MICRO LABS LIMITED

DERMA TODAY

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Dear Doctor,

Greetings from Micro Labs. We are happy to bring you "Derma Today" which contains latest and interesting news in the field of Dermatology.

This issue contains:

Should you require any article or, medical information, please feel free to contact us medicalservices@microlabs.in

Looking forward to your valuable feedback.

Best Regards,

Medical Team, Micro Labs Limited.

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New mutation identified in patients with xeroderma pigmentosum group–E in the DDB2 gene

Introduction

Xeroderma pigmentosum (XP) is an unusual autosomal recessive disease characterized by elevated susceptibility to heat, pigment changes and premalignant lesions in the skin's sun-exposed regions, unusually high prevalence of skin tumors, the presence of an increased tumor in the surrounding organs and tissues and, in some instances, neurological abnormality. XP impacts 45 people per million in Japan, 2.3 per million in Western Europe and 1 per million in the USA. It is divided into eight different groups of complementation, the XP variant (XPV) and the classical XP (XPA to XPG) relevant to influenced genes for DNA repairs. Seven of the genes (XPA to XPG) encode the proteins in the nucleotide excision repair (NER), eliminating UVR-induced disruption from DNA. NER consists of two paths: transcription-coupled NER (TC-NER) where the harm happens on the dynamically transcribed DNA strand and global genome repair (GGR) that exists all over the genome. XPC and XPE proteins are required only for GGR, whereas the remaining proteins (XPG, XPF, XPD, XPB, XPA) play a role in both TC-NER and GGR.

Most of the patients in classes XP-A, -B, -D, -F and -G have serious early-age sunburn results. In contrast to the TC-NER defect groups, the patients in the XP-C, -E and -V groups have normal sunburn reactions for skin type. Type E XP patients (singular harmful mutations in the XPE gene) draw from a malformed Damage Specific DNA Binding Protein 2 (DDB2) that risks identifying DNA damage through the DDB complex. Two subunits, DDB1 (p127) and DDB2 (p48), form the UV-DDB complex. UV-DDB has an important part to play in mammalian cells' p53-linked reaction to DNA damage. While cells are subjected to UV radiation, the following p53 accumulation operates DDB2 transcription which results in increased levels of UVDDBs. UV-DDB link with the cyclobutane pyrimidine dimers activates these GGR lesions and may inhibit mutations without impacting survival of UVs.

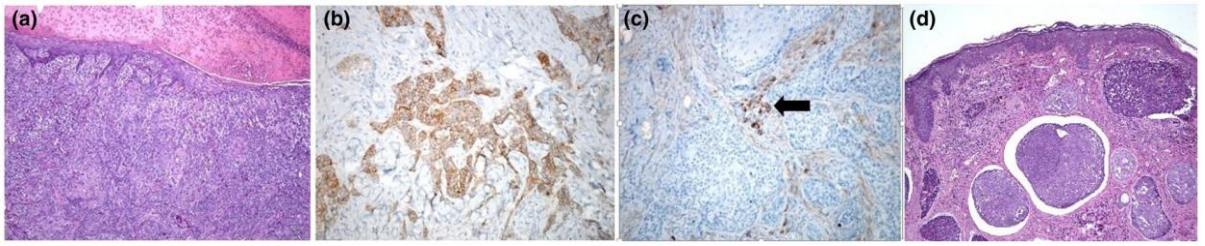
In the current study, authors have presented a family of seven members with a novel nonsense mutation (c.1063C>T (p. Arg355Ter) in the DDB2 gene that causes XP-E type together with their clinical, pathological, genetic, and biochemical findings.

Methods

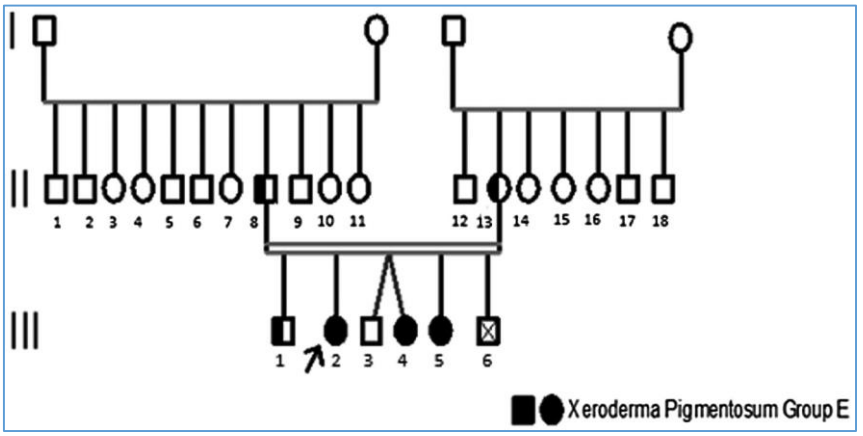
DNA was isolated from peripheral blood samples of the proband, and cancer predisposition genes were sequenced with next-generation sequencing. The demographic features and the laboratory, clinical, and histopathological findings of patients were evaluated.

