The Turkish Journal of Pediatrics 1996; 38: 261-264

ASSOCIATION OF XERODERMA PIGMENTOSUM WITH THROMBASTHENIA*

*Alev Hasanoğlu MD***, *Kıvılcım Gücüyener MD****, *Leyla Tümer MD*****
*Türkiz Gürsel MD******

SUMMARY: Hasanoğlu A, Gücüyener K, Tümer L, Gürsel T. (Department of Pediatrics, Gazi University Faculty of Medicine, Ankara, Turkey). Association of xeroderma pigmentosum with thrombasthenia. Turk J Pediatr 1996; 38: 261-264.

Xeroderma pigmentosum (XP) is an autosomal recessive disorder characterized by severe sun-sensitivity, early skin cancers and abnormal DNA repair. XP has a worldwide distribution with an approximate frequency of 1/250,000. It is classified into nine complementation groups, and distribution of patients among the various groups is related to ethnic origin.

To our knowledge, the association of XP with thrombasthenia has not been reported perviously; here a 12-year-old girl with this combination is reported. She was first noted to have skin erythema on exposure to sunlight at the age of six months and was diagnosed with XP. At the age of one she had the complaints of easy bruising and epistaxis. A diagnosis of thrombasthenia was made based on the absence of platelet aggregation response to ADP, collagen and adrenaline and reduced clot retraction. In clinical management, oral isotretinoin was given in order to supress tumor formation. *Key words: xeroderma pigmentosum, Glanzmann's thrombasthenia.*

Xeroderma pigmentosum (XP) and Glanzmann's thrombasthenia (GT) are two rare, autosomal-recessive hereditary disorders[1-6]. The typical clinical findings of both disorders are reported in a 12-year-old girl as the first example of this association.

Case Report

The patient was the second product of consanguineous parents. The pregnancy and delivery were uneventful, and psychomotor development in the first two years of life was normal. At the age of six months she suffered from hyperpigmented macules of the skin in sun-exposed areas. She also had had frequent ecchymosis, epistaxis and dental bleeding since infancy. A skin biopsy confirmed the diagnosis of XP.

Physical examination revealed hypo/hyperpigmented macules, ecchymosis and petechiae. Her eyelashes had fallen out with bilateral ectropion, and bilateral opacities were observed on the lower part of the cornea (Fig. 1). The rest of the physical examination revealed no pathology.

* From the Department of Pediatrics, Gazi University Faculty of Medicine, Ankara.
** Professor of Pediatrics, Gazi University Faculty of Medicine.
*** Associate Professor of Pediatrics, Gazi University Faculty of Medicine.
**** Pediatrician, Gazi University Faculty of Medicine.
***** Professor of Pediatrics and Pediatric Hematologist, Gazi University Faculty of Medicine.

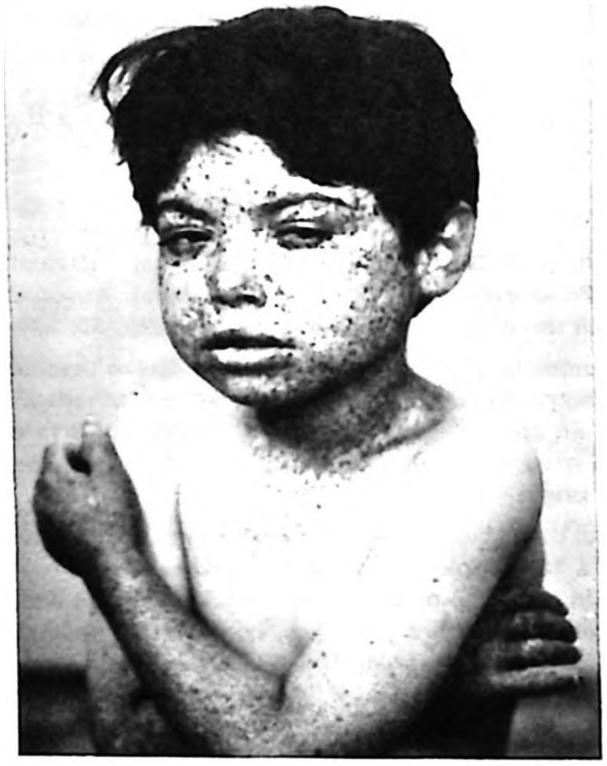

Fig. 1: Patient at 10 years of age.

Laboratory findings: electroencephalography, electromyography, computerized brain tomography and brain auditory evoked potentials were normal, ruling out auditory and neurologic involvement[7-9]. Hematological investigations including hemoglobin, leukocyte count and red blood cell morphology were normal. The platelet count was 239,000/mm^3. Platelets remained discrete, round and isolated in stained blood smears. The prothrombin and partial thromboplastin times were normal, but the bleeding time was greater than 15 minutes. Platelet aggregation response to ADP, collagen and adrenaline was impaired, and to ristosetin was normal (1.5 ng/ml).

