Skinning the Surface of Bone Abnormalities in Trichoiodiodystrophy

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INTRODUCTION

Trichoiodiodystrophy (TDD) is a rare autosomal recessive disease characterized by multisystem abnormalities: low birth weight, short stature, developmental delay, microcephaly, absent myelin in the brain, ataxia and altered reflexes, congenital cataracts, photosensitivity, ichthyosis and sulfur-deficient, brittle hair (Figure 1).

Bone abnormalities, which include central osteosclerosis, peripheral osteopenia, and hip abnormalities, such as coxa valga (Figure 1), subluxation and avascular necrosis, significantly impact the quality of life of TDD patients. Patients with TDD exhibit a diagnostic “tiger-tail” banding pattern in hairs examined utilizing polarized microscopy (Figure 2). The underlying cause of TDD involves mutations in the genes, XBP, XPD, TDDA, which collectively play a role in DNA repair and basal transcription (1). TDD1 gene, whose function is unknown, is also associated with TDD (1).

OBJECTIVES

• Characterize the bone abnormalities and clinical manifestations present in TDD patients examined at NIH.
• Identify TDD patients at risk for rapidly progressive bone abnormalities.

METHODS

• Reviewed clinical documents and imaging studies for the 32 TDD patients utilizing Clinical Research Information System (CRIS), as well as from clinical centers and hospitals around the world.
• Evaluated 611 radiographic images (x-rays, CTs, MRIs) for changes in bone structure, hip orientation and trabecular architecture.
• Assessed stage of avascular necrosis (AVN) as described in reference (2).
• Measured the acellular angle for the TDD patients exhibiting hip abnormalities (3, 4).

RESULTS

Figure 5: Two TDD patients (TDD548E & TDD4018E) with progressive degeneration of the femoral epiphyses.

Table 1: Clinical array of 32 TDD patients

SUMMARY & CONCLUSIONS

• Delayed bone growth, central osteosclerosis, peripheral osteopenia, hip degeneration or coxa valga were present in 31 (97%) of 32 TDD patients. Thus bone abnormalities are a common clinical feature of TDD.
• Hip abnormalities (subluxation and/or femoral head degeneration) were present in 5 (16%) of 32 TDD patients. Acetabular angle measurements did not correlate with the clinical and radiological findings for 4 of these TDD patients.
• All patients with hip abnormalities exhibited difficulty walking, typically beginning at an early age, followed by rapid worsening of ambulation over 4-5 years.
• Of the 5 TDD patients who received hip surgery, 2 died from post surgery complications and 2 remain bedridden following surgery. Thus, bone abnormalities, specifically hip degeneration, may significantly impact the TDD patient’s quality of life.

FUTURE DIRECTIONS

• Further analyze the characteristics of hip degeneration in order to gain an understanding of the causative factors and events preceding the degeneration of the femoral head, with the goal of improving diagnosis and treatment for TDD patients.

REFERENCES


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