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Xeroderma pigmentosum group D:
a clinical and genetic study of 19 Japanese cases

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Xeroderma pigmentosum (XP) is a rare autosomal recessive genetic disorder of DNA repair in which the ability to repair damage caused by ultraviolet light with an incidence of 1: 22,000 in Japan. From the clinical symptoms, XP is classified into 3 types, such as **XP cutaneous disease** (45% of Japanese XP), **XP neurological disease** (55% of Japanese XP), and **XP/Cockayne syndrome (CS) complex** (Extremely rare). Genetically, XP is classified into eight distinct groups: A though G and a variant form (V). XPA is the majority (55%) and XPV follows it (25%) in Japanese XP case.

Although the frequency of XPD is only 8% in Japan, there are the most diverse clinical symptoms. In contrast to Western XPD reports that there are many cases of XPD neurological disease, there are many patients with XPD cutaneous disease in Japan. In spite of the phenotypic and geographic differences, Japanese XPD cases have not been adequately studied.

	First visit (age)	Sex	Diagnosis	Sunburn	Pigmentary disorder	Skin cancer (onset age)	Neurological symptom	Severity Score	Gene analysis
1	39y	M	XPD	+	+	SCC, BCC, AK (35y)	–	D3, N0	cells not available
2	65y	F	XPD	+	+	SCC, BCC, AK (50y)	–	D3, N0	cells not available
3	3y	M	XPD	+	+	–	–	D2, N0	Under analysis
4	26y	M	XPD	+	+	BCC (12y)	+	D3, N3	Under analysis
5	42y	F	XPD	+	+	BCC (41y)	–	D3, N0	Under analysis
6	1y10mo	M	XPD/CS	+	+	SCC (2y4mo)	+(CS)	D3, N3	G47R/-
7	34y	M	XPD	+	+	–	–	D2, N0	Under analysis
8	3y6mo	F	XPD	+	–	–	–	D2, N0	Under analysis
9	57y	M	XPD	+	+	SCC (56y)	–	D3, N0	Under analysis
10	5y11mo	F	XPD	+	+	–	–	D2, N0	Under analysis
11	60y	F	XPD	+	+	BCC, AK (56y)	–	D3, N0	R601L/R601L
12	49y	F	XPD	+	+	+	–	D3, N0	Under analysis
13	60y	M	XPD	+	+	BCC (60y)	–	D3, N0	Under analysis
14	36y	F	XPD	+	+	–	–	D3, N0	Under analysis
15	1y1mo	M	XPD/CS	+	±	–	+(CS)	D2, N3	G47R/R616G
16	63y	M	XPD	+	+	BCC (60y)	–	D3, N0	No mutation in exon
17	62y	M	XPD	+	+	AK (50y)	–	D3, N0	R601L/R601L
18	4y4mo	F	XPD/CS	+	–	–	+(CS)	D2, N2	R636W/R636W
19	66y	M	XPD	+	+	AK (66 y)	–	D3, N0	R601L/del482

<Materials and Method>

19 cases were diagnosed to have XPD using cultured fibroblasts which demonstrated an increased DNA repair capacity by transfecting an XPD gene between 1998 and 2017. We conducted clinical, epidemiological, and genetic studies from medical records and examination data.

<Results>

- ◆ All 19 XPD patients had a history of sunburn.
- ◆ The diagnosis confirmed mean age of XPD was 35.6 years old.
- ◆ There were 15 cases of XPD cutaneous disease, 1 case of XPD neurological disease, and 3 cases of XPD/CS complex.
- ◆ 11 cases showed complications of skin cancer, the average age of onset was 44.4 years old. Skin cancer develops is obviously younger and more frequently than healthy people due to the photoageing and photocarcinogenesis in which lacking proteins involved in cleavage of damaged DNA in nucleotide excision repair.
- ◆ There was no relationship between UV sensitivity of patient cultured fibroblasts and severity of clinical type.

Summary and Conclusion

We examined clinical, epidemiological, and genetic studies in Japanese 19 cases of XPD who we experienced in 20 years. In Japan, XPD disease clasification was confirmed that most cases are cutaneous disease (15 cases), neurological disease (1 case), XPD/CS complex (3 cases) is rare. This frequency is obviously different from the Europe XPD case where the neurological disease is common, and there are regional differences.

Although the analysis number is still insufficient and genetic analysis is currently underway, clinical type (phenotype) - genetic type relation is inferred in Japanese XPD patients. It is suggested that R601L is associated with XPD cutaneous disease, G47R is associated with a severe XPD/CS complex, and R636W is related to a mild XPD/CS complex.