

## Corneal Changes in Spondyloepiphyseal Dysplasia Tarda

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**Background:** A new type of corneal opacity with prominent corneal nerve fibers as an ocular complication of spondyloepiphyseal dysplasia tarda (SEDТ).

**Case:** A 58-year-old woman, diagnosed with SEDТ at 5 years of age, underwent a complete ophthalmological examination.

**Observations:** The patient had no complaints and no history of eye disease. No relatives were reported to have suffered from SEDТ. Slit-lamp examination disclosed a diffuse opacity in the central cornea in both eyes, which was localized in the middle to deep stroma. Dot opacities in the central and paracentral cornea were located in the middle of the stroma in both eyes. Optically clear regions were observed in the peripheral cornea of both eyes. More interestingly, corneal nerve fibers were visible passing from the limbus to the central cornea in both eyes.

**Results:** The etiology of the corneal opacities of this patient with SEDТ is unknown. However, collagen and proteoglycan abnormalities in the skin of patients with SEDТ have been reported. Therefore, such abnormalities may also be present in the cornea and these alterations may lead to corneal complications. **Jpn J Ophthalmol 2000;44:29–32** © 2000 Japanese Ophthalmological Society

**Key Words:** Corneal opacity, prominent corneal nerve fibers, spondyloepiphyseal dysplasia tarda.

### Introduction

Spondyloepiphyseal dysplasia tarda (SEDТ) is a rare inherited disease of skeletal dysplasia of both the spine and epiphyses of the major long bones. The onset of SEDТ is in childhood and patients with SEDТ are characterized by their short stature with osteoarthritis of the major joints, such as the knee and hip joints. The inheritance of SEDТ has been described as mainly X-linked recessive. However, autosomal dominant and recessive cases have also been reported.<sup>1</sup>

Ocular complications of SEDТ have been reported in 4 cases and corneal opacities were the only ocular disorder. Punctate opacities through the entire depth

of the cornea was reported in 3 cases in one pedigree.<sup>2</sup> In the other case, peripheral nodular-shaped opacities in the deep stroma up to Descemet's membrane, and central fine, ground-glass opacities in the middle and anterior stroma were observed.<sup>3</sup>

We report a patient with SEDТ with a different type of corneal opacity, combined with prominent corneal nerve fibers. As far as we know, this is the first report of prominent corneal nerve fibers in a SEDТ patient.

### Case Report

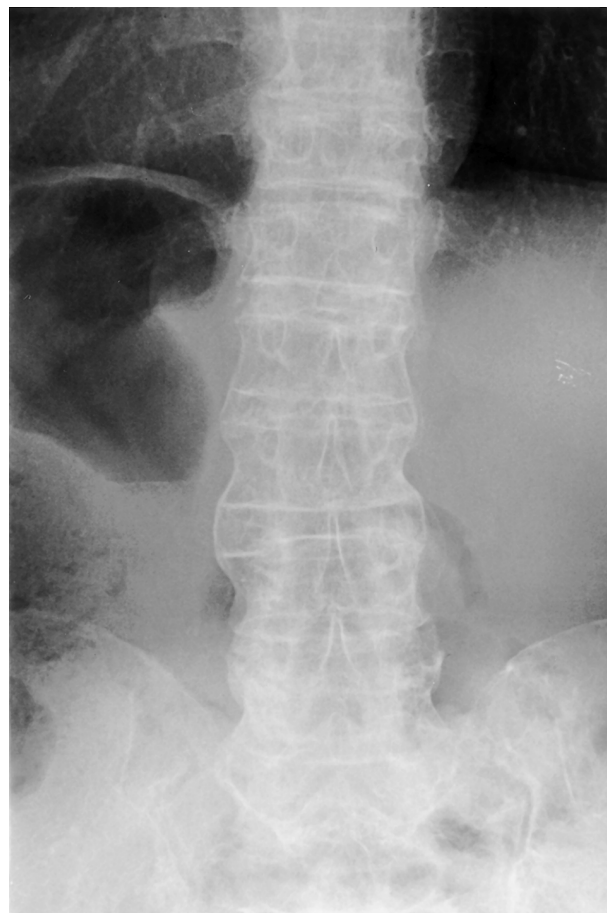
A 58-year-old woman was referred to our hospital for examination because of ocular complications connected with SEDТ. She had been diagnosed as having SEDТ by an orthopedist when she was 5 years old. The woman was 127 cm tall and weighed 39 kg (Figure 1). X-rays showed various irregulari-

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**Figure 1.** The patient is short in stature, only 127 cm tall.



