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Early-onset squamous cell carcinoma in xeroderma pigmentosum: A rare case

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Case Report

ABSTRACT

Xeroderma pigmentosum (XP) is a rare autosomal recessive genodermatosis characterised by photosensitivity, dry skin, pigmentary abnormalities, premature skin aging, and skin cancers at an early age. This case report aims to alert health professionals about this disease, considering the rarity of the disease and the need for an early diagnosis of patients with XP. A 4-year-old boy was referred to our department with multiple painful ulcerated masses over his head and face, which had developed over the past two years. At the age of 6 months, the patient started to develop hyperpigmented spots of numerous sizes on his face, and gradually spread to the other sun-exposed areas of his body. He also had dry skin, photophobia, redness, and watery eyes. Dermatological examination showed multiple ulcerated erythematous nodules at the temporal and frontotemporal region; multiple scaly, hyperpigmented macules, papules, and cutaneous horns at the facial region; multiple hypopigmented and hyperpigmented macules, generalised distributed, predominantly over the sun-exposed areas. A biopsy examination from one of the nodules showed keratinising squamous cell carcinoma (SCC). The patient was diagnosed with xeroderma pigmentosum and was treated with multidisciplinary assessment involving dermatology, paediatric, oncology surgery, ophthalmology, and otolaryngology. The diagnosis in this patient is made clinically based on history taking, physical examination, and confirmation of malignancy from biopsy. Early diagnosis of XP is crucial for decreasing the development of neoplasms, which could improve the patient's quality of life.

INTRODUCTION

Mutations in nucleotide excision repair (NER) cause xeroderma pigmentosum (XP), a rare autosomal recessive genodermatosis that results in inadequate deoxyribonucleic acid (DNA) repair following ultraviolet radiation (UVR) exposure**.** XP is defined by photosensitivity, xerosis, pigmentary irregularities, accelerated skin aging, early onset skin malignancies, and in certain instances, neurological and ophthalmic degeneration.[1–5] Compared to healthy individuals, patients with XP are at an increased risk of developing skin cancer, which can be classified as either non-melanoma skin cancer (NMSC) (e.g., basal cell carcinoma (BCC), squamous cell carcinoma (SCC), or melanoma skin cancer (MSC).[1,6–8]

XP was initially delineated by Moriz Kaposi and Ferdinand Hebra in their dermatology textbook published in 1870. Initially, xeroderma; parchment skin; or desiccated skin were the terms used to describe this condition, and subsequently, the term "pigmentosum" was inserted to reflect the greatly increased freckle-like pigmentation. The term "xeroderma pigmentosum" refers to the condition of desiccated and pigmented skin.[4]

XP has been reported worldwide in all races. The sex ratio is essentially equal. XP affects around one individual per one million population in the United States.[1] In Western Europe, XP

affects up to 2.3 individuals per one million live births.[9] The frequency of XP in the Middle East is approximately 15-20 individuals per one million population.[10] In Japan, the incidence of XP is up to 45 persons per one million population or 1 in 22.000 people.[4,11] Currently, there is no data on XP's incidence in Indonesia. It is more likely to occur in areas where consanguinity is common.[1,3,4]

The management of patients with XP relies on prompt diagnosis, continuous shielding from UVR exposure, early identification and treatment of neoplasm, symptomatic treatments, and multidisciplinary care.[1,4,11] The majority of individuals and healthcare professionals are unaware of this ailment, because of the rarity of the disease, resulting in the neglect of XP patients and their lack of adequate medical support. The objective of this case report is to raise awareness among health professionals about XP and emphasise the importance of early diagnosis.

CASE DESCRIPTION

A 4-year-old boy was referred from the paediatric department to our dermatology and venereology department with multiple painful ulcerated masses over his head and face present for the past two years. Initially, the masses started as pea-size bumps (±0,5cm), progressively expanded in size, became ulcerated, and frequently bleed upon exposure. The patient began to acquire hyperpigmented spots of varying size on his face at the age of six months, and they gradually spread to other parts of his body that were exposed to the sun. Those spot's colour tones were heterogeneous. His skin was very dry. His parents denied any exaggerated sunburn upon sun exposure, but for the past two years, the patient has experienced photophobia, redness, and watery eyes. No history of other diseases before. He was the second child, and his family did not have a history of a similar condition or consanguinity.

The dermatological examination disclosed ulcerated erythematous nodules with sizes 6x4x5cm and 2x3x1cm at the temporal region; ulcerated erythematous nodule with size 4x5x1 cm at the frontotemporal region; ulcerated erythematous nodule with size 6x7x0,5cm, covered with crusts at right facial enlarging to right ear region; multiple scaly, hyperpigmented macules, papules, and cutaneous horns at facial region; numerous hypopigmented and hyperpigmented macules, miller to lenticular size, generalised distributed, predominantly over the sun-exposed areas; xerosis skin (+) (Figure 1-A to 1-G).

