need or very young

Ovarian Tissue Cryopreservation

- The biggest concern is the possibility of reintroducing cancer back into the patient
- Although most grafts only last 2 years there is a reported case of one lasting 7 years
- Pregnancy rates are really unknown because usually one ovary is left in situ and it is impossible to know whether the ovary or the graft was where the ovulation occurred

Pregnancy Data 2022

- Embryo Cryo Live birth rate 35.3%. SAB rate 16.9%
- Oocyte Cryo Live birth rate 25.8%. SAB rate 9.2%
- Ovarian tissue Live birth rate 32%. SAB rate 7.5%
- Remember only a very small Percentage of patients come back to use their frozen embryos/eggs/tissue
- They may not need it, don't desire it, are deceased

GnRH Agonists

- MOA-Increases gonadotropin secretion which overloads the receptors leading to desensitization and suppression of gonadotropins secretion
- The question is- does it reduce the risk of ovarian insufficiency?
- Most studies agree that in premenopausal patients with breast cancer it does reduce the risk of OI- 14.1%in treated vs 30.9% in untreated
- Zong et al 10.3% treated and 44.5% untreated. Treated patients also had a longer disease free interval.

GnRH Agonists

- 60% of all Breast Cancers and 74% of triple negative breast cancers express the GnRH receptor
- Lambertino et al showed that ER negative patients has a longer disease free interval and overall survival when treated
- PROMISE Trial- no difference in ER- and ER+ survival when treated with GnRH agonists vs controls

Menopause and Menopausal Symptoms

- Specifically as it relates to cancer patients
- Each woman has a unique set of factors that influence their benefits and risks of treatment
- This “Personalized Medicine” approach allows us to tailor treatment to each patient’s specific disease process as well as to their needs
- Considerations include blood pressure, BMI, diabetes, smoking history, family history, type of cancer, receptor status and most important are quality of life issues

Symptoms to Discuss and Address

- Hot Flashes/Flush
- Vaginal and Sexual Symptoms
- Urinary Symptoms
- Mood/Depression
- Sleep Disorders
- Cognitive Issues
- Bone Density

Hot Flashes-Vasomotor Instability

- Affects 80% of all women in menopause
- Decreased estrogen leads to disinhibition of neurokinin 3 receptors which ultimately leads to dysregulation at the thermoregulatory center in the hypothalamus
- Heat loss is caused by skin vasodilation which results in hot flashes, chills and sweating
- Therapies are directed at these physiologic phenomena

Options for Therapy

- Hormonal- Estrogen and Estrogen/Progesterone

- Non-hormonal
- OTC-black cohash, primrose oil, flaxseed, Vit E, red clover, etc
- OTC options have been shown to be no more effective than placebo
- Prescription meds include Paxil, Veozah, Gabapentin, Clonidine, Oxybutynin

Paroxetine-Paxil

- MOA-selective serotonin reuptake inhibitor
- Metabolized in the liver
- Side effects include nausea, dry mouth, sexual dysfunction, anorgasmia, sweating and suicidal ideation
- In order to ameliorate VMS you have to push the dose which unfortunately increases the side effect profile

Fezolinetant-Veozah

- Fezolinetant is a neurokinin 3 receptor antagonist which directly targets the kisspeptin-nerokininB neurons to ameliorate VMS. Dose 45mg/day.
- Essentially blocks action at the thermoregulatory center in the hypothalamus
- This is contraindicated in patients with cirrhosis, significant liver metastasis and renal disease
- Side effects include abdominal pain, diarrhea, insomnia, hot flashes and liver dysfunction
- Recommended to follow liver functions q 3 months

Gabapentin

- GABA analogue used for seizures and nerve pain
- Use is off label
- Best to use for severe night VMS
- Major side effect is drowsiness/dizziness
- Initial dose is 300 mg/day with increase to TID

Clonidine

- Agonist of the alpha 2 adenoreceptor
- Decreases blood pressure and heart rate by relaxing arteries
- Side effects are dry mouth, anxiety, lightheadedness, constipation and depression
- Starting dose is .1 mg day. Increase to .3 mg/day
- Increasing the dose increases the side effects

Oxybutynin

- Used to treat overactive bladder by competing at the postganglionic muscle receptor thus relaxing the smooth muscle
- In 2 clinical trials it was effective in treating VMS
- This is also off label and could be considered in patients refractory to other treatments.
- Dosage is 5 mg BID-TID. Can increase to QID.
- Side effects are nausea, stomach pain, constipation, diarrhea, headache, weakness and sleep disturbances

In Summary

- No solutions that fit all patients
- Need to assess each patient and their unique set of issues
- Use a “Personalized Medicine” approach to tailor their therapy