**Figure 2.** X-ray photograph of patient's spine. Various changes of spine were found, such as vertebra plana, osteophyte of spine, irregularity of vertebra endplate, and narrowing of intervertebra.

ties of the spine, such as vertebra plana, osteophyte of the spine, sclerosis, and irregularity of vertebral endplate, and narrowing of intervertebra (Figure 2). She had no ocular complaints and no history of eye disease. SEDT has not been reported in her family. Her parents have neither eye disease nor corneal opacities.

At the first examination in our clinic, the best corrected visual acuity was 20/20 in both eyes; Vd = ( $1.0 \times +0.75$  cyl  $-0.5$  D Axis  $65^\circ$ ), Vs = ( $1.0 \times +0.25$  D). The axial length, measured with the auto axial length biometer (Tomey, Nagoya), was 23.4 mm in the right eye and 23.1 mm in the left eye.

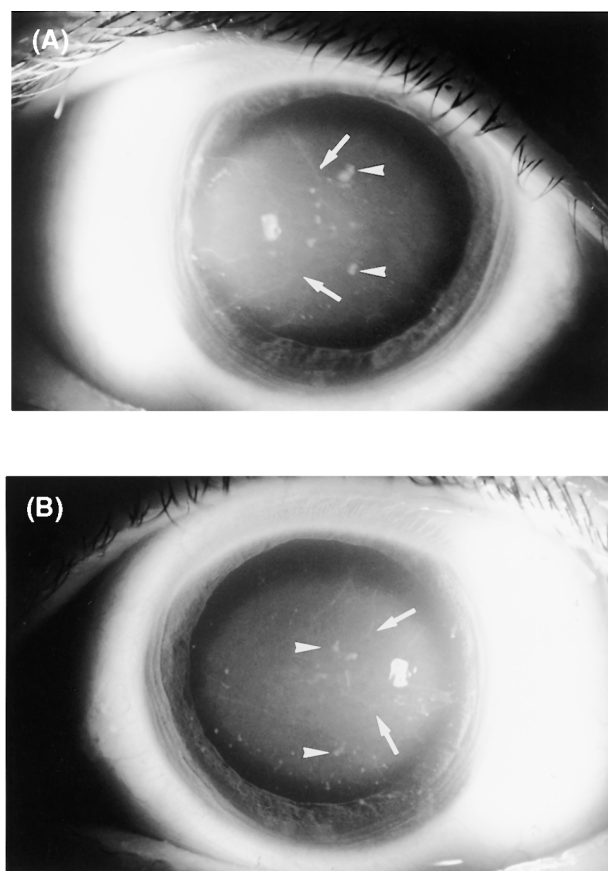
Slit-lamp examination disclosed a diffuse corneal opacity in the central cornea in both eyes (Figure 3). This opacity was localized in the middle to deep stroma. Besides this opacity, multiple dot opacities were found in the central and peripheral cornea in each eye. These dot opacities were localized in the middle of the stroma and were prominent in the

lower cornea of both eyes. However, these opacities were not observed in the most peripheral cornea in either eye.

In addition to the opacities, prominent corneal nerve fibers were found in both eyes. The nerve fibers were visible running from the peripheral to the central zone of the cornea.

The corneal diameter was 11 mm in both eyes. Corneal thickness determined by ultrasound pachymeter (Tomey) was  $473 \mu\text{m}$  in the right eye and  $478 \mu\text{m}$  in the left eye. The corneal sensitivity measurement by Cochet-Bonnet esthesiometer was 55 mm in the right eye and 60 mm in the left eye. Corneal topographic analysis by TMS-1 (Tomey) showed no prominent configuration in either eye.

