

Original Article

Clinicopathological characteristics of xeroderma pigmentosum associated with keratoacanthoma: a case report and literature review

Jin-Feng Zheng¹, Hai-Ying Mo², Zhen-Zheng Wang³

¹Department of Pathology, The General Hospital, Jinan Military Command, Jinan 250031, China; ²Department of Pathology, Zaozhuang Hospital of Zaozhuang Mining Group, Zaozhuang 277100, China; ³Department of Pathology, 456th Hospital of Jinan Military Command, Jinan 250031, China

Received July 17, 2014; Accepted August 16, 2014; Epub October 15, 2014; Published October 30, 2014

Abstract: Objective: To investigate the clinicopathological characteristics, diagnosis and differential diagnosis, and treatment of xeroderma pigmentosum associated with keratoacanthoma in an infant. Methods: The clinical manifestations of xeroderma pigmentosum associated with keratoacanthoma were assessed in an 18-month old boy. The morphological and histological features of the lesions were examined by light microscopy. Results: An 18-month old boy was admitted with unequal size, irregularly shaped brown spots, patches and depigmentation spots on his face. A well-circumscribed hemispherical mass measuring 3 cm × 3 cm with smooth surface and brown patches was observed beneath his left lower eyelid. Light microscopic examination of the skin lesions revealed epidermal hyperkeratosis, chronic inflammatory infiltration of the superficial dermal layer, and increases in melanocytes and melanin in the basal layer. Scanning microscopy showed that the mass beneath the left lower eyelid was cup-shaped, consisting of proliferating squamous cells with a central keratin plug. The squamous epithelium was acanthotic with hypergranulosis. The adjacent epidermis formed exophytic projections resulting in a silhouette likened to lips. An associated inflammatory reaction was observed within the stroma surrounding the mass. The patient was treated with a combination of antioxidant drugs, keeping the child from light and surgical excision of the mass. No recurrence has been observed. Conclusions: Xeroderma pigmentosum of infancy is a rare disease, and association with keratoacanthoma is even rarer. This condition should be considered in the differential diagnosis of freckles, Rothmund-Thomson syndrome and porphyria.

Keywords: Xeroderma pigmentosum, keratoacanthoma, clinicopathology

Introduction

Xeroderma pigmentosum (XP) is a rare autosomal recessive inherited disorder caused by exposure to ultraviolet radiation. The skin of patients with XP is sensitive to light, which can induce skin desquamation, brown spots and patches, and even skin tumors, eye damage and tumors in the viscera. Keratoacanthoma is a rapidly growing skin tumor, occurring primarily in older men but rarely in children. We describe here the clinical and histopathological features of an infant with both XP and keratoacanthoma.

Materials and methods

Clinical features

An 18-month male child was brought to our center by his parents. At age 3 months, he had

developed facial skin redness, blisters and desquamation after exposure to sunlight, a condition diagnosed as “eczema” by a local clinic. Anti-inflammatory ointments and other treatments were not successful. At age 6 months, brown pigmentation spots appeared on his face; the color of the spots deepened after irradiation, but became gradually weaker in the dark. At age 16 months, two grain size red papules appeared below his left lower eyelid. One gradually faded, but the other grew rapidly, being 3 × 3 cm in size after 1 month. At age 18 months, he was admitted to our hospital for diagnosis and treatment.

Physical examination showed that the patient's general condition and vital signs were normal, with no enlargement of superficial lymph nodes. Dermatologic examination showed visible brown, disfiguring spots and patches, of different



Figure 1. Photograph showing a brown patch on his face and a mass below his left eyelid.

sizes and irregular shapes on his face. In addition, a 3.0×3.0 cm hemispheric globular mass, with clear borders and a rough appearance, was observed below his left lower eyelid (**Figure 1**). Laboratory examinations showed nothing abnormal. A biopsy was taken of a patch on his facial skin and sent for pathological examination. In addition, the neoplasm below the left lower eyelid was resected and examined.

Tissue specimens were fixed with 4% formaldehyde, followed by conventional dehydration, paraffin embedding and sectioning. Sections were stained with hematoxylin and eosin (HE) and examined by light microscopy.

