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Original Research Article

Genetic study in 50 cases of carcinoma breast: a prospective study

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ABSTRACT

Background: Carcinoma breast is the leading cancer among urban Indian women. The main aim of our study was to focus on the chromosomal aberrations in patients of carcinoma breast.
Methods: Fifty case of carcinoma breast admitted in our institute between June 2009 to December 2011 were studied.
Results: In our study premature centromere division was seen in 50% patients while chromatid break was seen in 60% patients. 20% patients had an acenteric fragment. Break in the same locus in both the chromatids of a single chromosome i.e. chromosomal break was seen in 1 patient in 1p, 1q, 2q, 12q chromosome. Terminal deletion was seen 31 times in different chromosomes with most common being in 2q, 3q, 2p, 1q. Chromatid gap was seen in 24 chromosomes most common being in 1q, 2q, 3q, 6p while dicentric chromosomes was seen in 33.33% of patients.
Conclusions: Most common chromosome involved in chromosomal aberrations were 1q (CHTB, CHRB, CHTG); 2q (CHRB, TER del, CHTG); 1p, 12q (CHRB); 3q (TER del).

Keywords: Carcinoma breast, Chromosomal aberration

INTRODUCTION

In India breast cancer is the most common cancer followed by cervical cancer.[1] Worldwide it is the second most common type of cancer after lung cancer and fifth most common cause of cancer death.[2] Extensive work has revealed numerous relationship of the disease with age at menarche, age at menopause, parity, lactation but as such no clear picture is yet apparent. Prognosis is influenced by size of primary carcinoma, lymph node involvement, distant metastasis, grade of tumour, histological type of tumour, oestrogen/progesterone/Her2nu receptor, aneuploidy. Genetics play an important role in the development of carcinoma breast. About 5 to 10% breast cancers cases are thought to be hereditary. Having a first degree relative with breast cancer almost doubles a woman's risk. Having two first degree relatives increase her risk about 5 fold. In 2003, genetic analysis of systemic breast cancer progression suggested that in breast cancer, tumour cells disseminate in a far less progressed genomic state than previously thought, and that they acquire genomic aberrations typical of metastatic cells, thereafter, challenging the widely held view that the precursors of metastasis are derived from the most advanced clone within the primary tumour.[3] The aim was to study the changes in chromosomes in carcinoma breast patients.

METHODS

The study was conducted on 50 patients of carcinoma breast, in department of surgery, at Sri Guru Ram Das Institute of Medical Sciences and Research, Amritsar in conjunction with Guru Nanak Dev University from June 2009 to Dec 2011. All patients with cytological or histopathological proof of breast carcinoma were included in the study. Patients who had received neoadjuvant chemotherapy were excluded from study.

After thorough work up of the patient, 10ml of blood was drawn intravenously with disposable 22g needle and was transferred to heparinised vacutainer. Chromosomal aberrations study was done from peripheral blood lymphocyte culture using standard protocol by Moorhead et al and modified as per laboratory conditions. G banding was done according to Benn et al techniques with modifications according to laboratory conditions. Well spread metaphases were photographed using digital camera and the photographic prints thus prepared, were used for karyotyping. Karyotypes were analysed using ISCN-2005 (International System for human Cytogenetic Nomenclature).

RESULTS

Chromosomal aberrations study was done in 50 cases out of which 20 cases had culture failure. Rest 30 patients showed mutations. The detailed results are as follows

Number of cells studied (total metaphase studied= TMS) and number of total aberrations studied (TAS)

100-200 cells were studied in metaphase for 17 patients while 50-100 cells were studied in 9 patients. In 4 patients 20-50 cells were studied.

Table 1: Number of cells studied for metaphase and the range of aberrations seen.

TMS		TAS	
No. of cells studied for metaphase	**Frequency (no. of patients)**	**Range of aberrations**	**Average**
20-50	4	4-16	10
50-100	9	17-36	26.5
100-200	17	6-43	28

Premature centromere division (PCD)

Premature centromere division (PCD), a chromosomal alteration, is regarded as a phenomenon manifested as a loss of control of centromere separation and segregation and is characterized by distinctive separation of chromosome chromatids earlier than usual during interphase of mitosis. The number of patients with PCD was 15 out of 30 (50%) (Figure 1).

