Increased Levels of Leptin in the Absence of Obesity, with Ovarian Cancer

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Introduction

Ovarian cancer:
- Highest mortality rate of the various cancers that are unique to women
- Difficult to diagnose

Obesity:
- One-third of the world’s population has an excess of adipose tissue
- Precursor to many diseases; recognized as a risk factor for endometrial cancers

Leptin:
- Hormone that is stored in adipose tissues
- Primary function – send signals to the brain to aid in the body’s maintenance of weight

Obese persons have an excess of leptin in the blood which causes the hormone to be less effective as they develop leptin resistance. Studies suggest that obese women with higher levels of leptin may contribute to keeping ovarian cancer cells alive. Understanding more about the biochemical mechanisms for the development of ovarian cancer can provide more predictors, which in turn can increase the likelihood of an earlier diagnosis and increase the survivability of the disease.

Question

Leptin levels are directly correlated to obesity and obesity is related to ovarian cancer but, will normal-weight individuals with high leptin levels be more susceptible to developing and maintaining ovarian cancer?

What is Ovarian Cancer?

- **Diagnosis**: ultrasound, MRI and other tests that are not routine
- **Symptoms**: bloating, increased pelvic mass, fullness in abdomen, etc.
- **Number of Stages**: four
- **Cell types that cause Ovarian Cancer**: surface epithelium (most common & lethal), germ or stromal cells (rarest & least aggressive)
- **Mechanisms for Development/Progression**: not well understood, to date

What is Leptin?

- **Hormone**
- **Released by adipose tissue**
- **Signals to the brain when the body is full**
- **As body fat accumulates, leptin levels drastically increase**
- **Obese persons develop leptin resistance**
- **Desensitization to the hormone**
- **Studies suggest leptin metastasizes ovarian cancer cells in obese**
- **Unknown whether leptin metastasizes ovarian cancer cells in normal-weight women**

Research Studies

**What is the known relationship between obesity and cancer?**

- Per 10-units relative risk
  - BMI 30-24.9 = 2.53
  - BMI > 40 = 6.25

**Obesity, Leptin and Ovarian Cancer?**

Obese women with serous ovarian cancer and higher leptin levels had poorer prognosis

Figure 1: The above picture shows, what healthy ovaries look like without cancer on the left. The subsequent diagrams show the progression of the stages of ovarian cancer from I – IV.

Figure 2: The above diagram was adapted from The Influence of Leptin on the Process of Carcinogenesis by Modzeleska et. al. This diagram is a schematic representation of the procarcinogenic effects of leptin.

Tracking Clinical Outcomes

- Being overweight – worse survival and progression-free times
- Certain types of ovarian cancer breed differential expression of Ob-Rb (leptin receptor) and higher circulating leptin levels (found overweight group)
- Ovarian cancer cell lines express the active form of the leptin receptor (Ob-Rb) in overweight patients
- High leptin and Ob-Rb mRNA expression in certain ovarian cancer types – correlated to an overall poorer survival rate
- Obese women will have either a higher risk for developing ovarian cancer or a poorer prognosis

Analysis

- Normal-weight women = lower risk for ovarian cancer than obese women
- Obese women with high leptin = high risk for ovarian cancer
- Normal-weight women = better prognosis than obese women
- Outcomes due to obesity not leptin

Conclusion

- Learning more about mechanism for ovarian cancer could increase survivability
- Future research opportunity – compare leptin levels in women with varying BMI and the severity of their symptoms
- Future research opportunity – look into some other biochemical mechanisms that relate to obesity and ovarian cancer (look for correlational overlap)
- Discover more preventative methods, early diagnostic tools and symptom management techniques
- Save hundreds of thousands of women

Bibliography

