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Gaucher's Disease: Case Report with Stress on Eye Findings

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This interesting case report comes from an alumnus of Henry Ford Hospital—Dr. Carlos Petrozzi who was a medical resident here from July 1961 to 1964. The findings may be of interest to opththalmologists and others because of the rather specific changes in the bulbar conjunctiva which can be easily seen without special ophthalmic instruments.—Ed.

Gaucher's Disease

Case Report with Stress on Eye Findings

Angel O. Carbone, M.D.* and Carlos F. Petrozzi, M.D.**

The diagnosis of Gaucher's disease can be made, *ex visu,* with expediency if one is well aware of the external signs of the disease. In the case to be presented we have stressed the eye findings — an often unsuspected path to the diagnosis. We are including a biopsy report of the conjunctival tissue showing infiltration by Gaucher's cells, a finding only briefly mentioned in the literature available to us.

Case Report. — L.R.S., a single, 14-year-old Mestizo girl, came to the hospital because of progressive pallor and weakness of insidious onset. The patient was aware of a very slow-growing mass in the left flank region and, recently, of occasionally tarry stools.

Family history was negative. Physical examination, routine blood work and acid phosphatase determination carried out on the available relatives (mother and three sisters) was unrewarding. Past medical history was unremarkable.

Physical examination disclosed a well-nourished and well-developed girl with facial pallor and chloasma-like pigmentation over the nose and malar regions. There was a 5 cm diameter, hyperpigmented area surrounding a previous superficial injury in the left leg. There was a systolic murmur II/VI in the second and third intercostal spaces to the left of the sternum. Abdominal examination showed a massive hepatosplenomegaly. (Splenic longitudinal diameter was 37.5 cm; the lower border was palpated 17.5 cm below the costal margin. The spleen was freely movable on respiration. Its surface was smooth and its consistency harder than normal.) No murmurs were audible over the abdomen. The remainder of the physical examination was unremarkable.

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Figure 1
Chloasma-like pigmentation

Ophthalmological examination showed normal adnexae. The bulbar conjunctivae presented a brownish discoloration, almost triangular in shape, its base adjoining the sclerocorneal limbus. There was a small, subconjunctival hemorrhage in the left eye. In a concentric distribution, 4-5 mm from the limbus, there were multiple pigmented spots corresponding to the sites of perforation of the scleral vessels. Eye grounds showed normal discs. There was a retinal pallor and a hemorrhage with rounded edges overlying the right infero-temporal artery. Visual fields were normal. Visual acuity was O.D.: 8/10, corrected to 10/10 with -0.25 spherical and -0.50 cil. lenses at 180°; O.S. was corrected to 10/10 with the same lenses.

Laboratory work on admission was as follows: Hgb. 4.3gm%; WBC 1473/cubic mm; reticulocyte count, 5%; platelet count, 34,530/cubic mm; prothrombin time, 40%; serology lues: negative; BSP (5 mg/Kg/45'): 1.2% total bilirubin: 1.6mg%; direc-

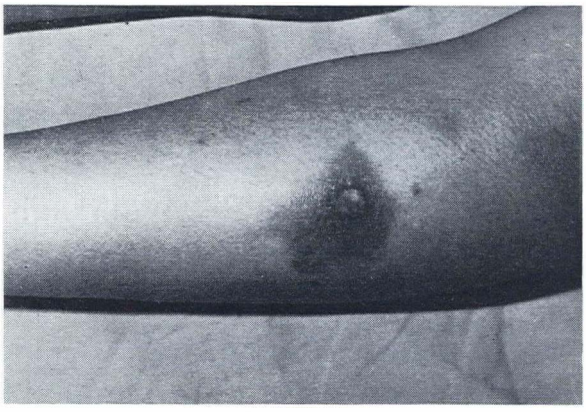

Figure 2
Left leg — pigmented halo around old injury

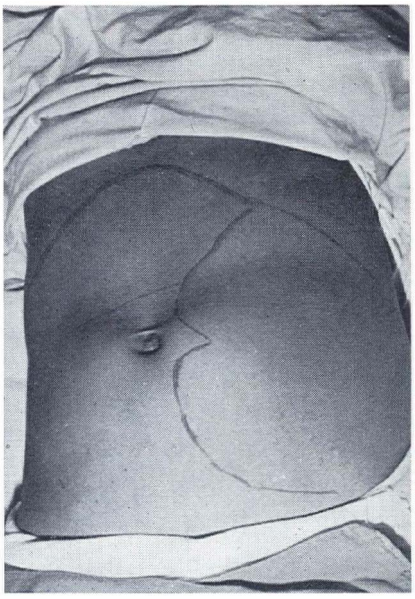

Figure 3
Massive hepato-splenomegaly

reacting bilirubin: 1mg%; alkaline phosphatase: 4.2 Bodnasky units; total proteins: 6.9 gm%; albumin: 3.3 gm%; globulins: 3.6 gm%; glutamic-pyruvic transaminase: 24 u%; acid phosphatase: 13.5 King-Armstrong units (control values in persons of same sex and age: 5 K-A units); total cholesterol: 285 mg%; occult blood in stools: positive, 2 plus, on three occasions. Blood glucose, creatinine, sodium, potassium, calcium and phosphorus were within normal limits. Urinalysis and stools for ova and parasites were normal. Bone marrow showed normo-erythroblastic hyperplasia, lack of hemosiderine; infiltration by Gaucher's cells. Studies with radioactive iron (Fe^{59}) showed normal marrow functioning and exaggerated red cell destruction in the spleen. Red cell half-life studied with $chromium^{51}$ was shortened to 15 days (normal: 30 days).

