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Xeroderma pigmentosum in eastern Turkey: a review of 15 cases*

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Aim: To determine the demographic and clinical characteristics of xeroderma pigmentosum (XP). XP is a rare autosomal recessive disease that is characterized by cellular hypersensitivity to ultraviolet radiation, development of cancers at an early age, severe actinic changes, and photophobia.

Materials and methods: In the dermatology clinic of Yüzüncü Yıl University, Van, Turkey, 15 patients who were diagnosed with XP were seen between April 2004 and May 2010. They were evaluated according to their age, sex, family history, parental relationships, age at onset of skin lesions, presence of cutaneous malignancy, and neurological and ophthalmologic involvement.

Results: The patients consisted of 8 males (53.33%) and 7 females (46.67%), and their ages ranged from 4 to 25 years (mean: 12.13). In 2 sibling cases, there was no parental consanguinity. Parental consanguinity was present in all of the other 13 cases (86.67%). The mean age at the onset of skin lesions was 1.4 years. Neurological involvement was not seen in any of the cases, but ophthalmologic involvement was seen in all of the cases. Skin malignancy was detected in 6 patients and actinic keratosis, keratoacanthoma, and multiple ulcers were observed in some of the patients.

Conclusion: XP is an inherited disorder and mostly affects the skin. Clinical signs and symptoms usually develop over time. In this series, malignancy developed in 40% of the patients during the follow-up period. This study is a large case series in which XP is clinically assessed.

Key words: Xeroderma pigmentosum, Turkey, skin malignancy, genodermatoses

Türkiye'nin doğusunda kseroderma pigmentozum: 15 olgunun değerlendirilmesi

Amaç: Kseroderma pigmentozum ultraviyole radyasyonuna karşı hücresel aşırı duyarlılıkla karakterize, erken yaşta kanser oluşumuna ilerleyebilen, şiddetli aktinik değişikliklerin ve fotofobinin görüldüğü otozomal resesif geçişli nadir görülen bir hastalıktır. Bu çalışmada kseroderma pigmentozum tanısı ile takip edilen hastaların demografik ve klinik özelliklerinin belirlenmesi amaçlandı.

Yöntem ve gereç: Nisan 2004-Mayıs 2010 tarihleri arasında dermatoloji kliniğimize başvuran ve kseroderma pigmentozum tanısı alan 15 hasta yaş, cinsiyet, aile öyküsü, anne baba akrabalığı, deri lezyonlarının başlangıç yaşı, deri malignitesi varlığı, göz ve nörolojik tutulum açısından değerlendirildi.

Bulgular: Olgular yaşları 4 ile 25 arasında değişen (ortalama 12,13) 8 erkek (% 53,33) ve 7 bayan (% 46,67) hastadan oluşuyordu. Kardeş iki olguda anne baba akrabalığı yoktu. Diğer 13 olgunun tamamında (% 86,67) anne-baba akrabalığı mevcuttu. Deri belirtilerinin ortalama başlangıç yaşı 1.4 yaş idi. Olguların tamamında göz bulgularına rastlanırken hiçbir olguda nörolojik tutulum gözlenmedi. Altı hastada deri malignitesi gelişirken bazı hastalarda aktinik keratoz, keratoakantom ve multipl ülserler tespit edildi.

Sonuç: Kseroderma pigmentozum genetik geçişli bir hastalık olmakla birlikte belirtilerinin çoğu dermatolojik bulgulardır. Klinik bulgular belli bir süre içerisinde ortaya çıkmaktadır. Klinik serimizde hastaların izlemi ile % 40'ında malignite gelişimi saptanmıştır. Bu çalışma kseroderma pigmentozum hastalığını klinik yönden irdeleyen geniş bir olgu serisidir.