Chromatid break (CHTB)

Where the breaks and re-joins affect only one of the sister-chromatids at any one locus. This was seen in 18 patients (60%) out of 30 (Figure 2.).

CHTB relation with chromosome

Most common chromosome involved in CHTB was CHR.1q followed by 3p.

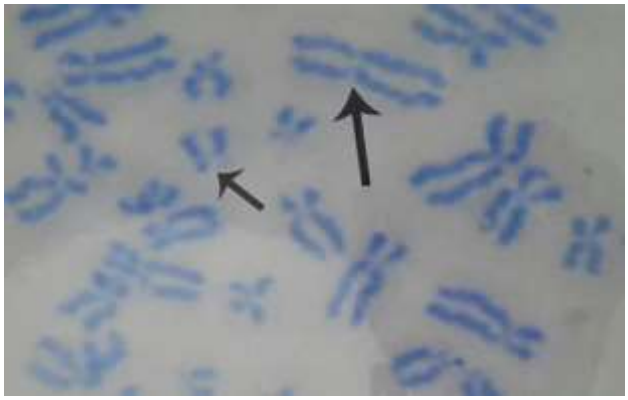

Figure 1: Metaphase showing premature centromere division.

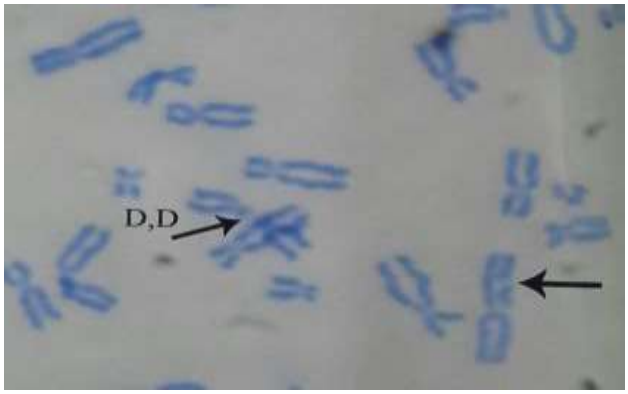

Figure 2: Metaphase showing acrocentric association and chromatid break (CHTB 1p).

Table 2: Number of chromosomes with chromatid break.

Chromosome	No. of chr+for CHTB	%
1p	4	9.7
1q	10	24.3
2p	1	2.4
2q	1	2.4
3p	5	12
3q	2	4.8
4q	3	7.3
5p	1	2.4
5q	3	7.3
6q	1	2.4
7q	1	2.4
10q	1	2.4
12q	2	4.8
13q	1	2.4
16q	2	4.8
Others	3	7.3
Total CHTB aberrations on CHR	41	100

Acenteric fragment

20% patients had acentric fragment positive that is the chromosome didn't have a centromere.

Chromosomal break (CHRB)

Which means break in the same locus in both the chromatids of a single chromosome. This was seen in 1p, 1q, 2q, 12q with 25% frequency in each of them.

Table 3: Chromosomes with chormosomal break.

Chromosome no.	Chrb+	%
1p	1	25
1q	1	25
2q	1	25
12q	1	25
No. of chr	4	100

Terminal deletion

Deletion involving the terminal part of a chromosome and leading to an adhesive terminus. Most commonly involved chromosome showing terminal deletion were 2q, 3q, 2p, 1q.

Table 4: Frequency of terminal deletions in various chromosomes.

Chromosome no	Frequency	%
1p	0	0
1q	3	9.6
2p	4	12
2q	5	16
3p	1	3.2
3q	5	16
4q	1	3.2
6p	0	0
6q	2	6.4
9q	1	3.2
11p	1	3.2
12p	0	0
12q	2	6.4
17q	1	3.2
18q	1	3.2
Others	4	12
CHR with TER del	31	100

Chromatid gap (CHTG)

A chromatid gap is a discontinuity in a single chromatid with minimal disalignment. This was Most commonly present on chr no. 1q, 2q, 3q, 6p.

