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Editorial Open Access

Gene-Environment Interaction and Risk of Ovarian Cancer

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Editorial

Ovarian cancer is the fifth most common type of cancer and second common cause of death among women in the world today. It is now recognized that cancer is actually a complex array of different diseases, with different genetics and different behaviors. Understanding the genetic alterations that are typical of cancer, there is a need to develop a completely revolutionarized research and a leading cause of gynecological disorder. As per statistics of Globocan 2008 and IARC, ovarian cancer is fifth most common cancer as well as fifth most common cause of cancer related mortality and morbidity in females. Nearly 28,080 new cases and 19,558 deaths per year with ovarian cancer have been reported from India as one of the example of developing country. Moreover, every fifth death from ovarian cancer is from India, this is very alarming signal and need of hour is to mitigate this menace.

Ovarian cancer is a silent killer in women and is the result of series of DNA alteration in a single cell or clone of that cell which leads to the loss of its normal function, aberrant or uncontrolled cell growth and often metastases. The symptoms are late to get revealed and vague and hence the survival rate is very low. The incidence of gynecological disorders is on rise in western countries as well as in developing countries. So established risk factors alone cannot provide explanation for current rising trend as multitude of other factors are involved in cause of cancer indicating need of new paradigm to be explored to understand the etiology of ovarian cancer. Moreover, along with the established risk factors, various cancers have also been reported in human studies to be associated with pesticides such as phenoxy acid herbicides, 2,4,5-trichlorophenoxyacetic acid, lindane, methoxychlor, toxaphenealdrin, dieldrin, endosulfan, Hexachlorocyclohexane (HCH), and 1,1,1-trichloro-2,2-bis(4-cholorophenyl) ethane (DDT). In India, forty percent of all pesticides used are Organochlorine Pesticides (OCPs). These compounds are stable, lipophilic and have half-life in decades. Hence, these compounds become concentrated in environment and have been detected continuously in human due to environmental exposure. OCPs owe their carcinogenic property due to their estrogen mimicking action. They act as an antagonist or agonist causing disruption in endocrine function hence these compounds are known as endocrine disruptors or xenoestrogens. The aberrant signal transductions orchestrate and the molecular events may manifest the etiology of ovarian cancer.

The OCPs have been implicated in plethora of diseases like, asthma, allergy, obesity, diabetes, hypersensitivity, fetal development and neurological disorders. Its role in various cancers has also started to get unravel indicating the role of environmental contaminants has long been suspected to be associated with cancer due to extensive use of OCPs and may support to be one of the reason of pathogenesis. The role of OCPs in many cancers like breast, testis, endometrial, prostate, etc. has been suggested predisposing factor but little light has been shed to unravel the association of such exposure with etiology of ovarian cancer. Hence it has remained mired in mystery and required investigation to establish the role of OCPs in genesis of ovarian cancer.

Ovarian cancer begins with transformation of cells that comprise the ovaries, including surface epithelial cells, germ cells, and the sex cord or stromal cells, and is generally hormone-dependent. Despite a great deal of research, the etiology of most hormone-related cancers remains a mystery. It seems that the hormones are necessary for the growth of cancerous tissues, but their involvement in the earlier steps of carcinogenesis is still unclear. The dominant theories of carcinogenesis invoke mutations as the ultimate cause of cancer, but most hormones are not strong mutagens. More recently, the field of epigenetic has begun to throw new light into the process that might contribute to hormonal cancers. It appears that mis-timed exposure of tissues to hormonally active agents can interfere with the subtle processes of gene silencing, and that disruption of these processes might be one factor that predisposes towards cancer. Exposure to cells having estrogen receptors to OCPs causes aberrant proliferation resulting in cellular control mechanism and homeostasis grinding to halt, and now its destinies lies for the pathogenesis of ovarian cancer. Several other ancillary processes such as genetic predisposition, altered immune surveillance, inflammation and subsequent oxidative stress may foster ovarian cancer and contribute to its pathogenesis. Several environmental factors continue to surface as potentially instrumental in explaining the wide global variation in the incidence and biological behavior of various tumors including tumor of ovary. One form of defense against cancer development involves a series of genes whose role is to metabolize and excrete potentially toxic compounds and to repair subtle mistakes in DNA. Much laboratory and epidemiological research over the past decade has concentrated on the identification of these genes and an assessment of their role in cancer etiology. Of particular interest has been whether the risk of cancer associated with a particular environmental exposure differs with respect to functionally different polymorphisms of these genes, i.e. gene–environment interaction. A possible hypothesis of gene environmental interaction for etiology of ovarian cancer following xenobiotic exposure is shown in Figure 1.

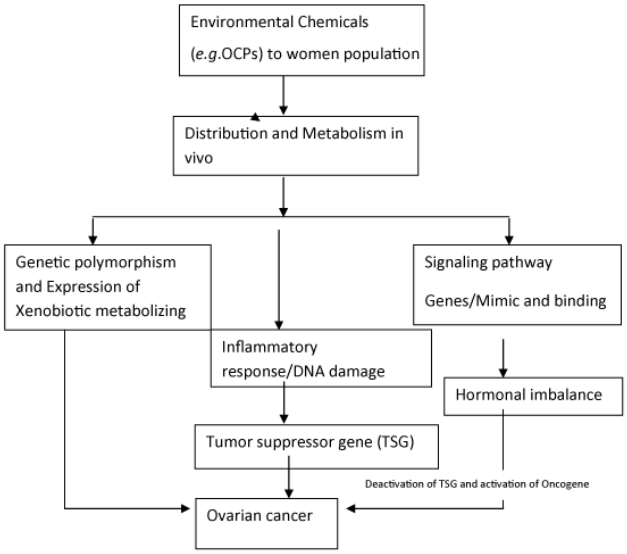

Figure 1: Organochlorine pesticide: Possible pathway leading to ovarian cancer

In conclusion, the etiology of ovarian cancer is still unclear. Interactions of environmental factors, interactions of genes, and gene-environment interactions may play an important role in the development of ovarian cancer. A large number of studies have been conducted for numerous genes and also for all common cancer sites, although results have been very inconsistent and therefore inconclusive. There is also much confusion about the meaning of 'gene–environment interaction', what type of studies should be conducted to pinpoint the mechanism and also how it should be measured. Furthermore, the very purpose of those studies is not clear; are they attempting to identify high-risk individuals, or are they simply trying to further understand the cancer process? Hence, further investigations are required to identify association of OCP with the incidence of ovarian cancer and high risk phenotypes. Such investigation will provide an evidence of gene-environment interaction and high risk phenotypes in the pathogenesis of ovarian cancer and will also highlight the importance of individual genetic susceptibility to ovarian cancer following exposure to environmental toxins.