Anahtar sözcükler: Kseroderma pigmentosum, Türkiye, deri malignitesi, genodermatoz

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Introduction

Xeroderma pigmentosum (XP) is a rare autosomal recessive genetic disorder that mostly affects the skin (1). XP was first reported in 1874 by Hebra and Kaposi (2). It is characterized by cellular hypersensitivity to ultraviolet (UV) light, photophobia, early onset of freckling, and neoplastic alternations on sun-exposed areas of body (1,3). The nucleotide excision repair enzymes that repair damage caused by UV light are deficient in XP. The excision repair-deficient XP strains have been classified into 7 different complementation groups and 1 variant group (1,2,4). In this study, we examined the demographic and clinical characteristics of xeroderma pigmentosum in 15 cases.

Materials and methods

A retrospective analysis was performed of 15 XP patients that were seen at the dermatology clinic of Yüzüncü Yıl University, Van, Turkey, between April 2004 and May 2010. Patients were evaluated according to their age, sex, family history, age at onset of dermatological lesions, presence of skin malignancy, and ophthalmological and neurological involvements.

Results

Dermatological and clinical features of the patients are shown in the Table. The patients ranged in age from 4 to 25 years (mean: 12.13) and consisted of 8 males (53.33%) and 7 females (46.46%). Only 2 sibling cases did not have a parental consanguinity; the remaining sibling patients (13 cases; 86.67%) had parental consanguinity. Patients 7 and 8 were siblings, as were patients 12, 13, and 14. In addition, patient 3 and patient 4 were relatives (the grandchildren of 2 siblings).

The mean age at the onset of dermatological lesions was 1.4 years. The UV light-exposed face, neck, and upper part of the body developed freckles and hypopigmented macules (Figures 1 and 2). All of the patients developed ophthalmological signs and/or symptoms including photophobia, conjunctivitis, and ectropion, but none had neurological involvement. Conjunctival malignant melanoma (MM) was detected in case 8. Skin malignancies were detected clinically and histopathologically in 6 cases. Patient 1 had a basal cell carcinoma (BCC) on the cheek; patient 4 had a pigmented BCC on the lateral left eyebrow edge; patient 6 had a well-differentiated squamous cell carcinoma (SCC) on the glabella and right auricula and a BCC on the left eyebrow and lateral orbital edge; patient 6 had a MM in the left conjunctiva and a SCC on the lip mucosa and upper lip edge; and patient 9 had a well-differentiated SCC on the left cheek and a well-differentiated SCC with microinvasion on the left upper eyelid. In addition, patient 4 had actinic keratoses on the face, patient 9 had a keratoacanthoma on the left cheek, and patients 6 and 11 had an ulcer on the arm and face, respectively.

Discussion

XP is seen worldwide and may affect all races (1). The prevalence shows variance in different populations; for instance, it is 1/1,000,000 in the United States, 1/250,000 in Europe, and 1/40,000 in Japan (1,5). The prevalence is higher in Middle Eastern countries such as Turkey, Israel, and Syria because of the high frequency of consanguineous marriages (1). Metin et al. reported that the prevalence of XP is high in Van, Turkey (6,7). In the literature, 12 XP case series from different parts of Turkey were reported (8). The present case series only consisted of the patients who applied to our clinic from eastern Turkey. A comprehensive epidemiological study is needed for the prevalence of XP in Turkey.

In this study, the parental consanguinity rate was 86.7%. This rate was consistent with previous reports by Khatri et al. (92.8%), Metin et al. (100%), and Gül et al. (83.3%), and was higher than that reported by Kraemer et al. (4,6,8,9).

The mean age was 12.13 years and the male-to-female ratio (0.8) was compatible with that in the study by Metin et al. (6).

XP is a genetically heterogeneous disorder and has been classified into 7 different complementation groups (XP-A to XP-G) and 1 variant group (XP-V) (1,3). Metin et al. detected only the XP-C complementation group in their series (10,11). Unfortunately, there was no DNA analysis in the present series.

Table. Dermatological and clinical features.

