

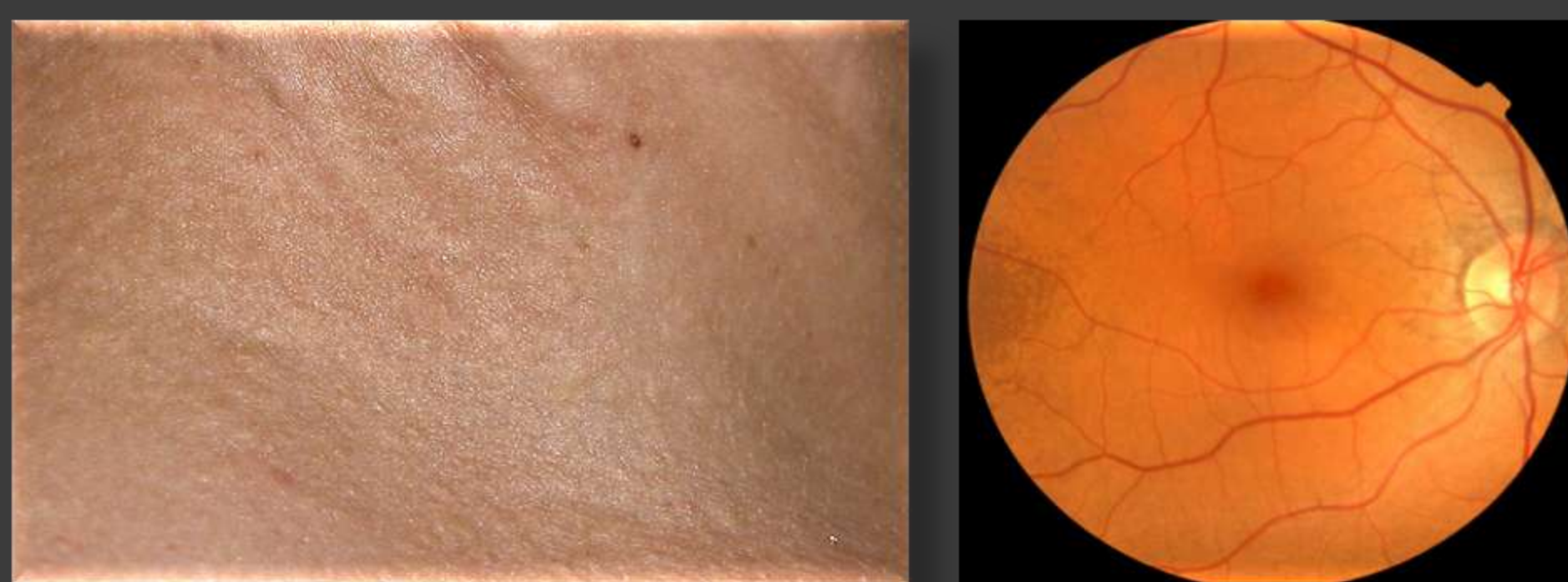
# FAMILIAL PSEUDOXANTHOMA ELASTICUM WITH NEPHROCALCINOSIS A CASE REPORT

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## Introduction

Pseudoxanthoma elasticum (PXE) is an autosomal recessive genetic disorder characterized by progressive calcification and fragmentation of elastic fibres. The estimated prevalence is 1 case in 25,000-100,000 individuals [1, 2]. PXE is caused by mutations in the ABCC6 gene. More than 300 pathogenic ABCC6 mutations are known. Two of these mutations are common: p.R1141X in exon 24, with a prevalence of 30%, and the Alu-mediated deletion of exons 23 to 29 (EX23\_29del; p.A999\_S1403del) found in 10-20% of patients [3]. Homozygosity is rare. PXE commonly involves the reticular dermis, the Bruch membrane of the eye, and blood vessels. Renal manifestations include hematuria and, rarely, nephrocalcinosis, although the significance of the later in the context of PXE has been called into question [4].



