

Total-Body Cutaneous Examination, Total-Body Photography, and Dermoscopy in the Care of a Patient With Xeroderma Pigmentosum and Multiple Melanomas

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Background: Xeroderma pigmentosum (XP) is an autosomal recessive disorder characterized by a defect in DNA repair and subsequent increased frequency of cutaneous malignant neoplasms, including melanoma. In patients with XP, patient and family education and aggressive UV radiation protection are the primary means of skin cancer prevention. An important secondary measure in decreasing morbidity and mortality in these patients involves early detection of skin cancers, particularly melanomas.

Observations: We describe a 39-year-old woman with XP who developed 38 primary melanomas along with 6 squamous cell carcinomas and 70 basal cell carcinomas over a 23-year period. During this time, a 3-fold management approach of total-body cutaneous examination, total-body photography, and dermoscopy was used

in the care of the patient. The thickest melanoma had a Breslow thickness of 1.07 mm, and the mean Breslow thickness of her detected melanomas was 0.18 mm. The ratio of benign to malignant biopsied suspicious melanocytic lesions during 23 years of follow-up was 0.9:1. All melanomas were treated using wide local excision, and she had no evidence of local or in-transit metastases of any of her malignant neoplasms at the most recent follow-up examination.

Conclusion: Monthly follow-up using total-body cutaneous examinations, total-body photography, and dermoscopy is an important 3-fold secondary management technique for this unique patient, allowing early detection of her melanomas.

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XERODERMA PIGMENTOSUM (XP) is a rare autosomal recessive disorder that was first described by Kaposi in 1874.¹ Individuals with XP are extremely sensitive to UV radiation and have high risks for developing actinic changes and cutaneous malignant neoplasms in sun-exposed areas.² Their rate of developing melanomas is 1000 times higher than the rate seen in the general population of individuals younger than 20 years.²⁻⁵

In addition to rigorous preventive efforts to avoid UV radiation-induced skin damage, frequent clinical monitoring and aggressive surgical intervention are needed to adequately manage these patients. In this case report, we describe a patient with XP who was diagnosed with 38 primary malignant melanomas over a 23-year period and was successfully treated for them.

REPORT OF A CASE

A 39-year-old woman with ataxia and a history of XP and multiple melanoma and non-

melanoma skin cancers was seen for her regular 6-week follow-up examination. Her diagnosis of XP had been made 36 years prior when she was evaluated by a dermatologist for extreme photosensitivity. As an infant, she was reported to cry incessantly on brief sun exposure and developed significant erythema and freckling at age 4 months after exposure to only wintertime sun. A biopsy specimen of her thigh at age 2 years revealed marked cellular crowding at the basal layer and dyskeratosis consistent with actinic damage. Throughout her adolescence, the patient and her parents were advised to adhere to a strict regimen of sun avoidance, protective eyewear, and vigilant sunscreen use. Apart from a few isolated yet significant sunburns sustained as an adolescent growing up along the beaches of the Florida Panhandle, the patient adhered fairly well to the sun avoidance regimen. Despite preventive efforts and provisions to avoid sun exposure, the patient continued to develop extensive actinic damage. Her first skin cancer was a basal cell carcinoma of the right lower eyelid at age 18 years, and the patient had developed 38

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melanoma and 76 nonmelanoma skin cancers by age 39 years (**Table**). All of the melanomas had been on her trunk and all 4 extremities, sparing the head and neck region. Twelve basal cell carcinomas and 4 squamous cell carcinomas had been detected and treated on her head and neck region. In addition to the skin cancers, the patient demonstrated ataxia and significant loss in visual and auditory capacities. Ocular abnormalities discovered under the care of an ophthalmologist included photophobia, decreased visual acuity, and multiple nevi within the irises. There was no evidence of ectropion or pterygium. The patient refused DNA repair testing. Magnetic resonance imaging of the posterior fossa at age 34 years was performed because of worsening ataxia and revealed cerebellar atrophy concomitant with unusually prominent third and lateral ventricles for a patient of her age. Intellectual and sexual development were not significantly affected by her disorder. The patient is married and has had 2 sons, who show no evidence of XP.

