Original Article

Iron Deficiency Anemia among High School Students

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During adolescence, various factors such as rapid growth of the body and iron depletion due to menstrual bleeding or other causes increase the iron requirement. For instance, Bothwell and Finch¹⁾ indicated that the average daily iron requirement is 1.0 mg for adolescent males compared to 0.6 mg for adult males, and 1.5 mg for adolescent females compared to 1.2 mg for adult females. Therefore, if males or females in adolescence do not have adequate diets to support positive iron balance as aforementioned, they might easily develop iron deficiency anemia. Although various problems concerning iron deficiency anemia in late adolescence have been reported by several investigators,¹⁻⁴⁾ few papers have been published concerning iron deficiency anemia in early adolescence. Therefore, various findings covering iron deficiency anemia in a group of high school students in Japan are presented in this paper.

Materials and Methods

Subjects studied were 5,002 students (3,040 males, 1,962 females) of a high school in Utsunomiya, Japan. They were ranged in age from 15 to 17. As a screening test for anemia, hemoglobin levels (cyanmethemoglobin method) were estimated in all students during June and July of 1970. In cases where hemoglobin levels were below 10.9 g/100 ml, routine examination of peripheral blood and determination of serum total protein levels, serum iron levels (Ramsey method⁵⁾) and total iron-binding capacity (Rath and Finch method⁶⁾) were carried out. In addition, social backgrounds, histories, complaints, symptoms and roentgenographic examination of the spleen on these cases were also investigated. Roentgenographic examination of the spleen was carried out as follows: roentgenographic settings—voltage; 70 KVP for 17 cm in anterior posterior diameter, ampere; 100 mA, time; 2 sec, focus film distance; 145 cm, 45° exposure angle for layer at 6 and 8 cm from abdominal wall in prone position. Procedure—tomography was taken in state of fast, 5 min after intake of a mixture of tartaric acid (1.5 g), sodium bicarbonate (2.0 g) and distilled water

(30 ml). Splenic area was estimated by tracing the splenic shadow which is visible below the stomach bubble with planimeter.

Results

Incidence of anemia:

Results of screening test for anemia on 5,002 high school students are shown in Table 1. Hemoglobin levels below 10.9 g/100 ml. were observed in 57 cases (1.9%)

Table 1. Incidence of anemia in high school students.

cases	hemoglobin level (g/100ml)				
	below 10.9 cases (%)	below 9.9 cases (%)	10.0-10.9 cases (%)	11.0-11.9 cases (%)	above 12.0 cases (%)
male 3040	57 (1.9)	21 (0.7)	36 (1.2)	154 (5.1)	2829 (93.0)
female 1962	164 (8.3)	63 (3.2)	101 (5.1)	365 (18.6)	1433 (73.0)

of 3,040 male students and 164 cases (8.3%) of 1,962 female students. Hemoglobin levels from 11.0 to 11.9 g/100 ml. were observed in 154 cases (5.1%) of 3,040 male students and 365 cases (18.6%) of 1,962 female students. Age distributions of students who showed hemoglobin levels below 10.9 g/100 ml. were as follows: 57.9% (15 years old), 29.8% (16 years old) and 12.3% (18 years old) in 57 male students, 47.6% (15 years old), 27.4% (16 years old) and 25.0% (17 years old) in 164 female students. Two hundreds and twenty-one cases (57 males, 164 females) whose hemoglobin levels were less than 10.9 g/100 ml were defined as patients, and further investigations were carried out.

Detailed hematological findings of the cases of anemia:

The results of peripheral hematological findings, serum iron levels, total iron-binding capacity and serum total protein levels are shown in Table 2. Red blood cell counts were normal in most of the cases. The low value of color index, mean corpuscular volume, mean corpuscular hemoglobin concentration, serum iron level and high total iron-binding capacity confined a state of iron deficiency. The reticulocyte counts in most of the cases were less than 0.2%. The platelet counts were normal or slightly above normal in most of the cases. The white blood cell counts were normal, and there was no significant granulocytopenia. Moderate anisocytosis was observed in a majority of the cases' blood film. Serum total protein levels were within normal range. Through detailed hematologic examinations as aforementioned, all cases except 1 male case of chronic myeloid leukemia were diagnosed as cases of iron deficiency anemia.

Social backgrounds of the cases of anemia:

The occupations of the parents were as follows: salaried worker 40.3%, agricultural worker 30.3%, independent professions 8.0%, business-men and -women 6.5%,

Table 2. Hematological findings of the cases of anemia.