A low dose (0.5 mg/kg/day) of oral isotretinoin was initiated since the patient had not developed skin neoplasm and no side effects or malignancy had been observed in two years.

Discussion

Xeroderma pigmentosum is a rare, autosomal-recessive disease characterized by severe photosensitivity and early skin cancers. Patients without neurological symptoms comprise 75 percent of cases and are diagnosed between six and 18 months of age. They reach the tumor stage before the age of 20, but a few run a more benign course as in our case[1, 2, 4-6]. XP has a worldwide distribution

with an approximate frequency of 1/250,000 with equal sex and race preponderence[4-6]. However, the incidences of both XP and thrombasthenia are relatively high in this country because of the high rate of consanguinity[10]. The distribution of XP patients among the various complementation groups is related to ethnic origin[5, 6].

In clinical management, strict, early measures to protect the patient from harmful radiation are necessary[3, 11]. The finding that tumor formation can be rapidly and reversibly supressed by isotretinoin therapy led us to administer low-dose oral isotretinoin to our patient[12].

The lifelong bleeding history, prolonged bleeding time and platelet aggregation pattern in our patient were consistent with GT. This autosomal-recessive disorder of platelet fnuction could be related to quantitative or qualitative abnormalities of platelet membrane glycoprotein IIb/IIIa complex[3]. Platelet dysfunction may also complicate a wide variety of heritable and acquired disorders such as heritable disorders of connective tissue, drug usage, disorders involving the hematopoietic system, uremia, congenital heart disease and liver disease[13]; however, in our case the patient's clinical and laboratory findings were discordant with these disorders.

Although the association of XP with two other diseases of DNA repair defects- Cockayne's syndrome and trichothiodystrophy- has been reported[1, 14], this is the first report of its association with thrombasthenia. Further case reports will shed light on the association of xeroderma pigmentosum and thrombasthenia.

REFERENCES

1. Bohr AV, Evans KV. Heterogeneity of DNA repair: implications for human disease and oncology. Pediatr Hem Oncol 1990; 7: 47-69.
2. English JS, Swerdlow AJ. The risk of malignant melanoma, internal malignancy and mortality in xeroderma pigmentosum patients. Br J Dermatol 1987; 117: 457-461.
3. Stuart MJ, Kelton JG. The platelet: quantitative and qualitative abnormalities. In: Nathan D, Oski F (eds). Hematology of Infancy and Childhood, Volume II. London: Saunders Co; 1987: 1436-1437.
4. Robbins JH. Xeroderma pigmentosum. Defective DNA repair causes skin cancer and neurodegeneration. JAMA 1988; 260: 384-388.
5. Robbins JH, Kraemer KH, Lutaner MA. An inherited disease with sun sensitivity, multiple cutaneous neoplasms and abnomal DNA repair. Ann Intern Med 1974; 80: 221-226.
6. Wood DR, Robins P, Lindhal T. Complementation of the xeroderma pigmentosum DNA repair defect in cell free extracts. Cell 1988; 53: 97-106.
7. Kenyon GS, Booth BJ, Prasher DK, Rudge P. Neuro-otological abnormalities in xeroderma pigmentosum with particular reference to deafness. Brain 1985; 108: 771-784.
8. Mimaki T, Itoh N, Abe J, et al. Neurological manifestations in xeroderma pigmentosum. Ann Neurol 1986; 20: 70-75.
9. Mimaki T, Tagowa T, Tanaka J, Sato K, Yabuuchi H. EEG and CT abnormalities in xeroderma pigmentosum. Acta Neurol Scand 1989; 80: 136-141.
10. Hiçsönmez G. Congenital qualitative platelet disorders in children. Report on 60 patients. Turk J Pediatr 1982; 24: 21-28.

11. Osguthorpe JD, Lang P. Management of xeroderma pigmentosum. Arch Otolaryngol Head Neck Surg 1987; 113: 292- 294.

12. Kraemer KH, DiGiovanna JJ, Moshell AN, Tarone RE, Peck GL. Prevention of skin cancer in xeroderma pigmentosum with the use of oral isotretinoin. N Engl J Med 1988; 318: 1633-1637.

13. Bithell TC. Qualitative disorders of platelet function. In: Lee GR, Bithell TC, Foerster J, Athens JW, Lukens JN (eds). Wintrobe's Clinical Hematology, Volume II. London: Lea and Febiger; 1993: 1397-1422.

14. Nuzzo F, Zei G, Stefanini M, et al. Search for consanguinity within and among families of patients with trichothiodystrophy associated with xeroderma pigmentosum. J Med Genet 1990; 27: 21-25.