

Discordance Between DNA Analysis and the Clinical Picture in a Case of Xeroderma Pigmentosum

Sir,
Xeroderma pigmentosum (XP) is a rare (2 cases/1,000,000 newborns), recessively transmitted genetic disease caused by the defective repair of UV-induced DNA damage. We can observe clinical signs and symptoms of photosensitivity, early skin ageing, depigmentation and a high incidence of basal cell carcinomas (BCC), squamous carcinomas (SCC) and, rarely, of melanomas. XP may also be associated with ocular disorders, deafness and neurological diseases (1, 2).

CASE REPORT

We present here the case of a 76-year-old woman affected by XP, which is characterized by discordance between the results of DNA analysis and the clinical picture. Upon anamnesis, she referred the onset of multiple lentigines, naevi and solar keratoses since childhood. She regularly sunbathed at the seaside and in the tropics without being sunburnt. She denied any hereditary disease and other dermatoses.

When she was 54 years of age she underwent surgical excision of a BCC followed, 10 years later, by the excision of 2 more BCC. In 1993, aged 73, the patient came to our department for the first time for removal of a melanoma on the right cheek and a BCC on the forehead. The history of many *de novo* occurring cutaneous cancers and the finding of many actinic keratoses on the photoexposed skin lead to a XP being suspected. Medical examination, routine blood tests, chest X-ray and abdominal ultrasound findings were all normal. No eye, auditory or neurological disorders were found.

A biopsy from photoprotected skin was taken to investigate the response of fibroblasts to UVC damage (2, 3). A small reduction in the results of an unscheduled DNA synthesis assay (UDS) and in a colony-forming ability test (CFA) were demonstrated. These results were considered compatible with a diagnosis of XP.

In 1995, we found a melanoma (III Clark level, 0.7 mm Breslow) and a SCC on the lower third of the right leg, and two BCC on the face. The patient is followed-up in our department to ensure early diagnosis and treatment of any new skin cancer.

DISCUSSION

XP patients can be classified into 8 groups (Table I) on the basis of genetic defects and the different incidence of skin cancer and

neurological disorders (2). In this case, the results of *in vitro* tests and the clinical picture were highly discordant. On the basis of the clinical data (late onset of skin cancer despite many years of recreational sun exposure, absence of photosensitivity, no involvement of other organs) our patient should be classified in the variant group (XP-V). Laboratory examination, however, demonstrated a reduced response of DNA repair mechanisms to UV damage. The rate of damage, that is higher in the classical form of XP, is present in our patient at the lowest detectable rate.

Many doubts have arisen recently about the sensibility and specificity of the tests used to classify XP, such as complementation group analysis and UDS study (3, 4). Cell fusion may demonstrate enzyme deficiency but it cannot identify the gene. Evidence of clinical and biochemical heterogeneity within individual XP complementation groups has been found: for example some patients in complementation group A have severe neurological abnormalities, while others do not (4). Published data has demonstrated the limits of the UDS test: in one family, two brothers were found to have depressed levels of UDS following UV irradiation, but only one of them had skin cancer. The other, despite many years of occupational sun exposure, remained tumour-free (4).

CONCLUSION

We conclude that in our patient the DNA repair system is fairly efficient and it has worked well for many years; skin cancer appeared only after many years of exposure to the sun. Our genetic probes could not have exactly located the affected gene. Further studies with more specific probes, which are not yet available, will let us identify the genetic defect and better classify the patient.

REFERENCES

1. Robert C, Sarasin A. Le xeroderma pigmentosum. Que peut-on attendre des études biologiques? Ann Dermatol Venereol 1994; 121: 434–439.