Results

Pathological features

Grossly, the skin biopsy tissue was beige in color, $0.3 \times 0.3 \times 0.3$ cm in size with a dark brown, toughened surface, with the cells showing irregular organization. The neoplasm below the left lower eyelid was hemispheric in shape and measured $3.5 \times 3.4 \times 3.4$ cm in size. A beige patch was observed, with the dome showing visible erosion in the center. The mass had clear boundaries, was pale beige in color, and showed a rough appearance on cross section.

Histologic examination of the skin biopsy showed epidermal hyperkeratosis, chronic inflammatory cell infiltrates of the dermis lamina, a large number of melanocytes in the basal cell layer, irregularly increased melanin, and tissue cells containing pigment (**Figure 2**). Histologic

examination of the resected mass showed a typical crater in the epidermis filled with keratin material. Lip-like epidermal hyperplasia was observed around the mass on both sides of the edge, as well as false epithelioma hyperplasia at the bottom of the mass. The epithelial mass was irregular in shape, indicative of compound angular formation, and had clear boundaries as well as containing large numbers of lymphocytes, eosinophils and tissue cells (**Figure 3**).

Our patient was treated by non-exposure to sunlight plus treatment with antioxidants and resection of the acanthoma. He showed good recovery, with no recurrence of tumor 8 months after surgery. He is being closely followed-up.

Discussion

XP is a rare autosomal recessive disease caused by defective DNA repair in various cutaneous and ocular cells following exposure to sunlight [1-3]. Its incidence is low, about 1:65000-1:100000, with 75% of patients diagnosed at age 0.5-3 years. XP is characterized by freckles and dry skin, similar to solar dermatitis, on exposed parts of the body, including the face, lips, conjunctiva, neck and legs. Some spots are pigmented, being gray or beige in color, whereas others may be depigmented. On occasion, visible scabby and bullous lesions may appear, similar to findings in patients with lupus. With age, eye damage increases, with patients experiencing ectropion and/or corneal opacity. Patients may also develop multiple visceral tumors on the head and neck and may experience nerve damage. Malignant tumors, including basal cell carcinoma, squamous cell carcinoma and melanoma, can also develop. XO shows no obvious racial predominance. The parents of this patient are not consanguineous, nor do they have any known genetic disorders.

Keratoacanthoma is a rapidly growing skin tumor, regarded as midway between a benign and malignant tumor or as a malignant tumor, equivalent to a highly differentiated squamous cell carcinoma. These tumors occur mostly on the head and face of elderly individuals. XP associated with keratoacanthoma is extremely rare in children. Our patient was only 18 months old at presentation. He had an about 3.0×3.0 cm hemispherical neoplasm on the skin below the lower eyelid, combined with facial erythema, blister, skin desquamation, brown spots

Xeroderma pigmentosum and keratoacanthoma in an infant

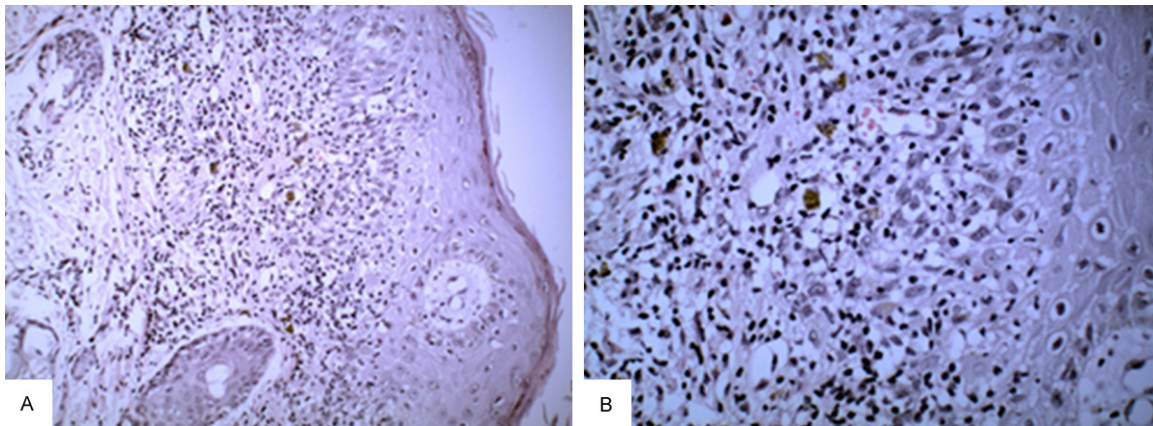


Figure 2. Histopathology of the brown patch, showing epidermal hyperkeratosis, increased numbers of melanin cells, and chronic infiltration of inflammatory cells into the dermis lamina. (A: HE \times 100, B: \times 200).