A radiological examination of the head showed soft tissue masses at the right mandibula and left temporal region, suggesting giant melanoma or abscess (Figure 2-A). The Multi-Slice Computed Tomography (MSCT) scan of the head revealed there were multiple solid masses in the right retroauricular and bilateral fronto-temporo-parietal regions, which erode the right temporal bone and extend into the masticator spaces and adjacent cutis-subcutis, indicative of malignant soft tissue tumours (Figure 2-B to 2-D). A biopsy was done from one of the lesions (the ulcerated erythematous nodules with size 6x4x5cm), and the histopathological examination showed keratinising SCC (Figure 3). Considering the patient's history, physical examination and supplementary assessments, the working diagnosis was XP.

In our department, the patient was treated with 10% urea cream (Carmed® 10%) applied twice daily as a moisturiser, normal saline compresses (0.9% sodium chloride), and Cuticell® (paraffin gauze dressing) applied four times daily to cover the right ear lesion. The patient was advised to reduce UV exposure, apply sunscreen with a minimum SPF of 30 daily, and cover the body with a hat, sunglasses, and long-sleeved clothing when exposed to the sun. The oncologist had planned for the patient to undergo chemotherapy; however, this has not yet occurred due to a deterioration in the patient's general condition.

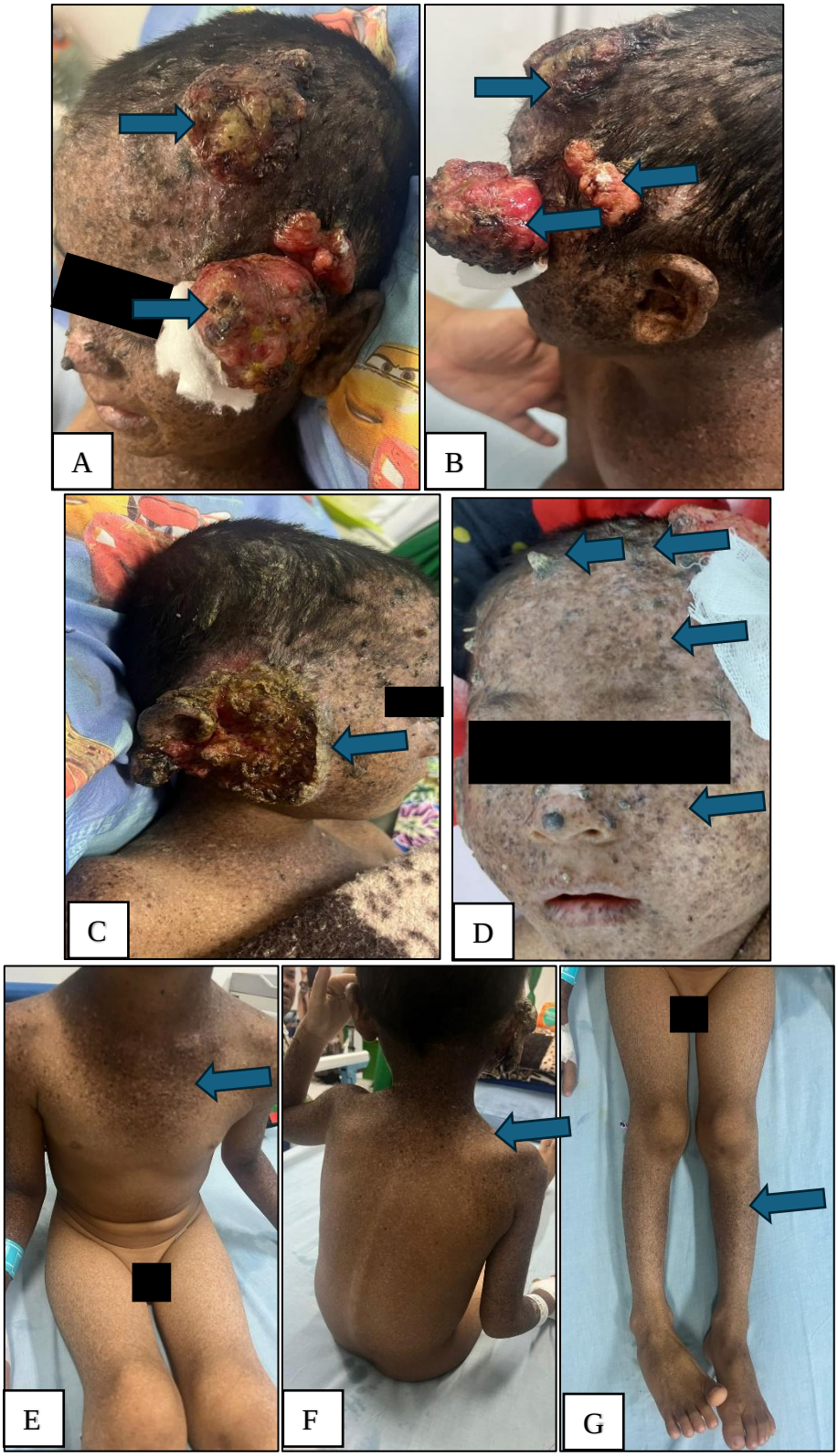

Figure 1. (A-B). Multiple ulcerated erythematous nodules at frontotemporal region; (C) Ulcerated erythematous nodules covered with crusts at right facial enlarging to right ear region; (D) Multiple scaly, hyperpigmented macules, papules, and cutaneous horns at facial region; (E-G) Salt and pepper appearance predominantly over the sun-exposed areas (the central part of the trunk was less affected).

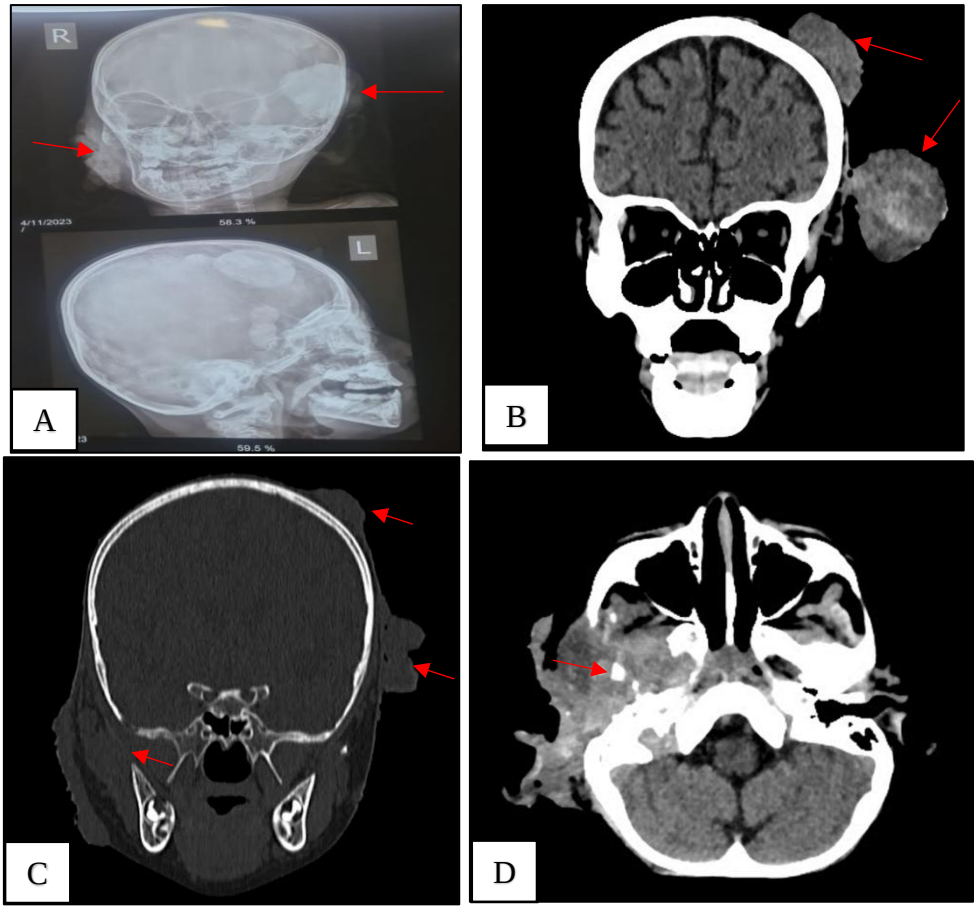

Figure 2. (A) Radiological examination from the head showed soft tissue masses at the right mandibula and left temporal region; (B,C,D) The MSCT examination from the head showed there were multiple solid masses at the right retroauricular and the left fronto-temporo-parietal region.

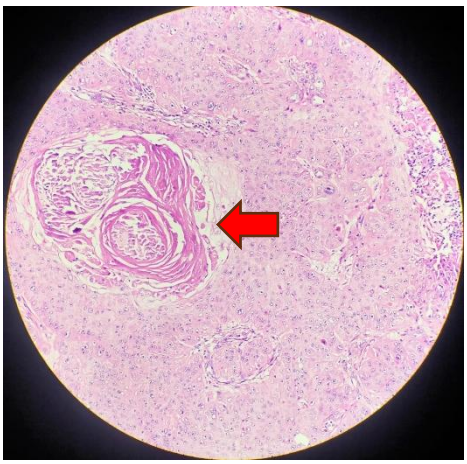

Figure 3. Histopathological examination showed pleomorphic cells and eosinophilic cytoplasm with keratinised masses (red arrow)