Results

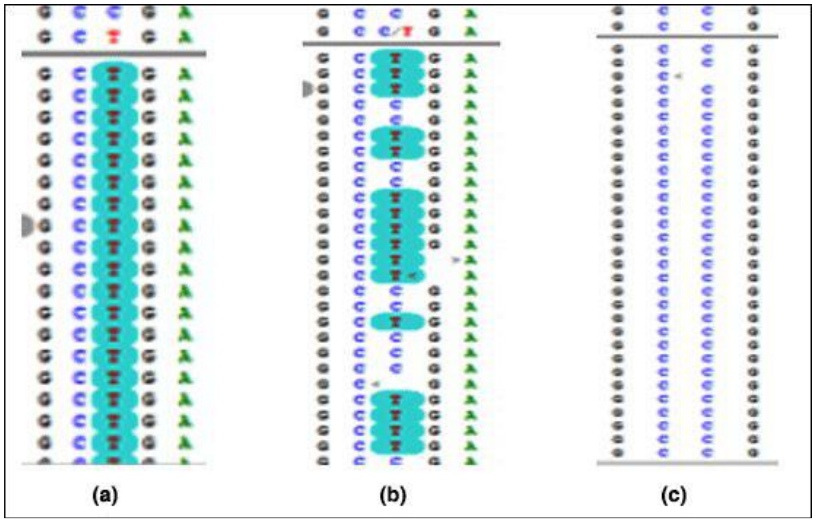
In the proband, squamous cell carcinoma was first diagnosed in the right-eye cornea at the age of 13 years and then in the left-eye cornea at the age of 15 years. Later, the patient was diagnosed with basosquamous cell carcinoma on the dorsum of the nose at the age of 18 years. After genetic analysis, a novel nonsense c.1063C>T(p. Arg355Ter) pathogenic variation that causes XP-E type was detected as homozygous in the DDB2 gene of the proband and her siblings, 11 and 5 years of age, and as heterozygous in her parents and a 22-year-old brother.



Basaloid cells and squamous cells in the tumor (H&E stain, 9100) (a), BerEP4 positivity in basaloid component (9200) (b) and EMA positivity (arrow) in squamous component (9200) (c), other tumor; basal cells show peripheral palisading and clefting away from the fibromyxoid stroma (H&E stain, 9100) (d)



Family pedigree of the patients



A novel homozygous (a), heterozygous c.1063C>T(p. Arg355Ter) variation(b) and normal (c)

Conclusion

Since early termination codon has arisen, the truncated non-functional Nonsense mutation synthesizes proteins or proteins with deleterious losses or gain-of-function activities. It is therefore important to avoid the development of pathological lesions that such patients with nonsense mutation stay away from agents that could cause DNA damage and develop a suitable lifestyle according to this condition.

Source: Karagün E, et al. Novel mutation identified in the DDB2 gene in patients with xeroderma pigmentosum group–E. Medical Genetics. Published online June 2020. https://doi.org/10.1111/ijd.14957

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Defaulters and Pattern of Treatment Default among Leprosy Patients: A 10-Year Analysis

Introduction

Based on current epidemiological evidence, leprosy continues to be a public health problem in India and in many other developing nations worldwide. Despite achieving the elimination target (prevalence below 1 per 10,000) in 2005, new cases are being detected continuously pointing towards a continuous transmission. The 1991 World Health Organization (WHO) dream resolution to eliminate leprosy as a public health issue and to expect fewer and fewer cases over time is challenged by the ongoing transmission of leprosy. India leads the global leprosy load with over 50% (0.127 million) of new cases reported annually from the country. Fortunately, this persistent infectious disorder is also curable if appropriate multidrug therapy (MDT) prescribed by WHO is taken: MDT-MB (rifampicin 600 mg and clofazimine 300 mg tracked monthly and dapsone 100 mg and clofazimine 50 mg daily) for 1 year and MDT-PB (Rifampicin 600 mg tracked monthly and dapsone 100 mg daily) for 6 months. The MDT, a polychemotherapeutic therapy launched by the WHO in 1982, has proven to be the strongest alternative available to combat leprosy and has undoubtedly been the key in meeting the elimination goal of the WHO. To this date, leprosy control strategy remains the key component in the absence of any vaccine. In India, the care of leprosy by public hospitals is given at no expense.