	Age/sex	Parental consanguinity	Family history	Age at onset of dermatological findings	Pigmented macules	Cutaneous malignancy	Other skin lesions	Eye involvement	Neurological involvement	Other findings
Case 1	22/M	+	-	1	+	BCC	-	Photophobia/ ectropion	-	-
Case 2	14/F	+	-	1	+	-	-	Conjunctivitis	-	Growth retardation
Case 3	4/F	+	+	2	+	-	-	Photophobia, conjunctivitis	-	Growth retardation
Case 4	5/M	+	+	2	+	Pigmented BCC	Actinic keratoses	Glaucoma	-	-
Case 5	5/M	+	-	2	+	-	-	Photophobia, conjunctivitis	-	-
Case 6	19/F	+	-	1	+	SCC BCC	-	Conjunctivitis	-	Hypertension, left ventricular hypertrophy
Case 7	2/F	-	+	1	+	-	-	Photophobia	-	-
Case 8	7/F	-	+	1	+	MM, SCC	-	Photophobia, conjunctivitis, conjunctival MM	-	-
Case 9	18/M	+	+	1	+	SCC	Keratoacanthoma	Ectropion, SCC at uppe left eyelid	-	-
Case 10	4/F	+	-	1	+	-	-	Photophobia	-	-
Case 11	10/M	+	+	1	+	-	-	Conjunctivitis	-	-
Case 12	14/M	+	+	2	+	-	Facial skin ulcer	Blepharitis, prominent conjunctival papilla	-	-
Case 13	10/M	+	+	2	+	-	-	Conjunctivitis	-	-
Case 14	12/F	+	+	2	+	-	-	Conjunctivitis	-	-
Case 15	25/M	+	+	1	+	SCC	-	Conjunctivitis	-	-

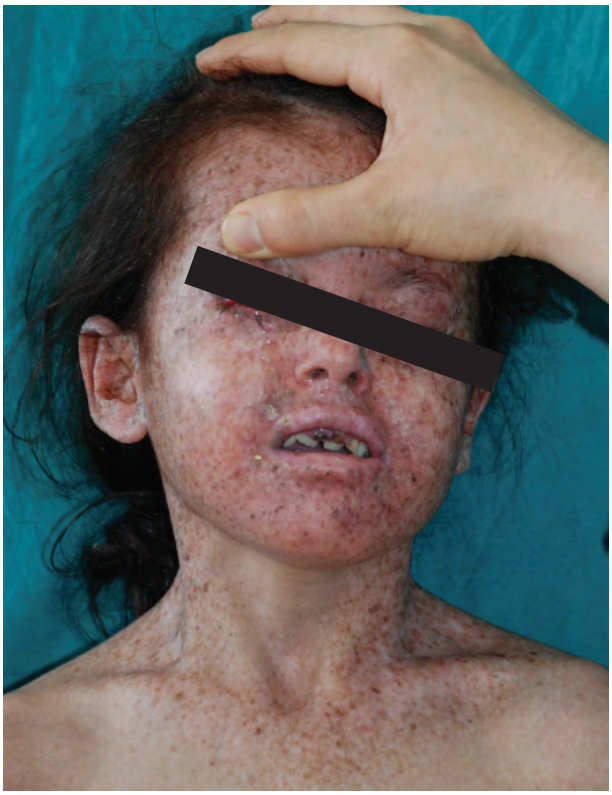

Figure 1. Multiple brownish lentigines of 1-4 mm on the face, neck, and trunk, and conjunctivitis (case 8).

