Ocular Involvement
in I-Cell Disease (Mucolipidosis II)
Light and Electron Microscopic Findings *

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Summary. A 5 1/2 year old boy with I-cell disease (mucolipidosis II) had bilateral corneal haziness, early cortical cataracts and bilateral prominence of his eyes associated with shallow bony orbits. He died of pneumonia at age 5 1/2 years. Light and electron microscopic examination of the ocular and orbital tissues revealed an accumulation of acid mucopolysaccharide positive, hyaluronidase resistant material in fibroblasts and histiocytes which had partially replaced Bowman's membrane and the anterior stromal cells of the cornea. Similar material, as well as glycolipid-like substance, was found in the conjunctiva and in the retrobulbar soft tissues.


Introduction

During the past two decades, disorders involving glycolipid and sphingolipid (GL) or mucopolysaccharide (MPS) metabolism have been separated into two groups on the basis of biochemical and morphological data [1, 2]. Recently, a third group, the mucolipidoses, has been delineated and subclassified. Patients in this group manifest a combined disorder of MPS and GL metabolism [3].

The purpose of this paper is to report the ocular findings in a case of mucolipidosis II (Leroy-Opitz syndrome), [4] also known as I-cell disease because of cytoplasmic inclusions (vacuoles) in fibroblasts and histiocytes of the affected individuals. Electron microscopic findings in the conjunctiva of such a patient have been described [5], but ocular abnormalities have not been documented previously.

* The clinical material was presented before the Los Angeles Dermatological Society, May 12, 1971, by Gerald I. Sugarman, M. D. (Archives of Dermatology, 106:411, 1972).
This patient was the first and only child of non-consanguineous Jewish parents. The child was the product of a full term normal pregnancy and weighed two kilograms at birth. He had physiological jaundice for the first ten days of life and at four months of age his anterior fontanelle was closed, the metopic ridge of his skull was prominent, and he had a peculiar facies and prominent tongue, similar to that seen in the mucopolysaccharidoses. Frequent colds, upper airway obstructions and multiple bouts of pneumonia complicated his first year of life. He had short stature, coarse facial features, small mandible, gingival hyperplasia, rigid pinnae, short neck, kyphoscoliosis, claw hands and feet with incurvation of the fourth and fifth fingers, and limited range of motion of many joints. His abdomen bulged due to hepatosplenomegaly.

His skin, including the eyelids, was thickened but had a soft texture. The conjunctiva appeared similarly thickened. He had bilaterally prominent eyes (Fig. 1a). The corneas were initially clear, but at five years of age corneal haziness and early cortical cataract formation were first noted on ophthalmological examination. There was no corneal stromal granularity [5]. No abnormalities of the fundus were described.

Radiological examinations revealed thick and short bones similar to those seen in patients with dysostosis multiplex. The orbits were shallow (Fig. 1b). Tissue cultures of skin fibroblasts revealed perinuclear refractile cytoplasmic vacuoles (inclusions) which were periodic acid-Schiff (PAS) positive and stained metachromatically with toluidine blue after treatment with chloroform-methanol. Hydrolytic enzymes, such as hexosaminidase, aryl sulfatase and beta galactosidase were reduced to 5-10 percent of normal values in the tissue cultured cells. These enzymes were present in normal amounts in the patients' plasma. There was no increased excretion of urinary MPS.

He continued to develop slowly and had multiple bouts of respiratory distress. In addition to speaking English, he had some understanding of and ability to speak Hebrew and showed no signs of mental deterioration. He died with severe pneumonia and acidosis at age 5½.

At necropsy, he weighed 11 kilograms and measured 75 centimeters in length. Cytoplastic vacuolations in connective tissue cells were found in the skin, bones, liver, spleen, pancreas, adrenal glands, heart, great vessels, kidneys, gastrointestinal tract, bone marrow, lymphoid tissue, thymus, peripheral nerves and skeletal muscles. The epiphyseal cartilaginous plates of bones appeared inactive. Severe myocardial hypertrophy, pneumonitis and Cushing-type ulcers of the duodenum were present. Permission to study the brain was not granted.

The right eye was removed with attached retrobulbar soft tissues. A thin layer of vacuolated fibroblasts and histiocytes replaced the normal anterior stromal cells over the entire cornea and, in some areas, Bowman's membrane was thinned or focally absent (Fig. 2a and b). Many of these cells stained with PAS and were also found to contain alcian blue and colloidal iron positive amorphous material which was resistant to hyaluronidase. The basal layer of the epithelium appeared edematous. The posterior stroma, Descemet's membrane and the endothelium were unremarkable and did not contain vacuoles. The adjacent conjunctival stroma was infiltrated by a moderate number of chronic inflammatory cells and increased numbers of thin-walled capillaries. The amount of colloidal iron positive material in histiocytes and in fibroblasts was less in this area than in the anterior corneal stroma. Sudan black and oil red 0 stains of frozen sections for neutral fats revealed only a small amount of such material, mostly in the cytoplasm of macrophages. In the lens, early posterior migration of nuclei and vacuolation of cortical cells was found. The remainder of the globe, including the retinal ganglion cell layer, was unremarkable.

Electron microscopy was performed on fragments of cornea, conjunctiva, and retrobulbar connective tissue obtained at the postmortem examination. The tissue had been formalin fixed for a period of three months. It was processed in a manner previously described by one of us [6]. Moderate amounts of fixation and postmortem artifact were encountered. Examination of the subepithelial cornea revealed histiocytes and fibroblasts with extensive vacuolation of their cytoplasm. Some of the vacuoles were membrane-bound, but others had only amorphous material as their lining. They contained fibrillar and granular material (Figs. 3 and 4). The cytoplasm of many corneal epithelial cells contained tonofilaments and there were frequent