Leprosy programs were combined with the general health systems in the second step of the National Leprosy Eradication Program (NLEP), for greater coverage and also to reduce the stigma connected with the disorder. About this, the default diagnosis in leprosy management system is a proven issue. While just about 5.5 percent of patients with leprosy died in 2016–17, considering the country's population, only a low proportion of the average may have major impacts. Normal of leprosy applies to a patient who refuses to complete the medication, either by refusing to take the medications properly or by declining to visit care centres. Treatment failure also results in subtherapeutic dosing, which can lead to the emergence of drug resistance and failure in the treatment, which will compromise the control programme. Many variables may contribute to default care. There is a shortage of studies on the default treatment and its associated

Factors from India during the last few years. This research was therefore performed with the objective of evaluating the magnitude of treatment default among patients with leprosy, its pattern over the past 10 years, and its correlation with clinicodemographic variables at a tertiary care centre.

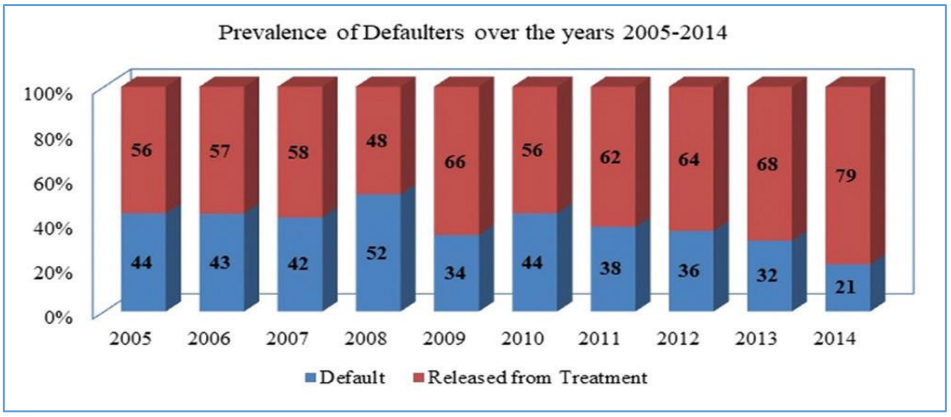
Methods

This was a retrospective study conducted at the urban leprosy center (ULC) attached to the dermatology department of a tertiary care centre. Data were obtained from the standard leprosy cards maintained at ULC from 2005–14. The following data were collected from the

preformatted cards: age, gender, residence, occupation, type of leprosy, treatment, time of default, and so on and analyzed to see the association of defaulter status with sociodemographic and disease-related variables.

Results

In a total of 743 cases, the rate of treatment default was 39.3%. The default status was found to have decreased significantly over the years from 2005–14 (P = 0.03). Majority of the treatment defaulters were migrants (47.9%) as compared with natives (29.7%) (P < 0.001). Regardless of the residential status, treatment default was more in pure neuritic (58.5%) and tuberculoid type (40.7%) as compared with others (P < 0.001). Smear negative cases (40.0%) were more likely to default than smear-positive cases (31.4%) (P < 0.001). Rate of defaulting was more among patients in the district where ULC was located than in the districts away from ULC (P = 0.017).



Trend of treatment default in leprosy cases from 2005–2014

Conclusion

The present study finds a general rising default pattern but the default rate is still strong and cannot be overlooked. The default prevalence was found to be correlated significantly with form of leprosy, profession, and residential status. Default therapy contributes to persistence of the disease, continued dissemination and promotes resistance growth. The causes leading to the default treatment can be diverse and need to be further studied and addressed for better compliance and control program success with the patient.

The key drawback of this research was that due to the retrospective sample nature the precise explanation for the average within the study population could not be ascertained. They recommend more study into the reasons of default using questionnaires of people returning following default to the treatment facility. It will help raising the average rating in resolving the cause and appropriate treatment of the patients.

Source: Mushtaq S, Dogra D, Faizi N, Dogra N. Profile of defaulters and pattern of treatment default among leprosy patients at a tertiary care hospital: A 10-year analysis. Indian Dermatol Online J 2020;11:355-60.