Physical examination revealed extensive actinic damage, with marked poikilodermatous changes and scarring (**Figure 1**). A new melanocytic lesion with irregularities was discovered on the patient's right calf that was absent in her most recent baseline photographs (**Figure 2**). Dermoscopic examination of the lesion was performed, and an excisional biopsy specimen was obtained for further histopathologic review of this suspicious lesion. Histopathologic review revealed a Clark level III melanoma with a Breslow thickness of 0.67 mm. As with the other 37 melanomas that she had developed, this melanoma was treated using wide local excision. The patient has been followed up regularly for the past 23 years by her dermatologist (A.B.C.) with the aid of total-body photography, total-body cutaneous examination, and dermoscopy.

COMMENT

Xeroderma pigmentosum is characterized primarily by defective DNA repair, resulting in an inability to repair UV radiation-induced DNA photoproducts. The manifestations of this defective repair mechanism usually begin in childhood as abnormal sun sensitivity, freckling, and skin cancers, including malignant melanoma.⁶ Sun protection and avoidance are the means of primary skin cancer prevention in this group of patients.⁷ The median interval between the onset of XP symptoms to the first neoplasm is 5 years, and almost 50% of patients with XP will develop skin cancer by age 8 years.⁸ The diagnosis of cutaneous melanoma in patients with XP is often difficult because of severe actinic damage, which includes telangiectasias, atrophy, hyperkeratosis, and extensive poikilodermatous changes that occur in sun-exposed areas. Because early detection is the most important management point in the prognosis of malignant melanoma, it is crucial to find a method that enhances the clinician's capacity for accurate discrimination of skin tumors in the diagnostically challenging context of XP.

Total-body examination,⁹ total-body photography,¹⁰⁻¹² and dermoscopy¹³⁻¹⁶ have been reported to increase the diagnostic accuracy of malignant melano-

Table. Findings of Malignant Neoplasms and Pigmented Nonmalignant Biopsied Lesions During 23 Years

Variable	No.
Malignant neoplasms	114
Basal cell carcinoma	70
Squamous cell carcinoma in situ	1
Squamous cell carcinoma	5
Malignant melanoma in situ	25
Malignant melanoma (Clark levels of II-III and Breslow thicknesses of 0.14-1.07 mm)	13
Pigmented nonmalignant biopsied lesions	33
Atypical melanocytic hyperplasia	14
Atypical melanocytic proliferation	4
Dysplastic compound nevus with mild atypia	3
Dysplastic compound nevus with moderate to severe atypia	2
Dysplastic junctional nevus with mild to moderate atypia	5
Dysplastic junctional nevus with moderate to severe atypia	4
Inflamed seborrheic keratosis	1

mas. Wang et al¹⁷ recently reported that the concomitant use of all 3 of these diagnostic tools allowed for early diagnosis of melanoma in 160 patients with classic atypical mole syndrome over a 10-year period. In addition, Malvey et al¹⁸ described the use of dermoscopy and clinical examination in the care of 2 patients with XP. We suggest that the combined approach of total-body cutaneous examination, total-body photography, and dermoscopy may be advantageous in the care of a patient with XP. Despite having 38 melanomas, the patient herein has had no deep local invasion or metastases, suggesting the success of this systematic approach for early detection. In our clinical experience, the combined 3-fold approach has rendered the distinct advantage of providing multiple references by which subtle changes can be appreciated within the diffuse areas of hypopigmentation and hyperpigmentation of the chronically inflamed and sun-damaged skin of our patient.

Having clinical photographs for review during examinations has afforded early detection and dermoscopic evaluation of new and changing lesions, thereby limiting the number of unnecessary biopsies. As described by Malvey et al,¹⁸ dermoscopy affords further delineation of individual tumors and their vascular structures in the markedly poikilodermatous skin of patients with XP. The thickest melanoma was 1.07 mm, and the mean Breslow thickness of her detected melanomas was 0.18 mm. The ratio of benign to malignant biopsied suspicious melanocytic lesions obtained using the 3-fold management technique described herein was 0.9:1, and 38 of 71 (53.5%) biopsied specimens of suspicious melanocytic lesions were indeed malignant. While prophylactic removal of all clinically atypical pigmented lesions would lead to increased sensitivity and decreased specificity, it would mean subjecting the patient to unnecessary surgery and to cosmetic disfigurement.^{19,20} In using the 3-fold approach during frequent follow-up examinations, we consider a benign to malignant ratio of biopsied lesions approaching 1:1 to be reasonable in the care of this particular patient. **Figure 3** shows a simplified algorithm-