Neck: plucked skin appearance

Eye: angioid streaks



Abdominal ultrasound: nephrocalcinosis

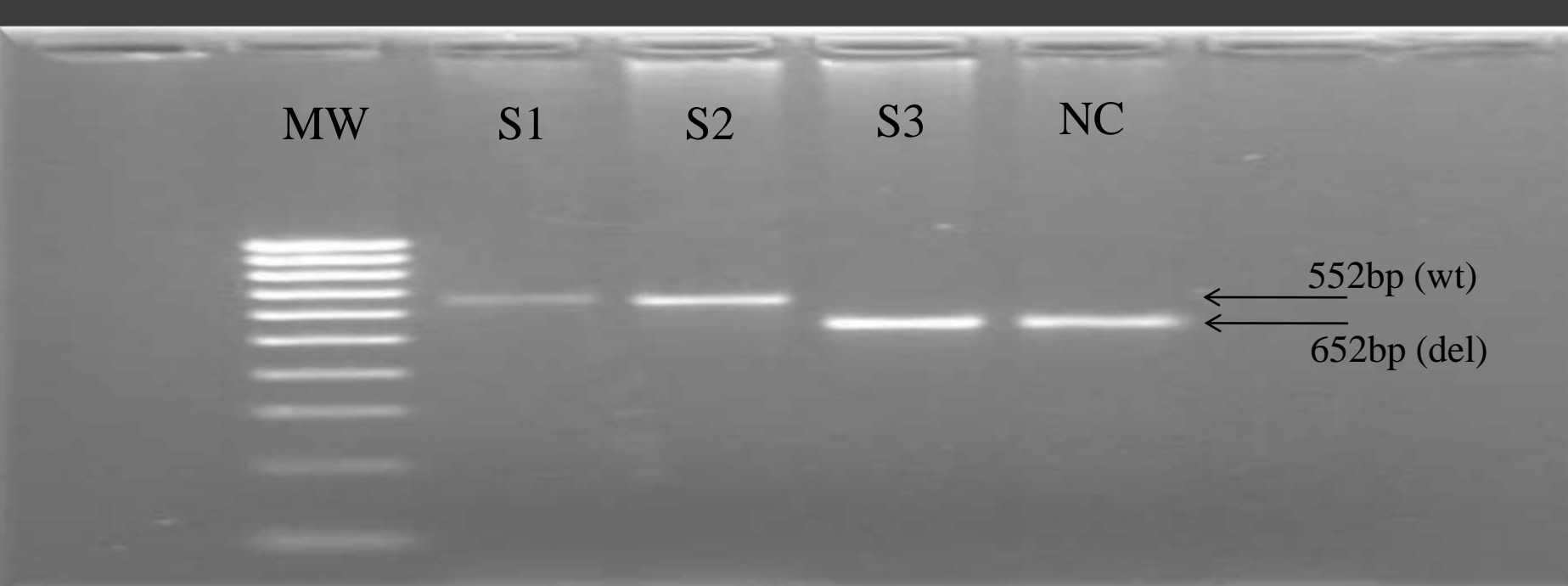
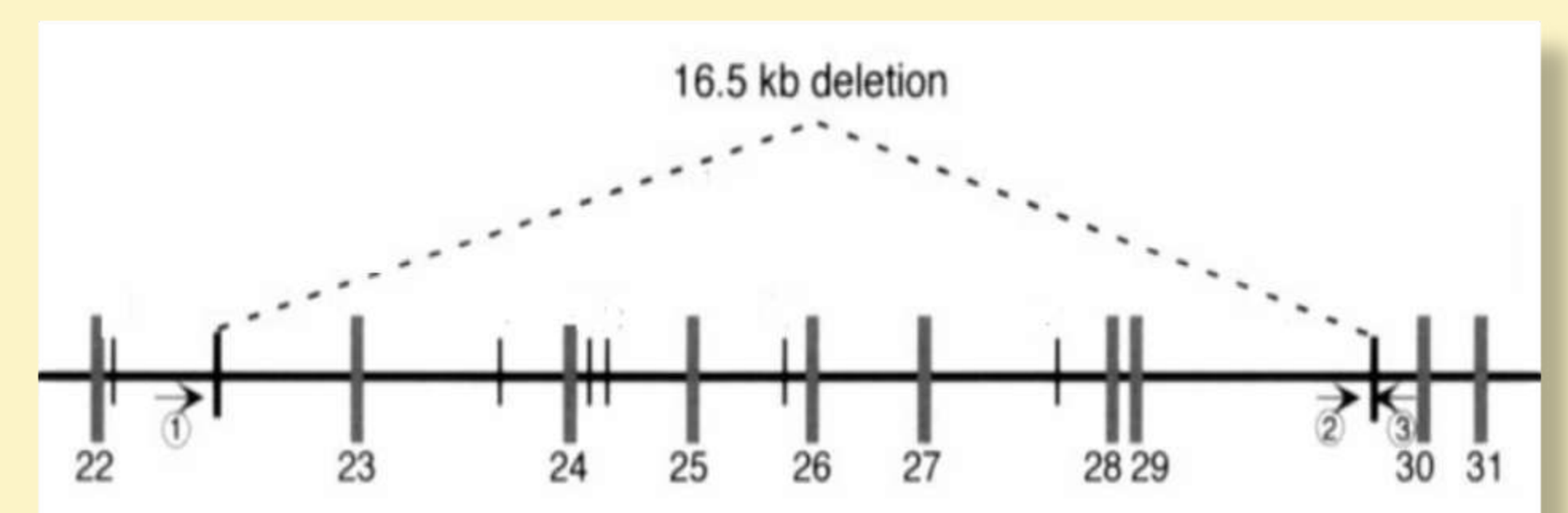
## Case Report