Chest x-rays were normal and in the Upper G.I. series no intrinsic alterations were found. The stomach was displaced to the midline by a huge spleen. Bone survey findings compatible with Gaucher's disease were noted in femora and humerii.

After iron therapy during the hospital course hemoglobin went up to 11.1 gm%, but the leukopenia and thrombocytopenia persisted. These facts and the intrasplenic hyperhemolysis led us to perform a splenectomy which resulted in an increase in the white blood cell count to 18,500/ cu mm. The platelet count was 367,000/ cu mm, in the immediate postoperative period.

Pathology reports showed the spleen increased in size (weighing 2,900 gm). Tissue sections had decreased lymphoid follicles with tissue invasion by Gaucher's cells.

Lobular structure was maintained in the liver, which had abundant Gaucher's cells, as did a mesenteric lymph node.

Microscopic examination of bulbar conjunctivae showed normal epithelium with areas of epidermoid metaplasia with Gaucher's cells. There were zones of elastosis in the underlying connective tissue.

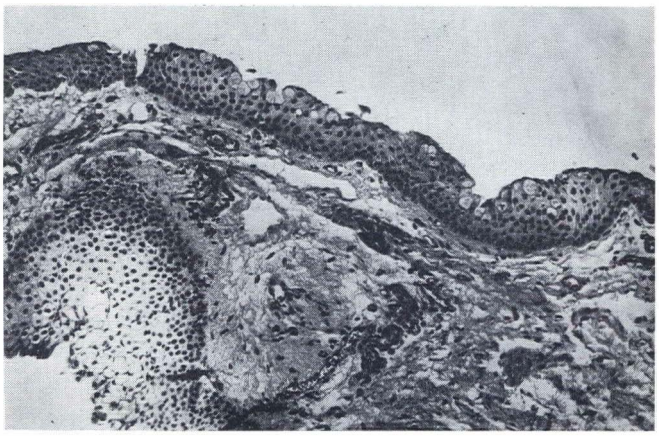

Figure 4
Conjunctivae showing the epithelium containing clear cells with trabeculated cytoplasm

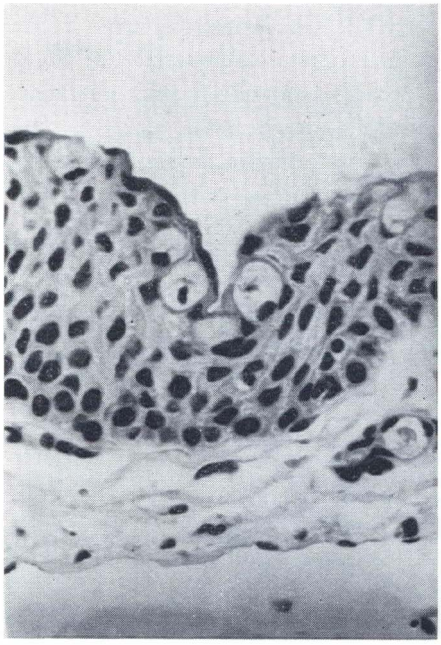

Figure 5
Detail of previous picture demonstrating Gaucher's cells intra-epithelially

General Discussion

From the clinical, laboratory, radiological and histological evidence, this is a case of Gaucher's disease. Although it is a genetically determined entity usually transmitted as an autosomal, recessive character, there are exceptional instances of autosomal, dominant transmission.[8]

The absence of neurological involvement, the slowly progressive clinical picture, and the delayed appearance of symptoms make this a rather typical case of "adult" or chronic Gaucher's disease.

We think it important to emphasize the basic enzymatic disturbance, the direct consequence of the underlying genopathy, and immediate cause of the glycolipid accumulation in the cells. Recent work along this path[2] has shown decreased activity of the kerasine-destroying enzyme.

Eye Aspects. — The most typical ocular lesion of Gaucher's disease is a wedge-shaped thickening of the bulbar conjunctiva. Its base adjoins the cornea. It is slow-growing and, as it matures, darkens to a peculiar brownish hue.[10] This is a pathognomonic finding of the disease.[3] East and Sabin, who examined the lesions histologically, found Gaucher's cells without being able to determine the kind of pigment responsible for the discoloration noted. Conceivably, and in analogy to the cutaneous changes, they are due to an exaggerated melanogenesis, whose origin is not known. Redslob and Gery[9] found, in once case, Gaucher's cells in the choroid. It is the only extant report of Gaucher's cell infiltration in nonconjunctival tissues. Reich, Seife and Kessler, cited by Thannhauser,[10] have described retinal edema accompanied by hemorrhage. The latter have been noted by Walsh[11] and are similar to the ones found in our case. They can be accounted for by a concomitant thrombocytopenia due either to bone marrow infiltration or increased splenic destruction, or both.

Eyb[6] reported a three-year-old boy with the infantile form of Gaucher's disease who displayed a perimacular degeneration similar to that seen in Tay-Sachs disease. In a personal communication to Walsh,[11] Tyler referred to two siblings, one of them a 15-year-old girl affected by a retinopathy similar to that in Tay-Sachs disease. The sister, five years older, had macular cherry-red spots and a diagnosis of Gaucher's disease. Bird[1] found ganglion-cell changes resembling those seen in Tay-Sachs disease in an 11-year-old boy with Gaucher's disease.

Collier[4] presented a two-year-old boy who showed seed-like retinal pigmentations distributed in a triangular fashion alternating with atrophic areas. There was accompanying macular degeneration.

These observations make one consider a kinship between Gaucher's and the genetically distinct Tay-Sachs and Nieman-Pick diseases.

Summary

A typical case is presented of the "adult" form of Gaucher's disease in a 13-year-old Peruvian Mestizo girl. After a brief diagnostic inquiry, the typical and atypical eye findings are discussed in some detail.

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