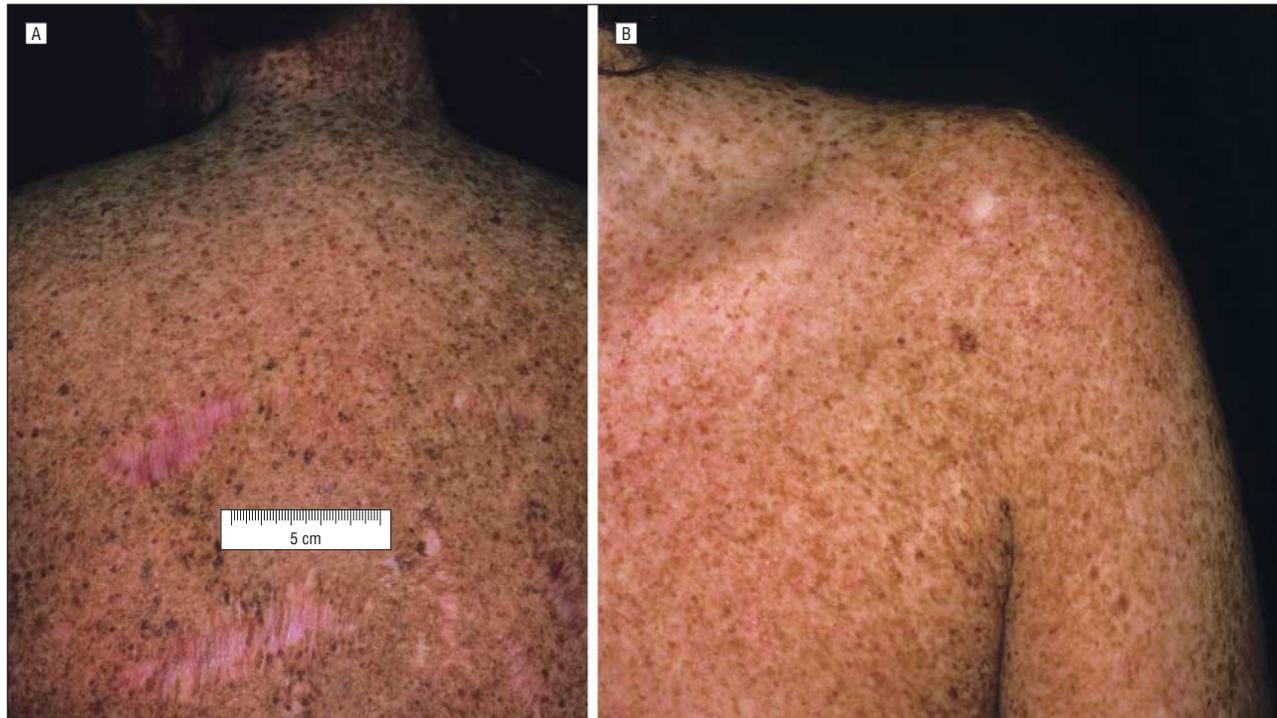


Figure 1. Notice the actinic, scarring, and poikilodermatous changes on the patient's back (A) and left upper chest (B), which create a diagnostically challenging environment.

mic approach that has been used in the care of this patient. Although this approach has proven helpful in the care of this particular patient with XP, it should not necessarily be applied to the management of all patients with XP, as other approaches may serve best for other dermatologists and patients.

During office visits, the entire cutaneous surface of the patient is examined, including the scalp, tip of tongue, and non-double-covered intertriginous areas. Eight representative baseline total-body photographs (patterned after the method described by Slue et al¹²) are reviewed in a stylized and consistent fashion in the context of thorough total-body examination. As each anatomical area is examined, the corresponding baseline photograph is viewed, and changes are noted, documented, and addressed accordingly using a low threshold for biopsy (**Figure 4**). Suspicious lesions are marked with blue ink at the 6-o'clock position and are then reviewed using dermoscopy and interpreted via a pattern analysis approach. With the aid of total-body photography and dermoscopy, one of us (A.B.C.) tracks for changes in clinically atypical lesions. In general, biopsies are performed if there is significant change noted on comparison with prior images.

