A newborn male was noted to have bilateral congenital corneal opacification. Findings from examination disclosed a variety of dysmorphic features, including cutis laxa, progeroid aspect, short stature, multiple hyperextensible subluxated joints, muscular hypotonia, and hyperreflexia. Bilateral penetrating keratoplasties were performed; histopathologic examination revealed diffuse epithelial thickening, loss of the Bowman layer, and stromal attenuation with anterior stromal scarring. Special stains showed no deposition of abnormal material in the corneas. Electron microscopy demonstrated absence of Bowman layer differentiation with a paucity of collagen fibers, as well as extensive small elastic fibers in the anterior stroma. The diagnosis of De Barsy syndrome was made, a rare progeroid syndrome associated with characteristic ocular, facial, skeletal, dermatologic, and neurologic abnormalities. De Barsy syndrome should be included in the differential diagnosis of congenital corneal opacification; its distinctive clinical features enable the clinician to easily differentiate it from other causes of congenitally cloudy corneas.


Congenital corneal opacification is associated with a variety of ocular and systemic disorders. We report a case of bilateral corneal opacification associated with De Barsy syndrome, a rare systemic syndrome associated with distinctive clinical features. To our knowledge, this is the first report of De Barsy syndrome in an English-language ophthalmic journal and the first description of light and electron microscopic corneal findings in this syndrome.

REPORT OF A CASE

A newborn male born to a 32-year-old, healthy, nulliparous woman was noted to have bilateral corneal opacification. The infant was the product of a 42-week gestation, complicated only by diet-controlled gestational diabetes. The mother, who received good prenatal care, was rubella immune at the beginning of her pregnancy and had negative findings for syphilis and hepatitis on serologic examination. There was neither a history of tobacco, alcohol, or other drug use during pregnancy nor a family history of congenital ocular abnormalities.

Shortly after birth, the patient developed respiratory distress and required transfer to the neonatal intensive care unit. The newborn, weighing 2721 g and measuring 44 cm long, was noted to have a variety of dysmorphic features: short stature with a small chest and pectus excavatum; skeletal dysplasia with short legs; multiple joint dislocations, especially involving the hands; marked redundancy of the skin typical of cutis laxa; frontal bossing; midfacial hypoplasia; and thin transparent skin with prominent superficial veins (Figure 1). During the patient’s 9-day hospital stay, the consulting ophthalmologist documented bilateral cloudy corneas and made a presumptive diagnosis of congenital hereditary endothelial dystrophy.
The patient was referred to a geneticist, who made a definitive diagnosis of cutis laxa. At age 5 weeks, the patient was referred to one of us (I.M.R.) for evaluation and possible surgical management of the corneal clouding.

On examination, height and weight were essentially unchanged from birth, well below the fifth percentile for age. No strabismus or nystagmus was present. Portable slit-lamp examination revealed bilateral diffuse, focally prominent corneal stromal haze, most prominent in the anterior stroma (Figure 2). The anterior chambers were of normal depth, the horizontal corneal diameter was approximately 9 mm in each eye, and tactile tensions were within normal limits. No obvious lenticular opacifications were noted. Only a red reflex was discernible through the corneal haze. The patient underwent penetrating keratoplasties in the right eye at age 4 months and in the left eye at age 12 months.

The corneal button from the right eye was bisected and half fixed in 10% neutral buffered formaldehyde for routine microscopy and the other half fixed in 2.5% glutaraldehyde and processed for transmission electron microscopy. Immunostaining for elastin (Elastin Products Inc, Owensville, Mo) was applied to some sections for electron microscopy. The left corneal button was processed for light microscopy. Light microscopic examination of both corneal specimens demonstrated diffuse epithelial thickening, absence of the Bowman layer, and attenuation of the stroma, most marked centrally (Figure 3A) with hypercellular scarring of the anterior superficial stroma. A variety of special histochemical stains, including Verhoeff van Giesen stain for elastic fibers, showed no abnormal deposits in the corneal stroma except for some mucopolysaccharide in the superficial stroma. The posterior stroma was compact. Although delicate, the Descemet membrane was intact, and the endothelium was well preserved and quite cellular.

Electron microscopy demonstrated loss of the normal architecture of the Bowman layer, with replacement of the normal random pattern and regular spacing of collagen fibers by a paucity of longitudinal and oblique collagen fibers (Figure 4). In contrast to the absence of elastic fibers in the normal cornea, the anterior stroma contained many small bundles of 10- to 12-nm elastic system microfibrils (Figure 4, upper inset) associated with foci of nonstaining amorphous material immunopositive for elastin (Figure 4, lower inset). Although the 2 basic components of elastic fibers were present (microfibrils and elastin), no mature elastic fibers consisting almost entirely of elastin were seen (Figure 5). The Descemet membrane had reduced evidence of the normal 100-nm fetal banding pattern that usually extends throughout the Descemet membrane in corneas of patients who are this age. The endothelium appeared normal.

