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Familial Palmoplantar Keratoderma, Malignancy and Sister Chromatid Exchanges

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SUMMARY

Sister chromatid exchange (SCE) study was done in six Bedouin patients (3 females and 3 males) from 2 unrelated families, with different palmoplantar keratoderma (MIM 144200 and 148400). To elucidate the validity of SCE study in distinguishing cancer - prone form noncancer-prone forms, the frequencies of SCEs among the 6 Bedouin patients was compared with that among 5 normal control cases.

INTRODUCTION

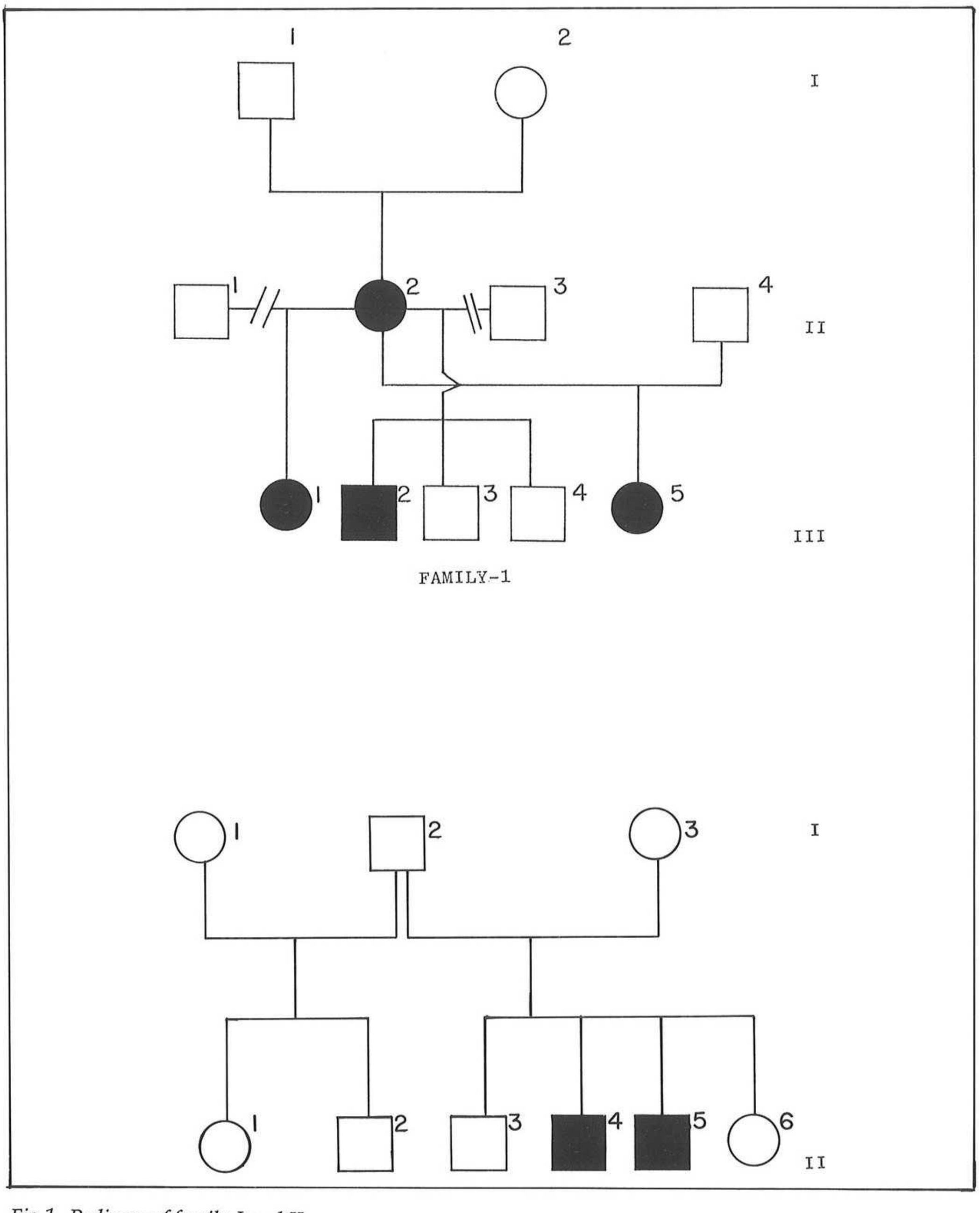
Various forms of familial palmoplantar keratosis (EPPK) have been described. They differ in their clinical manifestations, mode of inheritance and include both "nonsyndromic" and "syndromic" forms and the cancer-prone cases.[1-8] We report here the results of SCE study of 11 cases including the 6 Bedouins with FPPK and 5 phenotypically normal control cases.