Except for the past several years of clinical follow-up, total-body photography comparisons were performed via slides projected onto a carousel rearview screen. Although somewhat cumbersome, this modality served well for comparisons, particularly in light of the large screen size. In the past several years, the most recent sets of baseline images have been printed as glossy 6 × 4-in photographs, which are less cumbersome and are readily accessible during patient visits. In addition, during most years of clinical follow-up, Polaroid (Po-

laroid Corp, Waltham, Massachusetts) photographs of specific lesions with 1:1 magnification were conveniently obtained during the office visits and were given to the patient and her family for at-home monitoring of specific lesions for changes in the ABCD criteria (asymmetry, border irregularity, color variation, and diameter >6 mm). Although traditionally useful for its simplicity in obtaining immediate 1:1 magnification photographs, Polaroid photographing equipment is being phased out due to the advent and greater availability of digital photography.

The current literature²¹⁻²⁴ suggests that digital imaging systems are comparable with traditional 35-mm photography in terms of overall diagnostic quality, reliability, and storage and may become standard in dermatologic imaging. Recent technologic advances in digital imaging systems are available and have been used with success in total-body photography.^{20,22} This promising equipment may not yet be cost-effective for dermatologists in private practice without dedicated pigmented lesion clinics. Perhaps the most important issue in selecting an imaging monitoring modality is to maintain consistency when following up prospectively suspicious lesions to decrease the inherent variability of using digital and nondigital modalities.²⁰

The ideal management of patients with XP should also include early diagnosis of the disorder, followed by patient and family education. With our patient, ongoing verbal emphasis is made regarding sun protection and avoidance to avert irreparable DNA damage and resulting clinical changes and tumors. The patient has become more compliant and successful in her sun protective habits and precautions over the years as she has come to experientially understand the gravity of her condition and the det-

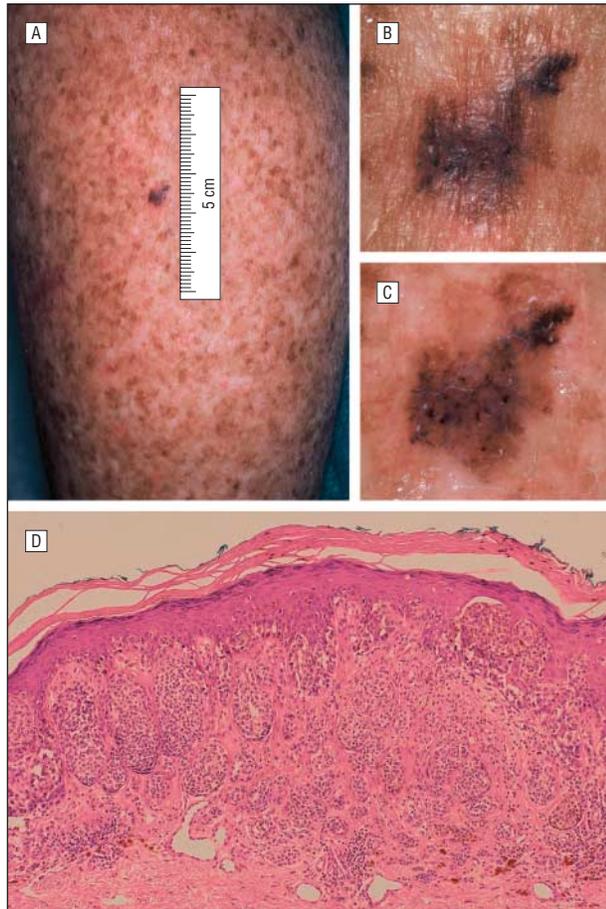


Figure 2. Dermoscopic and histopathologic views of a new irregular melanocytic lesion. New irregular melanocytic lesion arising on the patient's right posterior calf (A), with dermoscopic views of the lesion without (B) and with (C) oil immersion showing a malignant pattern (multiple colors, asymmetry in both axes, architectural disorder, nonuniform globules haphazardly dispersed throughout the lesion, and evidence of a structureless area with regression in the periphery of the lesion) that on histopathologic review (D) revealed a Clark level III melanoma with a Breslow thickness of 0.67 mm (hematoxylin-eosin, original magnification $\times 400$).

riments of unprotected sun exposure, particularly living along the Florida Panhandle. The patient's progressive proficiency in sun protection over the past 2 decades may be a contributing factor in the relative decrease in the annual number of basal cell carcinomas diagnosed, as shown in **Figure 5**.