2. Itoh T, Watanabe H, Yamaizumi M, Ono T. A young woman with

Table I. Xeroderma pigmentosum (4)

Disease and complementation group	Number of patients	%	Unscheduled DNA synthesis following UVC irradiation (% of normal)	CFA following UV irradiation (% of normal)	Skin cancer	Neurological disorders
XP-A	159	33.4	<2	<1	+++	+++
XP-B	3	0.6	3–7		++	++
XP-C	91	19.1	10–20	15	++	+
XP-D	59	12.4	25–50	1	++	–
XP-E	13	2.7	40–50		+	–
XP-F	16	3.4	10–20	40	+	–
XP-G	5	1.1	<2%; 25		+++	+
XP-V	130	27.3	100		+	–
Total cases	476	100				

xeroderma pigmentosum complementation group F and a morphoic basal cell carcinoma. *Br J Dermatol* 1995; 132: 122–127.

3. Lambert WC, Lambert MW. Diseases associated with DNA and chromosomal instability. In Alper JC, editor. *Genetic diseases of the skin*. St. Louis: Mosby Year Book 1991: 320–358.
4. Lambert WC, Kuo HR, Lambert MW. Xeroderma pigmentosum. *Derm Clin* 1995; (13) 1: 169–209.

Accepted July 30, 1998.

G. Tessari¹, F. S. D'Onghia¹, M. Stefanini² and A. Barba¹

¹Department of Dermatology, University of Verona, c/o Ospedale Civile Maggiore Piazzale Stefani 1 37124 Verona and ²Consiglio Nazionale delle Ricerche – Istituto di Genetica Biochimica ed Evoluzionistica, Pavia, Italy.

Post-herpes Zoster Scar Sarcoidosis

Sir,

CASE REPORT

A 70-year-old white woman presented a papular zosteriform eruption on her right upper thorax and right arm. Shiny, erythematous-purplish or flesh-coloured papules 2–3 mm in diameter were observed, isolated or closely arranged in little plaques (Fig. 1). The patient complained only of mild itching; no systemic signs and symptoms were referred. Two months earlier the patient had a C5–C6 right brachial palsy due to brachial herpes zoster. The histopathological pattern of a papula showed a dermal non-caseating granulomatous infiltrate with giant Langerhans-like cells and sclerosing evolution indicating scar sarcoidosis. Further clinical and laboratory investigations failed to reveal systemic sarcoidosis. Chest roentgenogram and liver ultrasonography were normal; X-ray of the hands and feet did not reveal osteolytic alterations. Spirometry and ophthalmology examinations were negative, as well as Mantoux test and skin tests.

DISCUSSION

The infiltration of scar tissue by non-caseating granulomas is a well-recognized form of cutaneous sarcoidosis (1–3). To our knowledge, it has been reported to occur in the site of previous herpes zoster only in one case (1).

Most of the patients with scar sarcoidosis have other systemic manifestations, particularly pulmonary changes; scar infiltrates may appear early in the disease or before parenchymal changes. Changes in scars in patients with sarcoidosis in remission may indicate exacerbation of the disease or may even be a marker for recurrences of thoracic sarcoidosis (4). A careful and prolonged follow-up in these patients is strongly recommended due to the potential risk of developing systemic sarcoidosis.

REFERENCES

1. Bisaccia E, Scarborough DA, Carr RD. Cutaneous sarcoid granuloma formation in herpes zoster scars. *Arch Dermatol* 1983; 119: 788–789.



Fig. 1. Papular zosteriform eruption of the right arm.

2. Olumide YM, Bandle EO, Elesha SO. Cutaneous sarcoidosis in Nigeria. *J Am Acad Dermatol* 1989; 21: 1222–1224.
3. Veien NK, Stahl D, Brodthagen H. Cutaneous sarcoidosis in Caucasians. *J Am Acad Dermatol* 1987; 16: 534–540.
4. Roegel E, Pauli G, Grosshans E, El Baz D, Dietemann-Molard A, Hutt JP. Sarcoides récidivantes sur cicatrices cutanées révélatrices de sarcoidose thoracique itérative. *Rev Pneumol Clin* 1984; 40: 81–83.

Accepted July 30, 1998.

Monica Corazza, Sandra Bacilieri and Renata Strumia
Dermatology Department, University of Ferrara, Via Savonarola 9,
I 44100 Ferrara, Italy.