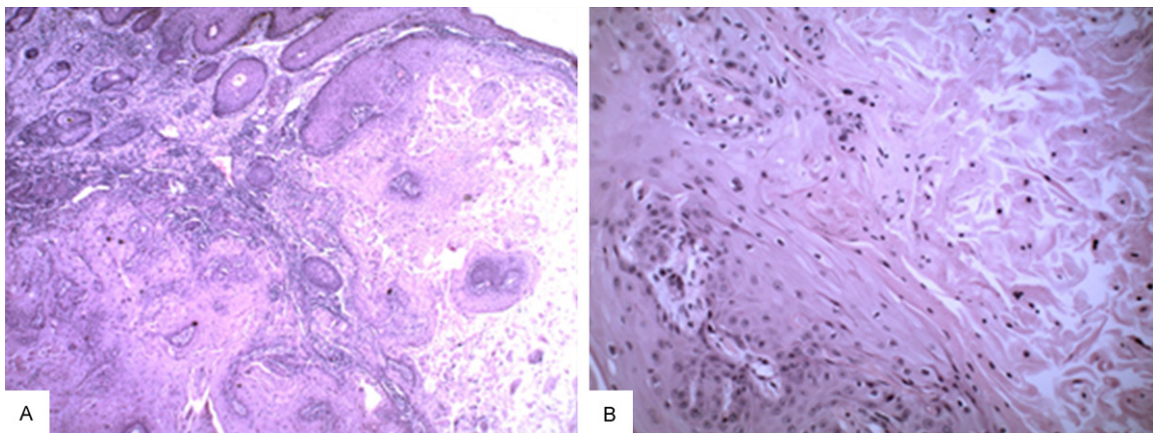


Figure 3. Histopathology of the cornification acanthoma below the left lower eyelid. A: The epidermis of the mass has a typical crater appearance. Lip-like epidermal hyperplasia was observed around the central area on both sides of the edge, with false epithelioma hyperplasia at the bottom of the mass. Inflammatory cell infiltration was also observed (HE \times 40); B: The epidermis of the mass filled with keratin material. False epithelioma hyperplasia was observed at the base of the mass (HE \times 100).

and patches. The diagnosis of XP associated with keratoacanthoma was confirmed by skin biopsy and histopathology.

The lesions in patients with XP are caused by exposure to ultraviolet radiation, which shows that the skin is sensitive to light [4]. It frequently manifests as skin desquamation, brown spots and patches, and may result in tumors on the skin and viscera, as well as damage to the eyes. It is unclear, however, whether XP can induce cornification acanthoma.

Pathological features

Xeroderma pigmentosum: Early pathological changes are hyperkeratosis and thinning at the

root level. Later, the epidermis is seen to shrink, with disordered arrangement of epidermal cell nuclei. The skin does not show typical growth. Rather, XP may be accompanied by solar keratosis, epidermal hyperkeratosis, chronic inflammatory cell infiltrates, increased numbers of melanocytes in the basal cell layer and irregular deposition of melanin. Long term manifestations include tumors and other histologic abnormalities.

Keratoacanthoma: These tumors, which usually occur on the face, head, neck, the back of the forearm and the hand, grow quickly. Histopathology shows that the epidermis is cavate, filled with a corneous plug, and that the hyperplastic epidermis contains keratin pearls.

Xeroderma pigmentosum and keratoacanthoma in an infant

The epidermis around the tumor is cratered, with extranuclear squamous cells and infiltration by inflammatory cells observed in the dermis.

Differential diagnosis

The differential diagnosis of XP includes freckles, Rothmund-Thomson syndrome and porphyria disease, while the differential diagnosis of keratoacanthoma includes squamous cell carcinoma.