Other preventive efforts described in the literature for patients with XP were considered over the years, including dermabrasion, dermatome shaving, reconstructive surgery, topical application of fluorouracil, and an oral regimen of isotretinoin. Nelson et al²⁵ described the use of dermabrasion in 2 patients with XP and its transient effect as the treated lentigines returned to baseline 4 to 5 months after the procedure. Dermatome shaving was reported by Epstein et al²⁶ and later by König et al²⁷ as a potential option for skin cancer prevention in patients with XP, as it involves removing portions of the damaged epidermis and allowing it to be replaced with a new epidermis arising from potentially less damaged stem cells from deeper-lying adnexal structures. Reconstructive surgery involving removal of all facial skin and subsequent grafting from abdominal skin was reported by Cox et al²⁸ in the care

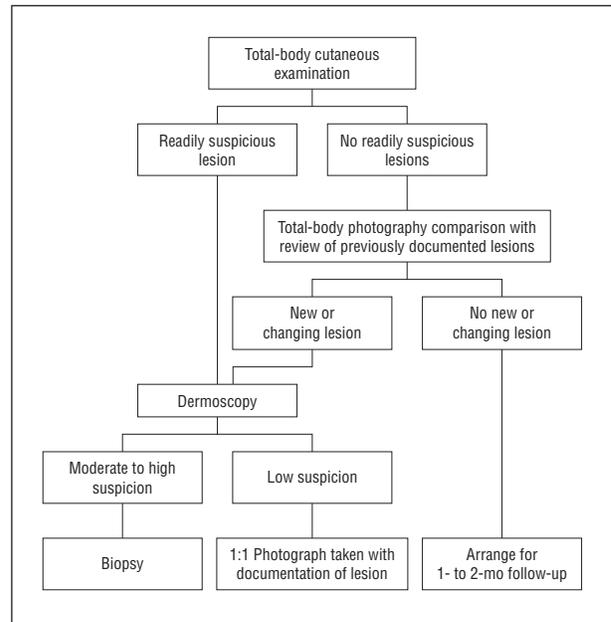


Figure 3. Algorithm for melanoma detection used in the management of this patient with xeroderma pigmentosum and multiple melanomas.

of a girl with XP. Topical application of fluorouracil has been reported to aid in the removal of actinic keratoses and as palliative treatment of unresectable facial squamous cell carcinomas.²⁹⁻³¹ A regimen of oral isotretinoin (2 mg/kg/d) was reported to decrease the frequency of skin cancers in 5 patients with XP, but its use was accompanied by significant toxic effects and was followed by an increase in the rate of detected skin cancers in 3 of the patients within months after cessation of the medication compared with the pretreatment rate.^{32,33} Of these described preventive measures, oral isotretinoin use was considered potentially appropriate in the care of the patient described herein and was recommended to her on several occasions when she was in her 20s. The patient declined the isotretinoin treatment in light of her and her husband's unwillingness to forgo childbearing while using the potentially teratogenic medication.

Selecting the appropriate interval between follow-up examinations has also proven to be an important factor in the care of this patient. In general, close follow-up has been associated with detection of melanomas in thinner stages as reported by Kang et al.³⁴ The mean interval between new skin cancer detection in our patient is 100 days, and the mean interval between melanoma or melanoma in situ detection is 330 days. In addition, 8 of her melanomas were discovered within 8-week intervals, while 3 were discovered within 6-week intervals. There have been instances when more than 1 melanoma was detected per office visit, and 4 melanomas were detected at one time during an extended-interval follow-up visit early in her care. In light of these experiences, a 4- to 6-week interval between examinations has been maintained for most years of follow-up to help ensure early diagnosis of her melanomas. This interval should not necessarily be applied to all patients with XP but was found to be appropriate for this patient, considering the rate at which she has developed cutaneous malignant neoplasms.