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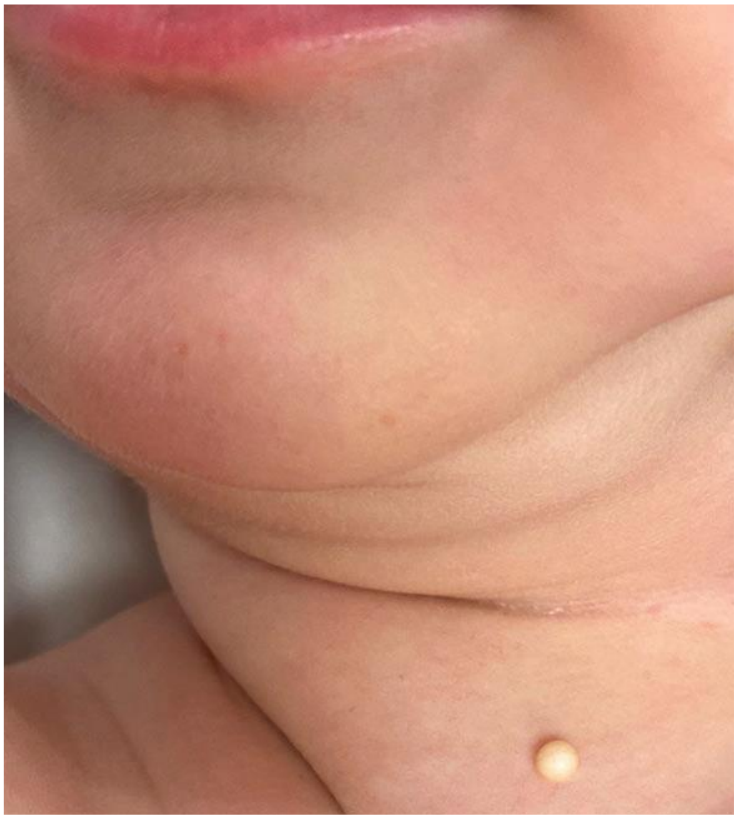
CASE STUDY

Midline Anterior Neck Inclusion Cyst in a child

An otherwise stable 9-month-old female baby born with a 4-mm yellow-white exophytic papule at the stage of the suprasternal knot on the anterior midline of the arm. The parents reported the lesion was present from birth, had not noticeably grown in size or changed in appearance, and was asymptomatic. Similar lesions have not had a family history. Ultrasonography was done and a 0.4 cm thin-walled cystic formation tended to emerge from the skin at the anterior midline of the arm. No fundamental area of the sinus has been established. A shave biopsy was done, and a cyst with epidermal inclusion was identified through histopathologic analysis.



Improper fusion of the anterior side of the neck during embryological development may trigger multiple congenital abnormalities in this area. The appearance and position of the lesion will be taken into consideration when formulating a clinical diagnosis of an anterior neck condition in the midline. Thyroglossal duct cysts develop around the anterior midline, but are subcutaneous and seldom at the sternal spot. Midline cervical clefts can occur anywhere along the anterior midline and appear as a thin vertical plaque of erythematous skin with a nipple like a higher-aspect

projection. Lastly, bronchogenic cysts normally act as a leaking sinus or thin subcutaneous nodule, and are generally found at the suprasternal notch.

In a case study of 7 patients with an identical abnormality that had been present since birth, the Midline anterior neck inclusion cyst (MANIC) was recently reported in the literature. Earlier, a milium-like cyst located at the anterior neck midline was identified in 2 additional case reports. This congenital lesion varies from other anterior midline neck defects in its superficial papular shape, which represents a broad milium, its midline position at the suprasternal notch point, and the histopathological characteristics of an inclusion cyst consisting of stratified squamous epithelium, keratohyaline granules, and central orthokeratin. MANIC was not correlated in the recorded cases of pathological internal abnormalities such as fistulas or tracts in the sinuses. Luckily, MANIC is a healthy, usually asymptomatic cyst that can be tracked with surgical excision, or extracted cosmetically. Spontaneous resolution was reported, too. MANIC, a newly described entity, has largely gone understated. To distinguish MANIC from other congenital developmental anomalies, the clinical clues of the characteristic appearance and precise location must be considered when assessing superficial midline anterior neck abnormalities.

Source: Rushin C, et al. Midline Anterior Neck Inclusion Cyst. JAMA Dermatol. Published online 2020. doi:10.1001/jamadermatol.2020.1089