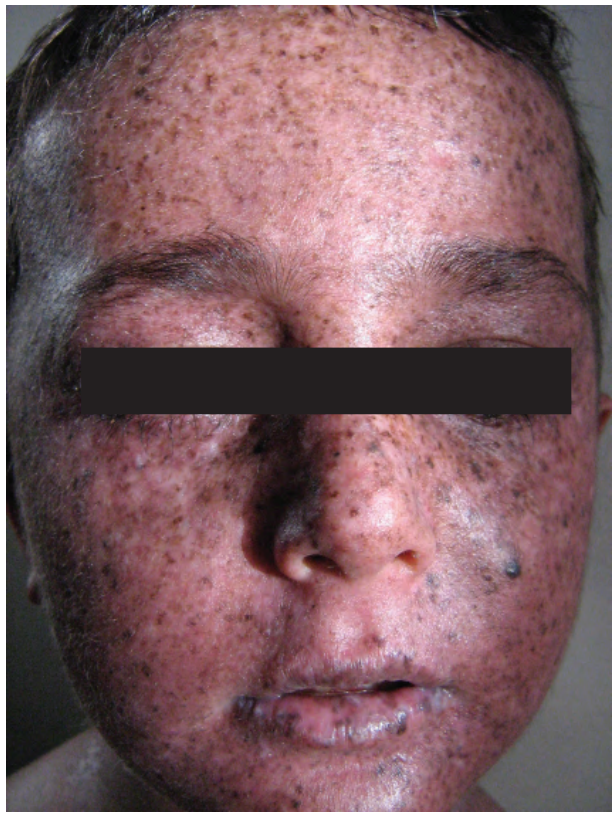

Figure 2. Multiple mousy dark brown and black lentigines on the face (case 5).

The age at onset of dermatological findings was 1-2 years in previous studies (1,3,9). It was 1.4 years in the present series. The first dermatological findings are severe sunburn reactions such as erythema, edema, and vesicles even after minimal sun exposure (1,8), and 50% of the patients only develop sun hypersensitivity without bullous or severe burns (1). Over the course of time, the patients develop dry and poikilodermic skin that may contain spots, freckling, atrophy, and hypopigmented macules (1,3,8). All of the patients had a history of early onset sunburn and dry and poikilodermic skin.

In XP, actinic keratosis, BCC, SCC, and, less commonly, MM may be seen on sun-exposed areas of the body at early ages (1,2). The other less common skin neoplasms are keratoacanthoma and angiosarcoma (1,12). The incidence of skin tumors in XP is 5 times greater than in the normal population (1,3,8,9). The incidence of skin lesion was 45% in a report by Kraemer et al. (9). In the series of 42 XP cases reported by Khatri et al., the incidence of SCC, BCC, and basosquamous cell carcinoma was 55%, 40%, and 4.8%, respectively. No MM was reported in their series (4). Metin et al. reported that the incidence of skin neoplasms including SCC, BCC, MM, atypical fibroxanthoma, and angioma was 81.25% (6). The incidence of skin neoplasms (1 patient had MM, the others had SCC, and no patients had BCC) was 75% in a study by Gül et al. (8). The incidence of skin neoplasm was 40% in the present study. All neoplasms were found on the sun-exposed areas of the face. Of the patients, 2 had BCC, 2 had SCC, 1 had both SCC and BCC, and 1 had SCC and MM. The diagnosis of MM in XP is very difficult because of severe chronic actinic skin damage and the poikilodermic appearance of the skin. Detailed body examinations, periodic taking of photographs of body lesions, and dermatoscopic examinations can facilitate the diagnosis of MM (13).

Ophthalmologic involvement is seen in almost 80% of XP cases (1). Severe photophobia, keratitis, corneal opacities, and vascularization are common findings. Photophobia and lacrimation are early-onset symptoms. Less frequent ophthalmological presentations are eyelash loss and ectropion. In addition, SCC and MM rarely develop in the UV light-exposed eye area (1,2,8,9,14). Photophobia, conjunctivitis, blepharitis, and ectropion were seen in our cases, and MM was detected in one case.

Neurologic involvement is seen in approximately 20%-30% of cases (2). The age at onset of neurological problems shows variation from the infantile period to the second decade (1). Microcephaly, severe mental retardation, sensorineural deafness, and ataxia have been reported in XP (1,8). Neurological symptoms are only seen in the XP-A, XP-B, XP-D, and XP-G complementation subgroups (1-3,9,11). No neurological manifestation was detected in the present cases.

The incidence of solid malignancy is 10-20 times higher than in the normal population (2,8). Brain, lung, oral cavity, gastrointestinal, kidney, and hematopoietic system cancers may be seen (2). There was no solid malignancy in the present cases.

