disease, make very difficult to believe that this relation is casual.

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Analysis of p53 gene mutations in parapsoriasis

Editor

The histological diagnosis of the initial stages of Mycosis Fungoides (MF) have not yet been established by exact morphological criteria.[1] The borderline between parapsoriasis and MF is not clear due to non-specific changes in the early stages of MF. The underlying molecular changes which may occur during progression or transition from parapsoriasis and early MF to advanced stages have not yet been clarified either.[2] However, abnormalities of cell cycle control genes and well-defined tumour suppressor genes may contribute to the disease pathogenesis and progression.

The p53 gene plays an important role in the control of cell death and proliferation, inducing cell cycle arrest and/or apoptosis in response to various cellular stress, and alterations of the p53 gene are commonly associated with malignant transformation.[3] The p53 gene mutations, one of the most common genetic alterations in human cancers, have been described in several types of haematologic malignancies.[4] By contrast, only a few studies have focused on p53 abnormalities in various categories of T-cell lymphomas and to the best of our knowledge, parasoriasis has not been studied so far.[5–10] Studies of p53 protein expression in primary cutaneous T-cell lymphoma have shown to be increased in the late stages of the disease. This prompted us to investigate the incidence of p53 gene mutations in parapsoriasis and its role in the pathogenesis.

Ten biopsy samples were obtained from the lesional skins on buttock, trunk and proximal limb sites but not from habitually sun-exposed skin of 10 patients formerly diagnosed as parapsoriasis. Haematoxylin and eosin stained slides were reviewed to confirm the diagnosis parapsoriasis. Female/male ratio was 4/6 and the mean age of the patients was 44.5 years (range 15–67 years). Four of the patients had a history of previous PUVA (psoralen plus ultraviolet A) therapy and three had UVB therapy. One patient had a history of topical corticosteroid ointment administration.

Genomic DNA was isolated using standard methods (Proteinase K incubation and phenol-chloroform extraction).

Exons 5, 6, 7 and 8 of the p53 gene were amplified by polymerase chain reaction (PCR) and heteroduplex analysis (HDA) with a sensitivity of 80–90% in small DNA fragments was used to investigate the point mutations in the central hydrophobic core of the molecule coded in exons 5 to 8 where most mutations seemed to be clustered.

The primary sequences of p53 genes were as below:
E5F 5′-TCA ACT CTG TCT CCT TCC TCT TCC-3′
E5R 5′-CTG GGC AAC CAG CCC TGT CGT-3′
E6F 5′-TTG CTC TTA GGT CTG GCC CC-3′
E6R 5′-CAG ACC TCA GGC GGC TCA TA-3′
E7F 5′-TAG GTT GGC TCT GAC TGT ACC-3′
E7R 5′-TGA CCT GGA AAT CTA CTG GGA CGG-3′
E8F 5′-AGT GGT AAT CTA CTG GGA CGG-3′
E8R 5′-ACC TCG CTT AGT GCT CCC TG-3′

Table 1 Review of the related data in the literature

Author	Diagnosis	Method	p53 mutation
Li *et al*.[5]	6 MF-tm stage	PCR/SSCP	0/6
McGregor *et al*.[6]	17 MF-tm stage	PCR/SSCP	6/17
			5/6 UVB type
	12 MF-plaque stage		0/12
Kapur *et al*.[7]	37 early MF	PCR/TGGE	1/37 polymorphism
			1/37 mutation
	17 MF-plaque stage		2/17 polymorpism
	4 MF-tm stage		1/4 polymorphism
Petit *et al*.[8]	4 MF-tm stage	DGGE	1/4
Dereure *et al*.[9]	24 MF-patch stage	PCR/SSCP	0/44
	17 MF-plaque stage		
	3 MF-tm stage		
Current study	10 parapsoriasis	PCR/HDA	0/10

SSCP, single stranded conformational analysis; DGGE, denaturing gradient gel electrophoresis; TGGE, temperature gradient gel electrophoresis.

Samples were HDA positive by visual inspection if two bands migrated apart from the wild-type bands. None of the patients were found to have p53 gene mutations by HDA.

Molecular analysis of p53 has been reported in only eight times in MF on an overall number of 141 patients from patches to tumour stage disease including cases transformed in large cell, more aggressive lymphoma (Table 1).[5–10] Relevant mutations have been found in only 15 patients, a significant number of them (6 of 15) occurring at dipyrimidine sites and resulting in a mutation spectrum strikingly similar to that usually found in non-melanoma skin cancer and characteristic of DNA damage caused by UVB radiation. Kapur *et al*.[7] also reported p53 gene polymorphism in the early stages of the MF. It is of interest that most reported MF cases showing p53 mutations are from advanced tumour stages or transformed aggressive large cell lymphoma but opposite to expected it is likely a rare, sporadic and rather late event associated with tumour progression.[4–8] p53 mutation was very rarely detected in patients with patch or plaque stages; our results revealing the lack of p53 gene mutations in parapsoriasis largely confirm these data. In our study, four of the patients had histories of previous PUVA therapy and three of them UVB therapy. It is noteworthy that no p53 gene mutations of UV type were detected in these cases. We cannot rule out mutations outside exons 5 to 8 which were not explored in this study. However, the majority of p53 gene mutations reported so far affect the central core domain involved in sequence-specific DNA binding and mutations outside exons 5 to 8 appear to be rare, representing less than 10% of p53 gene mutations in human tumours including lymphomas.[10]

We conclude that although the number of our patients is not sufficient to make strict comments, p53 gene mutations do not seem to have a role in the pathogenesis of parapsoriasis.

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