The Most Prevalent Form Of Cancer In Females

Breast cancer is the most prevalent form of cancer in females. There were 1.67 million cases reported worldwide in 201212.

The patient is diagnosed with invasive ductal carcinoma (IDC) which is considered rampant of all cancers. This form of cancer begins in the cells which line the milk ducts or lobules of the breast and infiltrate into the surrounding tissue1. Generally, cancer can be the result of DNA changes or mutations that can be inherited, which increases the risk of development5. However, DNA mutations linked to breast cancer are predominantly acquired2; this is significant for the patient as she has no previous medical history of breast cancer. Mutations in DNA can consequent in the mutations of genes and potentially alter the balance between controlled cell growth and death as normal function is distorted2. Risk also increases with elderly (e.g. post-menopausal) women, especially in individuals who experience a later onset of menopause5. This patient's case of IDC is acknowledged as hormone receptor-positive following immunocytochemical methods that observed the tumor mass as both estrogen receptor (ER)-positive and progesterone receptor (PR)-positive I.e. the cancer cells are growing in response to estrogen and progesterone steroid hormones.

Oestrogen is a steroid hormone that facilitates the growth, reproduction, and development of many mammalian tissues. It can be synthesized in extragonadal organs and tissues such as the mesenchymal cells of adipose tissue in the breasts, and its physiological actions moderated by its corresponding receptors, ER? and ER?3. These receptors are ligand-activated transcription factors that act by binding to DNA in the nucleus of cells10, both receptors uniquely contribute to carcinogenesis and tumor progression7. ER? (encoded by ESR1 gene located on chromosome 6q2510) is a key endocrine regulatory protein in ER-positive breast cancer, thus a primary indicator of endocrine responsiveness. Its structure is composed of a DNA-binding domain, an N-terminal AF1 domain, and a C-terminal ligand-binding region9. Oestrogen has high affinity and specificity for ER? where binding can activate a genomic pathway that initiates coregulator growth factors and G-protein coupled signalling4. The hormone is pivotal in cell cycle progression as it binds with cyclin-dependent kinase 4/6 (CDK4/6) to facilitate the G1 to S phase transition through cyclin D1 (CD1) activation. Dysregulation of this pathway is associated with tumorigenesis e.g. overexpression of CD14. Naturally, ER? is localized in the cytosol of cells where steroid hormone estrogen can passively diffuse through the cell membrane and bind specifically to the receptor. Post-binding, the complex can translocate into the nucleus and interact with the C-terminal ligand-binding domain of the receptor to induce a conformational change that initiates gene transcription10,11. RNA-polymerase and specific cofactors are recruited which bind to ER at the promoter through estrogen-response elements (ERE), enabling RNA-polymerase to generate a copy strand of the target genes. This mRNA strand is then exported from the nucleus to nearby ribosomes where it can be translated to proteins. Estrogen receptor promoter B associated factor 1 (ERBF-1) is critical for the transcription activity of promoter B in ER?-positive breast cancer cells; it is exclusively expressed in cells expressing ER? mRNA transcribed from promoter B and plays an important role in the expression of the ER? gene in breast cancer.

Progesterone receptors are also ligand-activated transcription factors. It is a vital regulator of

transcription and in initiating signal transduction pathways that are connected to proliferative signaling in breast cancer. PR-A and PR-B are the two prevalent isoforms of PR, made from the same gene but with differing translation sites29. Isoforms are typically expressed in response to ER?-mediated transcriptional events30; therefore, it is not surprising that the patient is both ER-positive and PR-positive. PR-B is significant in PR-positive cases as it acts in normal mammary gland development and has been expressed in proliferating cells. Post-binding with progesterone, the receptor experiences a conformational change and translocates into the nucleus where it can interact with coregulator molecules through progesterone-response elements (PRE)31. The receptors act with mitogenic protein kinases and cell-cycle mediators to elicit regulation of PR target genes and proliferative responses.