M±s.d.		%	M±s.d.		%
R.B.C. (×10 ⁴)			C.I.		
	below 350	10.0		below 0.79	51.0
402±56	351-399	27.9	0.81±0.11	0.80-0.99	47.5
	above 400	62.1		above 1.00	1.5
Hemoglobin level (g/100ml)			M.C.V. (cμ)		
	below 7.9	6.7		below 79	45.2
9.6±1.1	8.0-9.9	31.3	80.5±8.4	80-89	40.7
	10.0-10.9	62.0		above 90	14.1
Hematocrit (%)			M.C.H.C. (%)		
	below 29	14.9		below 29.9	65.2
31.8±3.1	30-37	82.2	29.2±2.2	30.0-32.9	30.6
	above 38	2.9		33.0-35.9	4.2
Reticulocyte (%)			Serum total protein level (g/100ml)		
	below 1.0	83.3		below 6.9	1.2
0.62±0.52	1.1-1.9	15.2	7.9±0.6	7.0-7.9	56.8
	above 2.0	1.5		above 8.0	42.0
Platelet (×10 ⁴)			Serum iron level (μg/100ml)		
	below 9.9	2.1		below 49	29.8
22.1±8.3	10-19.9	43.3	47.4±25.2	50-79	67.3
	20-29.9	41.8		above 80	2.9
	above 30.0	12.8			
W.B.C.			T.I.B.C. (μg/100ml)		
	below 4900	33.2		250-299	0
5460±1640	5000-7900	56.9	388.5±42.5	300-399	77.6
	above 8000	9.9		above 400	22.4

others 15.2%. Most cases were from middle class families in Utsunomiya. Geographically, Utsunomiya is located about 100 km northwest of Tokyo. It has a population of about 300,000, and is one of the representative of medium-sized Japanese cities. With respect to the social backgrounds, no significant relationship between the economic backgrounds and the cause of iron deficiency anemia was found.

Family histories and past histories of the cases of anemia:

No particular findings were shown in the family histories of the cases. Percentage of illness in the past histories of 221 cases were as follows: nothing extraordinary 89.6%, iron deficiency anemia 2.7%, blood loss anemia due to duodenal ulcer 1.4%, gastroenteritis 1.8%, nephritis 0.9%, hepatitis 0.9%, pneumonia 0.9% and rheumatic fever 1.8%. There were no cases who had histories of parasitic infection. The period and the duration of menses observed in 164 female cases were as follows: menstrual periods—normal was 110 cases (67.1%), oligomenorrhea was 53 cases (32.3%), polymenorrhea was 1 case (0.6%); duration of menses—normal was 156 cases (95.1%), hypomenorrhea was 2 cases (1.2%), hypermenorrhea was 6 cases (3.7%). These statistics showed that there were few cases who had had gastrointestinal or excessive menstrual bleeding in their past histories.

Complaints and symptoms of the cases of anemia:

The percentages of complaints of 221 cases of anemia were as follows: dizziness 29.3%, easy fatigability 12.5% and palpitation 11.3%; the remaining case (46.9%) had no complaints. Pallor of the conjunctiva was almost constant feature. No koilonychia, angular stomatitis or glossitis was demonstrated in any of the cases. Soft functional systolic murmur was demonstrated in the apex of the heart in 5% of the cases. The liver and the spleen were not palpable in any of the cases.

Roentgenographic examination of the spleen of the cases of anemia:

The average splenic area of the visible splenic shadow by tomographic examination was $13.3 \pm 4.0 \text{ cm}^2$ in 45 healthy adults as the author previously reported⁷⁾. Accordingly, cases who showed visible splenic shadow area which is greater than 30 cm^2 were defined as considerable latent splenomegaly. Although the spleen was not palpable in any of the cases, such considerable latent splenomegaly was demonstrated in 30 cases (52.6%) out of 57 male cases and 22 cases (13.4%) out of 164 female cases by tomographic examination of the spleen.