Materials and Methods

Family-I. A 40-years-old Beouin female with diffuse FPPK (148400) was ascertained in Jahra Regional Liaison-Community Genetics Programme with 3 affected children, from 3 unrelated husbands (Fig.I : III, 1, 2 & 5). Their ages were 16, 11 and 1 year respectively. The mother was worried regarding the prognosis.

Family-II. Two Bedouin brothers, aged 2 years and 2 weeks respectively, were recently described with patchy eczymatosis skin lesions followed by palmoplantar keratodermia and raised IgE.[9]

Peripheral blood of the 6 Bedouin patients with FPPK and 5 appropriate normal control cases were cultured for 72 hours in RPMI 1640 culture medium supplemented with 10% fetal calf serum, streptopenicilline and photohaemoagglutinin (PHA). Cultures were incubated at 37oC for 72 hours and 5 Bardu (10-25 ug/ml) is added to the cultures. The cells were allowed to complete 2 cycles of DNA replication before harvesting. The metaphase chromosomes prepared after arresting the cell division by colcemid and fixing in methanol:acetic acid (3:1) is stained with Hoechest-33258 fluorescent stain and exposed to a source of ultraviolet light and then stained with giemsa (FPG technique).[10] One sister chromatid shows bright staining and the other shows dull staining (Fig.2). Along the sister chromatid exchange points are seen as bright and dull stained chromatids