The main treatment approach for XP is to make an early diagnosis and to avoid sunlight and other UV lights. Experimental trials such as the topical DNA repair enzyme application are promising (1-3). In addition, gene therapy with retroviruses may be an alternative treatment in the future (1).

In conclusion, XP is more frequently seen in Turkish populations because consanguineous marriage is more prevalent. Studies related to the early diagnosis and treatment of XP are warranted for our population. Due to the increased incidence of skin malignancy, the patients should be instructed to avoid sun exposure and informed of the importance of regular dermatological examinations and follow-ups.

References

1. Metin A, Akdeniz N. Xeroderma pigmentosum. In: Tüzün Y, Gürer MA, Serdaroğlu S, Oğuz O, Aksungur VL, editors. Dermatology. 3rd ed. İstanbul: Nobel Tıp Kitabevleri; 2008. p.1721-36 (in Turkish).
2. Lim HW, Hawk JLM. Photodermatoses. In: Bolognia JL, Jorizzo JL, Rapini RP, editors. Dermatology. 2nd ed. St. Louis (MO): Mosby Elsevier; 2008. p.1333-94.
3. Rünger TM, DiGiovanna JJ, Kraemer KH. Hereditary disorders of genome instability and dna repair. In: Wolff KW, Goldsmith LA, Katz SI, Gilchrest BA, Paller AS, Leffell DJ, editors. Fitzpatrick's dermatology in general medicine. 7th ed. New York: McGraw-Hill. 2008. p.1311-25.
4. Khatri ML, Bemghazil M, Shafi M, Machina A. Xeroderma pigmentosum in Libya. Int J Dermatol 1999; 38: 520-4.
5. Bhutto AM, Shaikh A, Nonaka S. Incidence of xeroderma pigmentosum in Larkana, Pakistan: a 7-year study. Br J Dermatol 2005; 152: 545-51.
6. Metin A, Bekerecioğlu M, Uğraş S, Delice İ. Van'da kseroderma pigmentozum. Türkderm 2000; 34: 45-8 (in Turkish).
7. Kutluhan A, Bekerecioğlu M, Güney E, Metin A. Otorhinolaryngological aspects of Xeroderma pigmentosum. Auris Nasus Larynx 1999; 26: 457-66.
8. Gül Ü, Kılıç A, Gönül M, Külcü Çakmak S, Soylu S. Xeroderma pigmentosum: a Turkish case series. Int J Dermatol 2007; 46: 1125-8.
9. Kraemer KH, Lee MM, Scotto J. Xeroderma pigmentosum: cutaneous, ocular, and neurologic abnormalities in 830 published cases. Arch Dermatol 1987; 123: 241-50.
10. Khan SG, Metin A, Gozukara E, Inui H, Shahlavi T, Muniz-Medina V et al. Two essential splice lariat branchpoint sequences in one intron in a xeroderma pigmentosum DNA repair gene: mutations result in reduced XPC mRNA levels that correlate with cancer risk. Hum Mol Genet 2004; 13: 343-52.
11. Gozukara EM, Khan SG, Metin A, Emmert S, Busch DB, Shahlavi T et al. A stop codon in xeroderma pigmentosum group C families in Turkey and Italy: molecular genetic evidence for a common ancestor. J Invest Dermatol 2001; 117: 197-204.
12. Dilek FH, Akpolat N, Metin A, Ugras S. Atypical fibroxanthoma of the skin and the lower lip in xeroderma pigmentosum. Br J Dermatol 2000; 143: 618-20.
13. Green WH, Wang SQ, Cognetta AB. Total-body cutaneous examination, total-body photography, and dermoscopy in the care of a patient with xeroderma pigmentosum and multiple melanomas. Arch Dermatol 2009; 145: 910-5.
14. Halpern J, Hopping B, Brostoff JM. Photosensitivity, corneal scarring and developmental delay. Xeroderma Pigmentosum in a tropical country. Cases J 2008; 1: 254.