Discussion

As for the incidence of iron deficiency anemia in adolescent males, Leonard²⁾ reported that 0.9% of 4,221 recruits aged 18 to 20 showed hemoglobin levels below 10.4 g/100 ml and 0.2% of them showed hemoglobin levels below 10.4 to 12.0 g/100 ml. Brumfitt³⁾ reported that 1.1% of 2,000 recruits aged 17 to 21 showed hemoglobin levels below 12.0 g/100 ml. As to the incidence of iron deficiency anemia in adolescent girls, Bothwell¹⁾ reported that 12% of 750 female university students showed hemoglobin levels below 11.9 g/100 ml. In this study, hemoglobin levels below 11.9 g/100 ml were observed in 7.0% of 3,040 male students and 26.9% of 1,962 female students. In addition, the percentage of students who showed hemoglobin levels below 10.9 g/100 ml was greater in low teens than in high teens in both male and female students. According to these results, the incidence of iron deficiency anemia in adolescence seems to be higher in early adolescence than in late adolescence. This may be due to the facts that the growth of boys and girls in early adolescence correspond to the peak of adolescent growth spurt and that poor nutrition or iron depletion in this stage would easily create an added demand for available iron. As to dietary intake of iron, economic backgrounds in present day Japan do not seem to be closely related to the cause of iron deficiency anemia during adolescence. However, it is to be noted that there were some students who had to go on low caloric diets in order to avoid gaining weight. As to iron depletion, although menstrual or gastrointestinal bleeding is considered to be important, actually there were few cases who had had hypermenorrhea, polymenorrhea or gastrointestinal bleeding in this study. This fact suggests that iron depletion caused by excessive menstrual bleeding or gastrointestinal bleeding is not always the main factor in the cause of iron deficiency

anemia in adolescence. In the observation of menstrual periods in female case, 32.3% of 164 cases showed oligomenorrhea. This fact may suggest that ovarian dysfunction can be associated with this anemia as the author previously reported⁷⁾. It is to be noted that although the spleen was not palpable in any of the cases of iron deficiency anemia, considerable latent splenomegaly was found in 52.6% of male cases and 13.4% of female cases by roentgenographic examination. The real cause of such latent splenomegaly in iron deficiency anemia is not known. However, it seems that the cause of splenomegaly in this anemia is closely related to the fragility of red blood cells in this anemia. With respect to the fragility of red blood cells, it seems possible that abnormalities in lipid components in red blood cell membrane may play some role in the cause of fragility of red blood cells in this anemia. It has been reported that lipids such as cholesterol and phospholipids are important constituents of the red blood cell membrane^{8,9)} and such lipids in blood serum are constantly being incorporated into the red blood cell membrane.^{10,11)} Although the content of such lipids in red blood cells has not been investigated, as the author previously reported^{12,13)}, low content of serum linoleic acid content of unsaturated fatty acids composition in neutral lipids was demonstrated in some cases of iron deficiency anemia. According to the recent studies in this laboratory¹⁴⁾, low serum levels of total cholesterol, triglyceride and beta-lipoprotein were also observed in some cases of iron deficiency anemia. In addition to such abnormalities in lipid components in blood serum, content of vitamin E in red blood cells and blood serum is considered to be important as the cause of fragility of red blood cells in this anemia, because vitamin E is a strong antioxidant and prevents cell damage by lipoperoxidation of unsaturated fatty acids. Silber et al.¹⁵⁾ reported that vitamin E in red blood cells is localized to the red blood cell membrane and that rapid exchange of vitamin E takes place between the red blood cell and blood serum. Although the content of vitamin E in red blood cells in this anemia has not been estimated, as reported by the author previously^{16,17)}, low serum vitamin E level was demonstrated in cases of iron deficiency anemia. It has been reported¹⁸⁻²¹⁾ by many investigators that in a vitamin E deficient state, the red blood cells become fragile and get easily hemolyzed by H_2O_2 . Melhorn and Gross²²⁾ reported that an abnormal elevation of H_2O_2 hemolysis was observed in severe iron deficiency anemia in children. As reported by the author previously¹⁷⁾, abnormally elevated H_2O_2 hemolysis values were also observed in 11 out of 40 cases of iron deficiency anemia in adults. These facts suggest that the fragile red blood cells caused by abnormalities in lipid components and lack of vitamin E may play an important role in the cause of latent splenomegaly in iron deficiency anemia during adolescence. Besides those mentioned above, as the author previously reported⁷⁾, endocrinological imbalance such as the dysfunction of adrenocortex and ovary observed in this anemia may play some role in the cause of the latent splenomegaly. However, for sufficient explanation of these factors further investigations will be needed.

Summary

1. In a screening test for anemia on a group of high school students in Japan, hemoglobin levels below 10.9 g/100 ml were observed in 1.9% of 3,040 male students and 8.3% of 1,962 female students. Almost all of such students with anemia were the cases of iron deficiency anemia.

2. There were few cases who had excess menstrual bleeding, and almost half of the cases had no complaints.

3. Although the spleen was not palpable in any of the cases of iron deficiency anemia, considerable latent splenomegaly was found in 52.6% of 57 male cases and 13.4% of 164 female cases by roentgenographic examination.

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