Folic Acid Deficiency in Children with Nutritional Dystrophy

Studies on the Nutrition of Children in Hirosaki Area

(49th Report)

By

Narimasa Ooi

(大井 也昌)

From the Department of Pediatrics, School of Medicine, Hirosaki University, Hirosaki. Director: Prof. Ts. Arakawa

(Received for publication, July 26, 1956)

Among the children with nutritional dystrophy in this District, macrocytic anemia was not infrequently found.¹⁾ And such cases with the anemia responded sharply to folic acid.²⁾ In the present paper, the results of the folic acid load test performed upon children with or without macrocytic anemia will be discussed.

EXPERIMENTAL

Method and Material

The children subjected to this investigation were divided into 2 groups (Groups I and II); Group I included 6 boys who were healthy and free from ariboflavinotic signs,³⁾ and Group II included 19 boys who showed marked signs of ariboflavinosis as part manifestations of nutritional dystrophy.

The blood picture was examined just prior to the folic acid load test, and according to the mean corpuscular volume, the term of macrocytosis ($>95 \mu^3$) or microcytosis ($<79 \mu^3$) was used.⁴⁾

Folic acid load test was carried out as described in my preceding paper⁵⁾; pterolyglutamic acid excreted in the 24 hour-urine following oral ingestion of 10 mg. of pterolyglutamic acid was determined fluorometrically by means of my own procedure.⁵⁾

Results with Discussion

The results were shown in Tables I and II (Cf. Tables I and II). PGA excreted in the 24 hours urine following oral dose of 10 mg. of PGA was found to be 4.29 ± 0.61 mg. and 2.36 ± 0.81 mg. in Groups I and II respectively, showing a significant difference between them (Cf. Tables

TABLE I
Blood Picture and Folic Acid Excreted in the 24 Hour
Urine Following Oral Ingestion of 10 mg. of Folic Acid
in Children without Nutritional Dystrophy (Group I)

No. of Case	Name, Sex and Age (Years and months)	The 24 hour urine		Blood picture			
		Amount cc.	Folic acid mg.	Red cells (millions)	Hemoglobin (g%)	Hematocrit (%)	Mean corpuscular volume (μ^3)
1	K.M. ♂ 10y.7m.	1020	5.11	4.90	12.4	46	93
2	M.K. ♂ 11y.1m.	1060	4.17	4.90	12.4	45	91
3	K.K. ♂ 11y.6m.	620	3.16	4.80	11.6	47	97
4	K.H. ♂ 12y.3m.	1130	4.86	4.30	10.4	40	93
5	S.Y. ♂ 11y.5m.	1250	3.68	5.10	11.2	45	88
6	K.Y. ♂ 12y. 2m.	1380	4.29	4.50	10.8	41	91
Average			4.29	4.75	11.4	44	92
			±	±	±	±	±
			0.61	0.31	1.6	2.9	7.1

I and II).

On the other hand macrocytic anemia was found in 16 out of 19 cases of Group II—these 16 cases responded sharply to folic acid²⁾—, but in none of Group I (Cf. Tables I and II).

These two findings—a low excretion of PGA after oral test dose as well as a high incidence in macrocytic anemia in the children with nutritional dystrophy,—might be accepted as an evidence for the existence of folic acid deficiency in these children.

According to the general literature, anyone of the following 4 factors would contribute to the low excretion of PGA after its oral dose; a deficient intake of PGA, an increased requirement of it, the conjugation of it before excretion⁶⁾ and malabsorption from the intestine.⁷⁾ Stepp *et al.*⁸⁾ described that folic acid deficiency, which would manifest itself as in the form of macrocytic anemia as well as in the form of intestinal disturbance, was observed in cases of malnutrition, and that folic acid deficiency occurred, in general, not from a deficient intake of folic acid itself, but from protein deficiency accompanied by malnutrition, because protein deficiency brought out both an increased requirement for folic acid and a depression of the synthesis of folic acid by intestinal flora.

TABLE II
Blood Picture and Folic Acid Excreted in the 24 Hour
Urine Following Oral Ingestion of 10 mg. of Folic Acid
in Children with Nutritional Dystrophy (Group II)