Postoperatively, serial examinations under anesthesia demonstrated clear grafts, normal intraocular pressures, and healthy fundi. Unfortunately, the patient died at age 13 months, several weeks after receiving the graft in the left eye, of respiratory failure. An autopsy was not performed.

**COMMENT**

In 1968, De Barsy et al reported the case of a 22-month-old girl who had an “old-looking facies,” congenital generalized cutis laxa, mental retardation, hypotonia, hyperreflexia,
growth retardation, and corneal opacification associated with degeneration of the Bowman layer. Although 18 additional cases of children with the syndrome that now bears his name have appeared in the medical literature, we found no reports in an English-language ophthalmic journal.

De Barsy syndrome, likely inherited in an autosomal recessive manner, has not been associated with a specific chromosomal anomaly. The life expectancy is unknown, as all patients described in the literature were infants or children when the diagnosis was made. To our best knowledge, the oldest living patient described in the literature was 24 years old.

Skin biopsy specimens from patients with De Barsy syndrome demonstrate sparse short or fragmented, irregular elastic fibers and reduced elastin expression in skin cell cultures. The results of the histochemical elastic stains on the corneas in the present report were likely negative because of the small amount of elastin in these immature fibers. To our knowledge, this is the first light and electron microscopic examination of the corneal findings in this syndrome. Many of the clinical features in the syndrome may be related in part to a disorder of elastogenesis, such as the cutis laxa, some skeletal features, and even the presence of aberrant elastic fibers in the cloudy corneas. However, features such as muscle hypotonia, cataracts, mental retardation, and neurologic deficits are not readily explained by abnormalities of the elastic system. Investigators disagree as to whether abnormalities of collagen play a role in the phenotypic features of this disorder.

Further exploration of the corneal elastogenesis and associated changes in the present case is in progress.

The differential diagnosis of congenital corneal opacification includes a variety of ocular and systemic disorders. De Barsy syndrome is an unusual cause of congenital corneal opacification that is associated with characteristic ocular, facial, skeletal, dermatologic, and neurologic abnormalities. Classified as one of the “progeroid” syndromes, De Barsy syndrome has distinctive clinical features that enable the clinician to differentiate it from the other causes of congenital corneal opacification and progeroid syndromes.

### Clinical Manifestation of De Barsy Syndrome

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<tr>
<th>Location</th>
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<tbody>
<tr>
<td>Ocular</td>
<td>Corneal opacification</td>
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<td>Cataracts</td>
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<td>Facial</td>
<td>Frontal bossing</td>
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<td>Progeroid facies</td>
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<td>Large dysplastic ears</td>
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<td>Skeletal</td>
<td>Short stature</td>
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<td>Hyperextensibility of small joints</td>
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<td>Multiple joint dislocations and subluxations</td>
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<td>Dermatologic</td>
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<td>Atrophy of the skin</td>
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<td>Neurologic</td>
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<td>Brisk deep tendon reflexes</td>
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<td>Athetoid movements</td>
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Figure 4. Electron micrograph demonstrating loose superficial stroma with bands of elastic fibers composed primarily of microfibrils (arrow), focally positive for gold-labeled elastin amongst infrequent 30-nm collagen fibers (upper inset). Deeper elastic fiber clump (arrowhead) has multiple gold-labeled elastin cores (lower inset). E indicates epithelium (original magnification × 20714; insets, ×67770).

Figure 5. Electron micrograph demonstrating multiple small- and medium-sized elastic fibers (arrow) between the cell layers, with gold-labeling of scanty and poorly organized elastin cores (inset of arrowed fiber) (original magnification × 32400; inset, ×54000).
Opacification is common to both syndromes, our patient did not manifest the other clinical features associated with Cockayne syndrome. In addition, he demonstrated nearly all of the features most commonly associated with De Barsy syndrome such as cutis laxa (not associated with Cockayne syndrome); frontal bossing and a progeroid aspect; muscular hypotonia and hyperreflexia; hyperextensible joints (characteristically stiff in patients with Cockayne syndrome); growth retardation; and the presence of the characteristic features at birth (as opposed to after the first year of life in patients with Cockayne syndrome).5

In this case, the diagnosis of De Barsy syndrome was based primarily on the unique constellation of clinical features that clearly distinguish it from the other progeroid syndromes. These characteristic clinical manifestations also enable the clinician to easily differentiate it from the other systemic disorders associated with neonatal corneal opacification.

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REFERENCES