Liver Biopsy Findings of Malnourished Infants with Severe Rickets Studies on the Nutrition of Children at Hirosaki Area

(36th Report)

By

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In my preceding paper¹⁾ I reported liver biopsy findings of children who showed marked signs of ariboflavinosis and/or pellagrous skin lesions as part manifestations of nutritional dystrophy and who were not affected by any other severe illness.

In the present investigation liver biopsy was carried out on such infants, in whom clinical symptoms of rickets were conspicuous as compared with such signs as arisen from other nutritional deficiencies.

Materials and Method

In all the 22 cases biopsied, the diagnosis²⁾ of florid rickets was established both by clinical symptoms (rickety rosary, Harrison's sulcus and double joint of the wrist) and by radiological findings (cupping in the distal end of ulna or irregular and rough appearance of end of diaphysis of ulna and/or radius).

Angular stomatitis, cheilosis, swelling and/or atrophy of lingual papillae, hyperpigmentation of the skin and palpable or enlarged liver were recorded as part manifestations of nutritional dystrophy.³⁾⁴⁾⁵⁾

The method of needle biopsy of the liver and the description of histological findings of the biopsied specimens were the same as in my preceding report.¹⁾

Results and Comment

The results obtained are given in Tables I A and I B (Cf. Tables I A and I B). Fatty infiltration was found in 12 cases (Cases 1-4, 6, 8, 11-14, 18 and 21). Plant cell-like appearance of hepatic cells was seen in 12 cases (Cases 1, 7, 9, 10, 13, 15-17 and 19-22). Cloudy swelling

TABLE I (A)
Liver Biopsy Findings of Malnourished
Infants with Severe Rickets

Groups	No. of case (No. of biopsy)	Name, sex and age (y.m.)	Method of feeding for the first 12 months of life		Signs of nutritional dystrophy				Complications
			Mostly	Partly	Hyperpigmentation	Ariboflavinosis	Edema	Liver	
Group I	1 (227)	K.S. ♀ (0.4.)	Rice flour	M.M.*	++	—	+	2.5	
	2 (157)	M.J. ♂ (0.6.)	Rice flour + S.C.M.†	M.M.	—	—	—	6	Acute bronchitis
	3 (179)	S.S. ♂ (0.8.)	Rice flour		++	+	—	3.5	
	4 (176)	T.A. ♂ (0.10.)	M.M.	Rice flour	—	—	—	3.5	Prematurity
	5 (160)	S.M. ♂ (1.10.)	M.M.		—	—	—	5	
Group II	6 (263)	N.B. ♂ (1.2.)	Rice flour		++	+	—	3.5	
	7 (214)	Y.Sh. ♀ (1.0.)	Rice flour	S.C.M.	++	++	—	4	
	8 (255)	S.E. ♀ (1.3.)	Rice flour		—	++	+	5	
	9 (222)	N.S. ♀ (1.5.)	M.M.		—	—	—	4	
	10 (272)	K.H. ♀ (1.5.)	Powdered milk	Rice flour	—	—	—	6	
	11 (152)	S.H. ♀ (1.7.)	Powdered milk	Rice flour	—	++	—	7	
	12 (171)	S.Y. ♂ (1.3.)	Powdered milk		++	+	—	3.5	
	13 (319)	A.H. ♂ (1.3.)	M.M.	Powdered milk	—	+	—	3.5	
	14 (175)	I.S. ♀ (1.8.)	Rice flour		±	++	—	3.5	
	15 (279)	S.H. ♂ (1.10.)	M.M.		—	+	—	5	
Group III	16 (249)	O.K. ♂ (3.3.)	Powdered milk	Rice flour	—	++	—	3.5	
	17 (271)	F.K. ♂ (2.8.)	Rice flour	S.C.M.	—	—	—	2	Pertussis
	18 (252)	N.F. ♀ (2.11.)	Rice flour		—	++	—	4	Tetany
	19 (223)	Y.K. ♂ (2.3.)	Rice flour	M.M.	+	++	+	3.5	
	20 (224)	S.Y. ♀ (2.6.)	M.M.	Powdered milk	—	—	—	6	
	21 (170)	M.M. ♂ (2.10.)	Rice flour	S.C.M.	+	+	—	4	
	22 (236)	I.T. ♂ (3.2.)	Rice flour	M.M.	+	++	+	4	

TABLE I (B)
Liver Biopsy Findings of Malnourished
Infants with Severe Rickets

Groups	No. of case (No. of biopsy)	Change in hepatic cells					Change in nuclei of hepatic cells	Hypertrophy of kupffer's cells	Cell infiltration inthe portal tracts	Diffuse fibrosis
		Fatty		Cloddy swelling	Plant cell-like appearance	Zonal necrosis				
		Crops	Droplets							
Group I	1 (227)	++	++	+	+	+	+	+	+	
	2 (157)	+	++						+	
	3 (179)	##	++	+			+		+	+
	4 (176)		+			+	+		+	
	5 (160)			++						
Group II	6 (263)		++	+					+	
	7 (214)			+	++				+	
	8 (255)		##	++		+				++
	9 (222)				##		+			
	10 (272)				##					
	11 (152)	+	++	##					+	
	12 (171)	+		++						±
	13 (319)	+			++		+			+
	14 (179)		+	##						++
	15 (279)			+	##		+	+		+
Group III	16 (249)			++	++					++
	17 (271)			##	+					
	18 (252)	##	##							
	19 (232)				##					
	20 (224)			+	##		+			
	21 (170)	+		+	++					
	22 (236)				##					

occurred in 14 cases (Cases 1, 3, 5, 6-8, 11, 12, 14-17, 20 and 21), zonal necrosis in 3 cases (Cases 1, 4 and 8), and diffuse fibrosis in 8 cases (Cases 3, 8, 12-16 and 22).