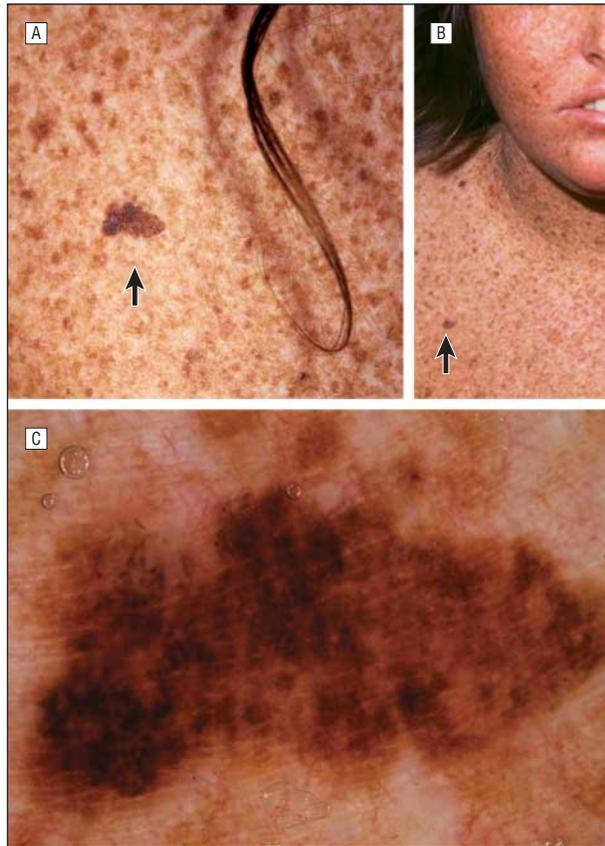


Figure 4. Example of interval changes in a melanocytic lesion from the previous baseline photograph. Melanocytic lesion on the patient's right upper chest (A) shown in comparison with the previous baseline photograph (B) that had an indeterminate pattern of neither benign nor overtly malignant features on dermoscopy (C) and proved histologically to be a malignant melanoma in situ.

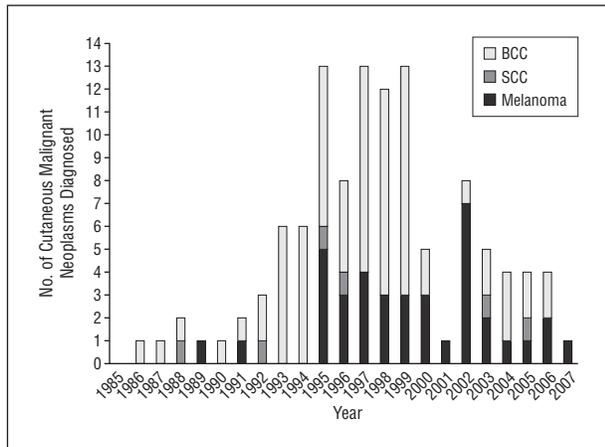


Figure 5. Graph of annual cutaneous malignant neoplasms diagnosed during 23 years of clinical follow-up. BCC indicates basal cell carcinoma; SCC, squamous cell carcinoma.

The outlined 3-fold approach of total-body cutaneous examination, total-body photography, and dermoscopy as described herein is time consuming and may seem excessively so in light of its use every 4 to 6 weeks during follow-up visits. Zalaudek et al³⁵ recently described the significantly increased time required to supplement

complete-body examination with dermoscopy and concluded that the extra time and effort were reasonable in light of the morbidity and mortality potentially prevented by skin cancer detection. Similarly, we consider the extra time and effort involved in using the 3 aforementioned detection modalities not only reasonable but also perhaps necessary in the care of this particularly high-risk patient.

In conclusion, we describe a patient having XP with a large number of melanomas. Many of her newly discovered melanomas occurred within a follow-up interval of only 6 weeks. Providing adequate dermatological care for such a patient can be a daunting task. The described aggressive method of surveillance has been central in the management and care of this unique patient and has allowed for early detection of her melanomas. The combination of short-interval total-body cutaneous examination, total-body photography, and dermoscopy may prove useful to other clinicians in the management of similar patients with XP.

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