Dicenteric chromosome was present in 33.33% patients

A dicentric chromosome is an abnormal chromosome with two centromeres. It is formed through the fusion of two chromosome segments, each with a centromere, resulting in the loss of acentric fragments (lacking a centromere) and the formation of dicentric fragments (Figure 3).

Table 5: Frequency of chromatid gaps seen in different chromosomes.

Chromosome no	Frequency	%
1p	0	0
1q	5	20.8
2p	0	0
2q	3	12.5
3p	2	8.3
3q	3	12.5
4p	1	4.1
4q	0	0
5q	1	4.1
6p	3	12.5
6q	0	0
9q	1	4.1
12q	1	4.1
Others	4	16.6
No. of chr with chtg	24	100

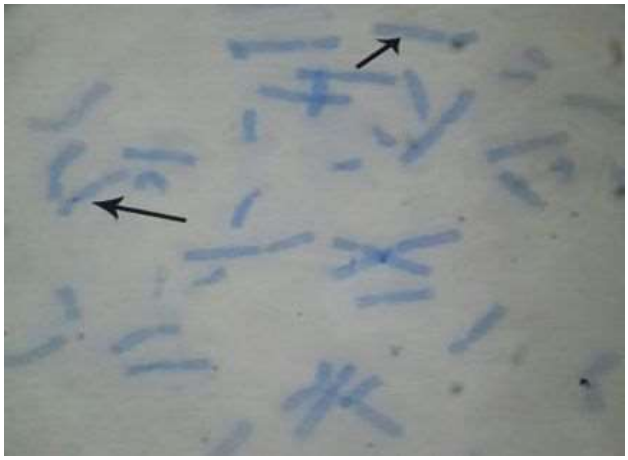

Figure 3: Metaphase showing chromatid break (CHTB) and dicentric chromosome (DIC).

Complete centromere separation was present in 13.33% cases.

DISCUSSION

The most common chromosomal aberration in our study was chromatid break (60%) followed by premature centromere division and dicenteric chromosome. The most common chromosome affected by structural aberration in our study was chr no. 1 followed by 2, 3, 6, 12.

Majority of recent studies also found involvement of CHR no 1, 3, 6. Thompson F et al study showed involvement of CHR no 1 an 6. Analysis of specific chromosome segments revealed that the most consistent tendency was over representation of 1q, 3q and 6p.[4] Cervantes et al in his study showed that the most common non-random chromosomal abnormalities in breast cancer involved were 1, 3, 6, 11, 16 and 17.[5]

Malamoumitsi showed variety of genetic changes, none of them was unique or specific in all the studied cases. The most consistent regions of gain were 1q, 20q and 8q while of loss were 3p and 6q.[6] In study by tren J et al, most often structural rearrangements included 1, 7, 11 and 6 (24.7%, 10.3%, 9.1% and 7.0% breakpoints respectively).

In our study premature centromere division was seen in 50% patients while chromatid break was seen in 60% patients. 20% patients had an acenteric fragment. Break in the same locus in both the chromatids of a single chromosome i.e. chromosomal break was seen in 1 patient in 1p, 1q, 2q, 12q chromosome. Terminal deletion was seen 31 times in different chromosomes with most common being in 2q, 3q, 2p, 1q. Chromatid gap was seen in 24 chromosomes most common being in 1q, 2q, 3q, 6p while dicentric chromosomes was seen in 33.33% of patients.

CONCLUSION

Most common chromosome involved in chromosomal aberrations were 1q (chromatid break, chromosomal break, chromatid gap); 2q (chromosomal break, terminal deletion, chromatid gap); 1p, 12q (chromosomal break); 3q (terminal deletion).

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Ethical approval: The study was approved by the institutional ethics committee

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