FAMILY-1

Fig.1 Pedigree of fmaily I and II

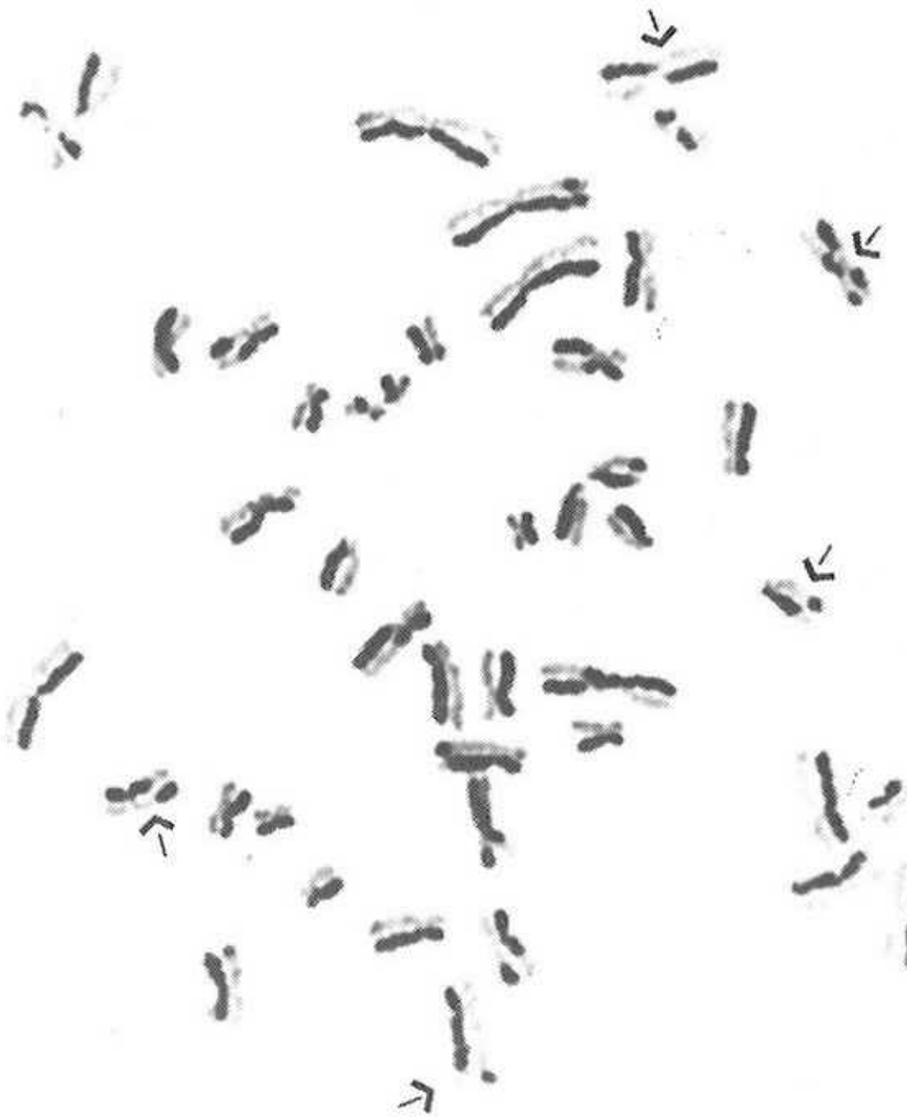


Fig.2 A metaphase plate showing differential staining of sister chromatid exchanges (SCEs). Arrows indicate sites of chromated exchanges, as visualised by FPG staining technique.

indicating exchange of DNA. The baseline SCE frequency in human tissues usually varies in the range of 10 + 5 per cell. The frequency of SCE in the 2 unrelated families were compared with that of phenotypically normal control cases (Table 1) The frequency of spontaneous chromosome aberrations, and SCE were analysed to find out the possible causal-relationship or predisposition to malignancy and DNA repair machanism. There was no increase in the frequency of spontaneous chromosome aberrations as compared to controls.

Discussion

The SCE technique is used as a tool of choice for the detection of mutagenic/carcinogenic effects on cells, and in the detection of neoplastic/clastogenic changes in dividing cells. The 6 Bedouins, patients with FPPK were tested by SCE technique to elucidate the possibility of being of the cancer-prone form. Data were compared with that of the 5 appropriate normal control cases.

It is well known that a variant of FPPK (MIM 148400 and 148500) is prone for late onset esophageal carcinoma. In Liverpool, Howell-Evans et al4 reported [2] kindred who were restudied by Harper et al [3]. They added 2 families each with one case of esophageal cancer with tylosios. In Oxford, shire and Allison[7] described another family with multiple members having this association. In 1980, Yesudian et al[9] studied genetic tylosis with malignancy in a South Indian Pedigree. Age of onset of tylosis appears to be a feature distinguishing the cancer-prone from the non-prone forms. Thylosis is late onset in the form with esophageal cancer[5].

Our observations of sister-chromatid-

Table 1. Frequency of SCE in FPPK (Family A & B) and controls

Subjects	No of cells	No of SCE Total/per cell		Range No. of SCEs per cell
Familial Palmoplantar Keratodermia				
Family-I				
II-2.	30	222	7.4	2-16
III-1	30	333	11.3	6-15
III-2	30	285	9.5	5-15
III-5	30	344	11.46	5-20
Family-II				
II-4	30	373	12.43	6-13
II-5	30	312	10.40	5-9
Control cases				
a. Male	30	275	9.17	2-16
b. Female	30	308	10.26	3-6
c. Female	30	251	8.37	3-14
d. Female	30	266	8.87	3-14
e. Female	30	263	8.77	2-14

exchange analysis in the two families, provides an "indirect" evidence of "non-proneness" to malignancy, in two families.

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