A 40-year-old female with a previous diagnosis of PXE, was admitted at the Nephrology Outpatient Clinic for nephrocalcinosis. Examination of the patient revealed the presence of characteristic bilateral and reticular papillary lesions with yellowish-color in the neck region (plucked chicken appearance), ocular abnormalities (atrophy of the retinal pigment epithelium, typical angioid streaks, peau d'orange of the fundus) and nephrocalcinosis.

The diagnosis of pseudoxanthoma elasticum had been previously established by skin biopsy in 1998. The proband has two sisters, one of which also has a diagnosis of PXE and nephrocalcinosis. Microscopic and gross hematuria was reported in both affected sisters. Abdominal ultrasound confirmed bilateral cortico-medullary nephrocalcinosis, Calcium and phosphorus levels in blood and urine were normal. Hyperparathyroidism, renal tubular acidosis, hypervitaminosis D and hyperoxaluria were excluded. Renal biopsy showed only minor glomerular abnormalities, and immunofluorescence was negative. Positive immunohistochemistry for type IV collagen excluded Alport syndrome as the cause of hematuria. Medullary sponge kidney was identified by excretory urography.

## Material and Methods

Genomic DNA was used as a template for PCR amplification of the region spanning introns 22 to 29 of ABCC6 [5]. The oligonucleotide cocktail used generated a 552bp PCR product for the normal sequence (primers 2 and 3), and a 652bp product for the deletion mutation (primers 1 and 3).



PCR analysis of the deletion mutation: S1-proband; S2-affected sister, S3-unaffected sister; NC-unrelated unaffected control.

## Results

Both sisters with PXE (S1 and S2) were homozygous for the EX23\_29del mutation. The third sister (S3) did not carry this deletion.

## Discussion

There are occasional reports of diffuse visceral calcifications in PXE. PXE-associated nephrocalcinosis was previously noted in four patients belonging to different families [4, 6, 7]. This is the first report of familial co-occurrence of PXE and nephrocalcinosis with medullary sponge kidney. These sisters' peculiar phenotype could be due to their unusual genotype, that was previously classified as a "severe" genotype [8]. Homozygous deletion mutations cause complete loss of function of the ABCC6 protein, and are associated with earlier age of onset and multiple organ involvement. On the other hand, other genetic and environmental factors, such as diet [9], are known to be important in the development of PXE, and are likely to be shared by the two affected sisters.

## References

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