Freckles or sallow or taupe spots, more prominent in summer and less prominent in winter. Histopathological examination of freckled skin shows capillary expansion, skin atrophy and angle of damage.

Rothmund-Thomson syndrome: As with XP, Rothmund-Thomson syndrome is a rare autosomal recessive inherited disease, usually occurring during the first year of life. It manifests as red brown pigmentation or pigment loss in the face, limbs, neck, and hips. Histopathology of the skin shows shrinking, red pigmentation of the palms and expansion of blood capillaries. Many of these patients have abnormal hair, mental retardation, and early cataract.

Porphyria disease: Porphyria disease is caused by an abnormality in porphyria metabolism, diagnosed by the presence of porphyria in blood, stool and urine.

Squamous cell carcinoma: Acanthoma can be easily confused with squamous cell carcinoma of the skin. Acanthomas show rapid growth; and are distinguished by round, solid colored nodular lesions, with clear boundaries. The center is filled with a keratin-like substance. The cells are well differentiated and these tumors are often accompanied by vascular proliferation and infiltration by inflammatory cells.

Treatment and prognosis

Patients with XP experience irreversible skin damage upon exposure to light. Treatment is based on avoiding this exposure and may include avoidance of being outdoors and use of sunscreen and dark ointments. In infants and young children with XP, avoiding light for long periods of time can alter calcium concentrations of calcium ions, affecting bone growth and development. These problems may be avoided by dietary supplementation with vita-

min D, vitamin A and nicotinamide or zinc sulfate [5]. Treatment with anticancer drugs, including isotretinoin or fluorouracil [6] can reduce the incidence of skin cancer in XP. However, these drugs have obvious adverse reactions and are not recommended for children. Enzymatic treatment and gene therapy have shown good results, but these agents are still in clinical trials [7, 8]. Surgical resection is effective in patients who have developed tumors.

Patients with XP have a poor prognosis, with about two-thirds dying before age 20 years. Many of these patients will develop multiple malignant tumors within 3-4 years of diagnosis, with widespread metastasis of these tumors resulting in death.

Acknowledgements

This work was partly supported by The President Fund (Grant No. 2011M03) from The General Hospital, Jinan Military Command, China.

Disclosure of conflict of interest

None.

Address correspondence to: Dr. Zhenzheng Wang, Department of Pathology, 456th Hospital of Jinan Military Command, 25 Wuyingshan Road, Jinan 250031, Shandong Province, China. Tel: +86 531 51613575; Fax: +86 531 51613575; E-mail: zhenzhengw456@163.com

References

- [1] Chen J, Deng D, Zhou X and Wang X. One case of Xeroderma pigmentosum with a family history. *J Clin Dermatol* 2012; 41: 45-46.
- [2] Rademakers S, Volker M, Hoogstraten D, Nigg AL, Mone MJ, Van Zeeland AA, Hoeijmakers JH, Housmuller AB and Vermeulen W. Xeroderma pigmentosum group A protein loads as a separate factor onto DNA lesions. *Mol Cell Biol* 2003; 23: 5755-5767.
- [3] Sugawara K. Xeroderma pigmentosum genes: functions inside and outside DNA repair. *Carcinogenesis* 2008; 29: 455-465.
- [4] Mellon I, Hock T, Reid R, Porter PC and States JC. Polymorphisms in the human xeroderma pigmentosum group A gene and their impact on cell survival and nucleotide excision repair. *DNA Repair* 2002; 1: 531-546.
- [5] Ali JT, Mukasa Y and Coulson IH. Xeroderma pigmentosum: early diagnostic features and

Xeroderma pigmentosum and keratoacanthoma in an infant

- an adverse consequence of photoprotection. *Clin Exp Dermatol* 2009; 34: 442-443.
- [6] Stockfleth E. Topical management of actinic keratosis and field cancerisation. *G Ital Dermatol Venereol* 2009; 144: 459-462.
- [7] Zahid S and Brownell I. Repairing DNA damage in xeroderma pigmentosum: T4N5 lotion and gene therapy. *J Drugs Dermatol* 2008; 7: 405-408.
- [8] Menck CF, Armelini MG and Lima-Bessa KM. On the search for skin gene therapy strategies of xeroderma pigmentosum disease. *Curr Gene Ther* 2007; 7: 163-174.