No. of Case	Name, Sex and Age (Years and months)	The 24 hour urine		Blood picture			
		Amount cc.	Folic acid mg.	Red cells (millions)	Hemoglobin (g%)	Hematocrit (%)	Mean corpuscular (μ^3)
1	H.S. ♂ 10y.1m.	1260	1.78	4.10	7.50	42.0	102
2	H.M. ♂ 9y.10m.	1440	5.88	4.30	9.30	43.0	100
3	K.A. ♂ 9y.8m.	1560	2.88	3.85	8.20	39.0	101
4	K.Z. ♂ 9y.3m.	2320	0	4.10	8.90	41.0	100
5	T.R. ♂ 9y.1m.	1020	1.65	3.80	7.90	37.0	97
6	T.O. ♂ 8y.11m.	640	3.66	3.80	7.90	35.0	92
7	H.S. ♂ 8y.11m.	1260	1.62	3.85	8.90	37.0	96
8	T.T. ♂ 8y.9m.	1000	1.69	3.85	7.90	36.0	93
9	K.K. ♂ 8y.8m.	1400	1.27	3.65	7.50	38.0	104
10	K.M. ♂ 8y.8m.	820	3.12	3.20	7.50	37.0	115
11	I.M. ♂ 8y.7m.	1180	1.55	3.85	8.20	40.0	103
12	K.K. ♂ 8y.5m.	1360	0.52	3.90	7.90	41.0	105
13	M.M. ♂ 8y.5m.	1600	0.42	3.90	6.80	36.0	92
14	I.K. ♂ 8y.5m.	1440	2.33	3.50	6.70	36.0	102
15	N.S. ♂ 8y.5m.	1160	2.28	3.90	7.50	38.0	97
16	S.M. ♂ 8y.5m.	1800	2.85	3.80	7.50	39.0	102
17	S.E. ♂ 8y.4m.	1300	0.92	3.75	6.40	37.0	98
18	W.T. ♂ 8y.4m.	1080	6.01	3.85	7.50	39.0	101
19	K.S. ♂ 8y.4m.	1400	4.46	3.50	7.90	42.0	120
Average			2.36 ± 0.81	3.81 ± 0.14	7.78 ± 0.39	38.5 ± 1.7	101 ± 3.7

In cases of macrocytic anemia of children with nutritional dystrophy in Hirosaki area, a gradual improvement of blood picture was observed after a continuous administration of skimmed milk for 3 months⁹⁾ without any dose of folic acid. So protein deficiency might play an important rôle for the development of folic acid deficiency in these children.

As will be seen from Fig. 1 (Cf. Fig. 1), a relatively high value of the PGA excreted after its oral dose was seen in 3 cases (Cases 2, 18 and 19) in which macrocytic anemia had been demonstrated. This apparent

Fig. 1. The folic acid excretion in the 24-hour urine following oral ingestion of 10 mg. of folic acid and mean corpuscular volume of red cells in children with nutritional dystrophy.

discrepancy might be well explained, if the following items are taken into consideration: (1) hepatic changes have been not infrequently demonstrated in the liver specimens biopsied from children with nutritional dystrophy,¹⁰⁾ (2) macrocytic anemia has been found with a high incidence among those children with nutritional dystrophy whose liver has shown histological alterations in the biopsied specimens,¹¹⁾ and (3) in hepatic diseases, according to Inoue,¹²⁾ a relatively large amount of folic acid, not citrovorum factor, is excreted into urine after subcutaneous injection of 10 mg. of folic acid due to a disturbance of utilization of folic acid.

SUMMARY

Macrocytic anemia was found in 16 out of 19 cases of children with nutritional dystrophy.

PGA excretion in the 24-hour urine after oral dose of 10 mg. of PGA

was lower in the majority of the children with nutritional dystrophy than in normal subjects, but in a few cases with macrocytic anemia, a relatively high value of the PGA excreted after the test dose was found. In these cases a disturbed utilization of folic acid due to hepatic changes of these children was suggested.

CONCLUSIONS

Folic acid deficiency will occur in the children with nutritional dystrophy. The occurrence is highly probable from the low excretion of PGA after its oral dose as well as the high incidence in macrocytic anemia among these children.

References

- 1) Arakawa, Wada & Takahashi, Tohoku J. Exp. Med., 1951, **55**, 61.
 - 2) Wada & Arakawa, *ibid.*, 1952, **56**, 47.
 - 3) Youmans, J. Am. Med. Ass., 1950, **144**, 307.
 - 4) Wintrobe, Clinical Hematology, 3rd ed., 1952, p. 101, Lea & Febiger, Philadelphia.
 - 5) Ooi, A Simple Method for the Urinary Folic Acid Assay, applicable to Folic Acid Load Test, this Journal, in press.
 - 6) Steinkamp, Shukers, Totter & Day, Proc. Soc. Exp. Biol. & Med., 1946, **63**, 556.
 - 7) Girdwood, Lancet, 1953, No. 6776, 53.
 - 8) Stepp, Kühnau & Sohroeder, Die Vitamine und ihre klinische Anwendung, 2nd ed., 1952, 510, Ferdinand Enke Verlag, Stuttgart.
 - 9) Wada, Hirosaki Igaku (Jap.), 1955, **6**, 232.
 - 10) Sato, Tohoku J. Exp. Med., 1955, **63**, 93.
 - 11) Wada & Sato, *ibid.*, 1952, **56**, 259.
 - 12) Inoue, Vitamins (Jap.), 1956, **10**, 75.
-