From the results shown above, it will be said that liver biopsy findings of the malnourished infants with severe rickets showed no qualitative differences from those of the children with nutritional dystrophy without severe rickets.

In 1903 Fujinami⁶⁾ found a gross fatty liver on autopsy of a girl, about 11 years, who had been fed on high-carbohydrate-low-protein diet and developed severe rickets.

According to Nakamura,⁷⁾ fatty infiltration, congestion, infiltration of cells in the lobules or in the portal tracts, hyperplasia and hypertrophy of Kupffer's cells were found in the autopsied livers of the infants whose disease had been diagnosed as rickets with starch injury.

Okamoto⁸⁾ reported that fatty infiltration and congestion of the liver were found in experimental rickets of young rabbits.

Prof. Sano,⁹⁾ Tohoku University, made clinical and radiological examinations upon over 30,000 infants in Tohoku district, and found that malnutrition was frequently found among infants in rural villages and that a considerable proportion of these infants were suffering from florid rickets and that disturbance in liver functions was revealed in these malnourished infants with rickets.

Gillman and Gillman¹⁰⁾ autopsied 150 cases of African infants with malnutrition (infantile pellagra) and found that severe rickets was recognized in over 50% of cases under one year of age and in 38% of cases with the age of from one to two years. In the majority of the autopsied livers, they found marked fatty infiltration.

In my present investigation, fatty infiltration, cloudy swelling, plant cell-like appearance of hepatic cells and necrosis were identified in the biopsied specimens of the livers from the malnourished infants with severe rickets, and these lesions are in my own opinion ascribable to the malnutrition especially due to high-carbohydrate-low-protein diet, as was discussed in my previous paper.

Differences in histopathological findings of the lesions of the malnourished infants from the view point of age:—All the 22 cases examined are divided into 3 groups according to their age; Group I consists of 5 cases under the age of 12 months; Group II, of 10 cases of the age from 13 to 24 months, and Group III, of 7 cases of the age from 27 to 39 months. Tables II, III and IV show the frequency of three kinds of liver changes—fatty infiltration, cloudy swelling and plant cell-like appearance of hepatic cells—in each group. A glance over these tables will give the impression that fatty infiltration occurred most frequently in Group I,

TABLE II
Incidence in Fatty Infiltration of Hepatic Cells
in Groups I, II and III

Fatty infiltration \ Group	I	II	III
+	4	6	2
—	1	4	5
Total number of cases	5	10	7

TABLE III
Incidence of Cloudy Swelling of Hepatic Cells
in Groups I, II and III

Cloudy swelling \ Group	I	II	III
+	3	7	4
—	2	3	3
Total number of cases	5	10	7

TABLE IV
Incidence of Plant cell-like Appearance of Hepatic
Cells in Groups I, II and III

Plant cell-like appearance \ Group	I	II	III
+	1	5	6
—	4	5	1
Total number of cases	5	10	7

cloudy swelling in Group II and plant cell-like appearance of hepatic cells in Group III. And at least the incidence in plant cell-like appearance of hepatic cells in each Group (according to the age of the infants) is statistically significant. So it will be said that plant cell-like appearance of hepatic cells occur more frequently in Group III than in Groups I and II, and that fatty liver may occur oftener in Group I than in Group III, and cloudy swelling oftener in Group II than in the other groups.

Gillman and Gillman¹⁰⁾ found in the biopsied liver of African pellagrins that fatty liver occurred more frequently in infants than in adults,

while plant cell-like appearance of hepatic cells was, as they state, found more frequently in adults than in infants.

This tendency to develop fatty liver more easily in infants is observed in the results of my present investigation as well as in those of my previous report.¹⁾ In a word, the younger the infants the more frequently fatty liver may occur, and the older the infants the more frequently plant cell-like appearance of hepatic cells in the biopsied livers of malnourished infants. Cloudy swelling may occur the most frequently in Group II among three groups. The differences of incidence in these three kinds of hepatic changes may be due to the differences in age of these malnourished infants.

SUMMARY

In 22 biopsied liver specimens of malnourished infants with severe rickets, fatty infiltration was found in 12 cases, cloudy swelling in 14 cases, plant cell-like appearance of hepatic cells in 12 cases and zonal necrosis in 3 cases.

These histopathological findings showed no qualitative differences from those obtained from children with nutritional dystrophy without severe rickets.

Fatty liver was found more frequently in younger infants than in the older, and plant cell-like appearance of hepatic cells more frequently in older infants than in the younger.

CONCLUSIONS

Liver biopsy finding of malnourished infants with severe rickets is not different qualitatively from that of those infants without same, so that the liver finding identified is to be ascribed to malnutrition alone.

Fatty liver occurs probably more frequently in younger infants, while plant cell-like appearance is seen in older infants.

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