DISCUSSION

XP arises from mutations in nucleotide excision repair (NER) mechanisms. The NER system is responsible for eliminating UVR-induced nucleic acid photoproducts such as pyrimidine 6–4 pyrimidine dimers and cyclobutane pyrimidine dimers. Mutations in genes associated with NER lead to defective DNA repair, resulting in the accumulation of DNA photoproducts that may be tumourigenic. Eight mutant genes have been found in XP, including XPA, XPB(ERCC3), XPC, XPD(ERCC2), XPE(DDB2), XPF(ERCC4), XPG, and XPV (DNApol η).[4,12–14]

Patients with XP frequently exhibit distinct clinical manifestations such as photosensitivity, xerosis, freckle-like hyperpigmented macules (lentigines) and poikiloderma (salt and pepper appearance), which are predominantly observed on sun-exposed skin. They also have an increased risk of cutaneous malignant tumours, premature photoaging, and in some cases neurologic and ophthalmologic degeneration. In comparison to healthy individuals, XP patients exhibit skin cancer incidence up to 10.000 times higher for NMSC, including BCC and SCC, whereas MSC is estimated to be up to 2.000 times more prevalent in XP.[1,6,15] The median age of onset of NMSC and MSC in patients with XP is 9 and 22 years, respectively, representing a reduction of over 50 years in the age of onset for the first NMSC and a reduction of over 30 years for the first MCC compared to the general population.[1,7,16]

A reported study from 11 cases of XP showed that the most common malignancy seen was SCC (63.6%) followed by BCC (27.2%).[17] In our case report, the patient developed multiple ulcerated masses over his head and face at the age onset of 2 years old, with one of them confirmed as SCC. This is far earlier than the onset stated in the literature which typically presents at 9 years old for NMSC. In XP, the disease manifestations result from the interplay between genetic risk (mutation in NER mechanism) and environmental exposure (UV exposure). In our case, the patient's parent reported that the patient spent a significant amount of time outdoors playing. Exposure to UV rays increases the carcinogenic photoproducts, meanwhile XP patient has a mutation in the NER mechanism that is responsible for eliminating these photoproducts. As a result, skin cancer arises.

The diagnosis of XP relies on clinical presentation and biopsy confirmation of malignancy.[1,3,18] The 2017 clinical practice guideline for the diagnosis of XP by the Japanese Dermatological Association indicated that a definitive diagnosis can be confirmed through supplementary investigation such as DNA repair tests and genetic analysis.[11] Nonetheless, these tests are not currently available at our institution. The diagnosis was confirmed by a biopsy, which showed pleomorphic cells and eosinophilic cytoplasm with keratinised masses, which is consistent with keratinising SCC.

There is no cure available for XP. The management of patients with XP relies on early diagnosis, continuous shielding from ultraviolet radiation, prompt identification and treatment of neoplasms, symptomatic treatments, and interdisciplinary care. Patients must embrace a lifestyle that reduces UV exposure, utilise UV-blocking apparel, and apply sunscreens with elevated SPF ratings with at least SPF 30 on a daily basis.[19] XP patients who received an early diagnosis and used strict sun protection had fewer skin cancers and lived longer than their affected siblings who did not use strict sun protection.[1] Cutaneous neoplasms are managed similarly to those in patients without XP. Standard procedures encompass electrodesiccation and curettage, surgical excision or Mohs micrographic surgery, and chemotherapy.[1,20] Overall survival can be extended by reducing sun exposure and maintaining regular follow-ups to detect potential early malignancies.

CONCLUSION

Xeroderma pigmentosum is a rare disease that is important for health professionals to recognise. It is crucial to detect the disease at an early stage to prevent and safeguard against the detrimental effects of UVR, thereby significantly reducing the occurrence of complications, particularly skin malignancies.

CONFLICT OF INTEREST

The authors declared no conflict of interest. Informed consent was obtained from the patient legal guardian (parents) for publication of this case.

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DATA AVAILABILITY STATEMENT

There's no data availability in this case report. If any question regarding the case report, reader can email us through the corresponding email.

SUPPLEMENTARY MATERIAL(S)

This manuscript does not contain any supplementary material.

AUTHORS CONTRIBUTIONS

All authors contribute equally in the process of preparing, reviewing, and finishing the manuscript. All authors agreed for this final version of the manuscript to be submitted to this journal.

DECLARATION OF USING AI IN THE WRITING PROCESS

Authors did not use AI and AI-assisted technologies in the writing process.

LIST OF ABBREVIATIONS

XP: Xeroderma pigmentosum; NER: nucleotide excision repair; DNA: deoxyribonucleic acid; UVR: ultraviolet radiation; NMSC: non-melanoma skin cancer; MSC: melanoma skin cancer; BCC: basal cell carcinoma; SCC: squamous cell carcinoma.

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