

Second Malignancy - A Rare Phenomenon

Pages with reference to book, From 345 To 347

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The development of a second malignancy, in the same patient, with a different histologic type and/or morphological site is an increasingly appreciated phenomenon in cancer patients. Factors incriminated for this development include genetic makeup of an individual¹, cytotoxic chemotherapeutic intervention for the first malignancy², radiation therapy³, endocrine therapy⁴ and immunotherapy⁵. Second malignancy is more frequently associated with a first haematological malignancy in childhood⁶. The time difference between the development of two malignancies and the actual risk of developing subsequent second malignant neoplasms highly variable⁷⁻⁹, yet it is directly proportional to the clinical stage of first malignancy at the time of initial diagnosis¹⁰. The precise mechanism by which a second malignant neoplasm develops is not yet fully understood but exposure to a shared mutagen, abnormal oncogene activation, or an aberrant expression of tumour suppressor genes are usually implicated". This study reports the local experience of second malignancy in a teaching hospital at Kamchifmrn 1991-1996.

malignant neoplasm, at a different site/organ and having a different histopathological variant proven on biopsy, were included in the analysis. Tumours exhibiting a mixed or totally undifferentiated/anaplastic histology were excluded from the study and so were the cases having an incomplete information or without documentary evidence of diagnosis.

A total of 2417 cases of malignant neoplasm with a proven histopathological diagnosis were seen from 1991-1996 with a male to female ratio of 1.2:1 (1359 males and 1058 females). Second histologically proven malignancy was found in 31 (1.3%) cases. No case of a third or subsequent malignancy was found in this series. The youngest patient was 23 years of age and the oldest 72 years. Majority of the cases (77.4%) were between 35-64 years of age with a mean age of 50.6 years and a male to female ratio of 1.6:1.

Average interval between the occurrence of first and second malignancy was 2.5 years (range 7 months to 7 years). In 58% cases, one of the two malignancies was either haematopoietic or lymphoid in origin (Table I). The tumours were representative of almost all the morphological sites.

Twenty-seven cases had treatment for the first malignancy (Table II), which included radiotherapy, chemotherapy, surgery, endocrine therapy or any combination. Twenty-six percent cases had received radiotherapy for their first malignancy and sixty-one percent were given chemotherapy either alone or as combined modality treatment.

Comments

The identification and reporting of malignant tumours is increasing due to awareness and availability of better diagnostic tools¹². The improved life expectancy of cancer patients, due to advances in management, have also led to increased appreciation of their subsequent problems while in remission. One of these is a much higher risk of developing a second or subsequent malignancy in these patients^{13,14}.

A 1.3% frequency of second malignancy found in this study is significantly lower than 21% reported in other series^{6,7,9,15}. The tumour pairs showed that a substantial number of cases were having lymphoid or haematopoietic origin as the first or subsequent malignancy, which is in accordance with other studies⁶. These cells of lymphoid or hematologic origin have a proportionately higher number of cells

inproliferative/mitotic phase in the body, where they are easily influenced by the mitogenic or mutagenic stimuli. This is also so because lymphoid and haematological malignancies are relatively easily diagnosed and many have a much better prognosis/survival (like chronic myelogenous/lymphoid leukemia orlymphoma). The second malignant tuour, in the present study, showed a wide spectrum of morphological distribution and tissue of origin, which is similar to other reports¹⁶.

The time interval between the development of two malignant neoplasms is variable^{7,17}. In this study the interval was relatively less than others. Patients with malignant tumours do not survive longerm our country due to multitude of reasons, this reduces the chances of a subsequent malignancy and only those cases of second malignancy are seenwho develop first malignancy ofalow anaplastic grade or if the second subsequent malignant tumour develops early. That is why the time interval for the second malignancy development is reflected as shorter in this study. This scenario is bound to change with more successful treatment and increase in life expectancy after the first malignancy.

The actual risk of a second, always fatal malignancy is significantly higher after the first malignancy^{6,7,9,15}. This risk increases if first malignancy was of higher anaplastic grade with a clinical stage III/IV, implicating many yet unknown immunological and biological factors^{10,18}. The development of subsequent malignancy may be spontaneous or triggered by genetic, immunological, cytotoxic drugs, radiation, growth factors, immunomodulators, or endocrine manipulations. The exact and precise mechanism is yet to be explored in depth. A lot of genetic workup, genetic analysis like BRCA1 and BRCA2 especially in high risk population groups and family pedigree mapping are required at least in high risk population to understand the basis of this high familial or individual susceptibility.

Malignant tumours in our part of the world are generally occurring at a younger age and tumours at younger age in colored races tend to be more aggressive and anaplastic as are already reported so¹⁹⁻²² and are of advanced clinical stage at the time of initial diagnosis¹⁹⁻²³. There is more aberrant immune system due to a higher rate of infectious diseases, there is late diagnosis and non-availability of appropriate and timely treatment^{1,18-20}. All this when translated, indicate a logically higher expectancy of second malignancy in our population which is likely to be seen in future with improved life expectancy due to integration of more successful treatment protocols in routine clinical practice.

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