Second Malignancy - A Chance or Probability!

Pages with reference to book, From 320 To 321

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With the decline in infectious diseases, cancer is becoming a major health problem in the developing world with its morbidity, complications, and mortality. Number of cases identified and reported are increasing due to better health education, awareness, improving diagnostic facilities and availability of these facilities to a greater proportion of the population.

The last two decades have witnessed significant and remarkable advancement in terms of screening[1], early detection, prevention[2] and treatment of cancer. A number of effective cytostatic and cytotoxic agents are becoming available which have better tolerability, biOavailability and utilization[3]. Surgery has become more applicable with early detection at a stage of local and regional disease. The impact of newer iniinunomodulators, genetic manipulations, growth factors, receptor amplification/downregulation, biological response modifiers, endocrine manipulation and many newly emerging modalities are encouraging but need to be evaluated in detail to be inducted in clinical practice[4-6]. The cumulative effect of all these advancements are a higher cure rate, a prolonged disease free survival, a more sustained remission and an improved life expectancy.

The improved life expectancy of cancer patients has brought newer dimensions into the focus. A new dimension worth mentioning and seeking attention is development of a second and a third malignancy[7], of a different histology at a different site/organ, subsequently over the years. This risk is ten times higher than normal age matched controls[8]. The SEER study (Surveillance, epidemiology and end results data) showed 1168, 910 tumours in 1092, 234 patients indicating 76,696 patients (7.0%) having more than one malignant tumour[9].

The development of a second malignancy can be spontaneous or triggered by cytostatic/cytotoxic chemotherapy[10], radiation therapy[12] immunotherapy[13-16] or endocrine manipulation[17]. These may have a direct effect or mediated through genetic alteration. The genetic makeup of certain individuals make them more susceptible to development of either first or subsequent malignancy. This is also explained by the close association of genetic diseases with tumours[18] The precise mechanism by which second cancer develops is not clear but exposure to a shared mutagen, abnormalities in oncogene activation and aberrant expression of tumour suppressor genes are implicated[19,20]. Environmental and life style factors like smoking are also believed to be contributory in development of a subsequent malignancy[21,22]. No definite etiologic factor or mechanism could be implicated in a number of cases of second malignancies[23]. Second malignancy is commonly associated with survivors having a haematologie malignancy in childhood[24]. Commonly found second malignancies are osteosarcoma, soft tissue sarcoma, breast cancer, leukaeniia. thy roid cancer, CNS tumours, mclanoma, non-melanomatous skin cancers, renal cancer and lymphomas[25,26]. Unusual tumours like squamous cell carcinoma, as young as in 12- 18 years old children, are also reported as second nmlignancy[27,28], The time interval elapsed between the first malignancy and the development of a subsequent malignancy is highly variableand has been reported as short as three years to as long as over thirty years[26,29-32].

The risk of a second malignancy varies between 0-15% at 10 years and 5-21% at 20 years after first malignancy[21,24,29,33-35]. A much higher risk of 22% at 5 years for a second (almost always fatal) malignancy, is being reported with head and neck cancers treated with conventional modalities[36]. The elevated risk of a second cancer remains relatively constant over tune, but the absolute risk increases substantially[24]. It is reported that patients with stage 111 andIV disease have an increased risk of

second malignancy regardless of age suggesting the significance of tumour related biological factors[37]. A further impairment in patients immune status is reported after a diagnosis of second malignancy, making them even more susceptible to all sorts of infection and further malignancies[37,38].
The persons or families with genetic diseases are at a higher'risk. They need to be identified and a long follow up is indicated. A better understanding of environmental and life style associated risk factors and their possible influences is indicated. Very unusual tumours can develop at unusual age and it should not be overlooked. The tumour pairs which are closely related should be identified for further workup. The tinie interval between the first and subsequent malignant tumours can not be predicted so continued surveillance of long term survivors of childhood cancer is stressed and descriptions of unexpected tumour pairs may target families for studies on genetic abuormalities[23]. Second malignancy is almost always fatal so its early recognition is highly desirable. Most patients in the developing world are diagnosed at stage III or IV, having a much higher risk of subsequent cancer development. Late diagnosis and treatment makes very few survive long enough to have a second neoplasin, but with better diagnosis and treatment there is going to be a greater number of cases of second malignancies.

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