The corneal endothelium was analyzed by noncontact specular microscopy (Sp-1000; Nidek, Nagoya). The cell population of the endothelium was 3154/



**Figure 3.** Corneal changes in this spondyloepiphyseal dysplasia tarda patient. (A) Right eye. Diffuse corneal opacity is observed in central cornea. Multiple dot opacities are also observed in central cornea as well as in mid-peripheral cornea (arrowheads). Corneal nerve fibers are visible in middle stroma of cornea. Nerves are more prominent in central cornea in correspondence with area of opacity (arrows). (B) Left eye. Diffuse and dot corneal opacities are observed (arrowheads). Corneal nerve fibers are also visible in left eye (arrows).

mm<sup>2</sup> in the right eye and 3204/mm<sup>2</sup> in the left eye. The coefficient of variation in the cell area was 27.1% in the right eye and 28.4% in the left eye. In the right eye, the cell shape was hexagonal in 73.6% of cells; in the left eye, in 61.5%. No significant abnormality in these three parameters of the corneal endothelium was found.

## Discussion

We report a novel type of corneal opacity with prominent corneal nerve fibers in an SEDT patient. Previous studies have reported the presence of nodular corneal opacities in the peripheral zone of the cornea and diffuse corneal opacity in the anterior

and middle anterior stroma of the cornea.<sup>3</sup> Prominent corneal nerve fibers in patients with SEDT have never been reported. In our patient, corneal opacity was found throughout the corneal stroma, but was more prominent in the deep stroma. In addition, nodular opacities were present in the central and mid-peripheral zone of the cornea. The prominent corneal nerve fibers were observed running from the limbus to the central cornea in both eyes. This is the first report of prominent corneal nerve fibers in patients with SEDT.

One may claim that corneal opacity may not be associated with SEDT. However, these corneal changes were found in both eyes, and the stage and the characteristics of the corneal opacities were similar in both eyes. Moreover, neovascularization was not present in either eye, and there was no history of eye disease or systemic disease that might cause such corneal opacities. Corneal opacities have been described in the previously reported cases of SEDT, although the type of corneal opacity was different.<sup>2,3</sup> For these reasons, we believe that the corneal opacity in this patient is associated with SEDT.

The prominent nerve fibers in our case were found in both corneas and were much more prominent than those seen in individuals of similar age. Prominent corneal nerve fibers have been reported to occur with aging as well as in diseases such as multiple endocrine neoplasia, neurofibromatosis, and Refsum syndrome.<sup>4-7</sup> Our patient did not have such a disease. These observations suggest that there may be a relationship between SEDT and the prominent corneal nerve fibers. However, the etiology of prominent corneal nerves is also unknown, and this is the first report of prominent nerve fibers in an SEDT patient. Further studies of the corneas of other SEDT patients will be needed to establish this relationship.

The etiology of the corneal opacities is unclear. However, collagen abnormalities have been reported in the soft skin of SEDT patients.<sup>2</sup> For example, the collagen fibers have been reported to be significantly larger in diameter in SEDT patients than in normal subjects.<sup>8</sup> It is unclear what causes the larger diameter collagen fibers in SEDT patients. In type V collagen, the diameter of the collagen fibers is known to be restricted.<sup>9,10</sup> Interestingly, type V collagen is present in the cornea as well as in the arthrosis.<sup>11</sup> Therefore, there is a possibility that the abnormality of collagen fibers in the arthrosis and in the cornea of SEDT patients may be related to type V collagen.

In addition to the collagens, proteoglycans such as keratan sulfate have been shown to restrict the space

between collagen fibers in the stroma. An abnormality in the metabolism of proteoglycan derived from dermal fibroblast cells of SEDT patients has been reported.<sup>12</sup> This abnormality may induce changes in the distance between the collagen fibers, leading to the opacity of the stroma in SEDT patients.

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