Aplastic Anemia in Srinagarind Hospital

Paithoon Boonma
Suriya Amornpun
Chittr Sitthi-amorn

Department of Medicine, Faculty of Medicine, Khon Kaen University.

ผู้ป่วยโรคโลหิตจางอะพลาสติคในโรงพยาบาลศรีนครินทร์

ไพฑูรย์ บุญมา พ.บ., สุริยา อมรพันธ์, จิตร สิทธิอมร พ.บ.
ภาควิชาอายุรศาสตร์ คณะแพทยศาสตร์ มหาวิทยาลัยขอนแก่น

ศึกษาผู้ป่วยโรคโลหิตจางอะพลาสติค ที่ได้รับการวินิจฉัยจากภาควิชาอายุรศาสตร์ โรงพยาบาลศรีนครินทร์ ในช่วงเวลาประมาณ 4 ปี มีผู้ป่วยทั้งสิ้น 125 ราย แต่สามารถศึกษาได้เพียง 78 ราย โดย 68 ราย (ร้อยละ 87.18) จัดเป็นโลหิตจางอะพลาสติคชนิดรุนแรง (severe aplastic anemia)

สาเหตุของโรคโลหิตจางอะพลาสติคไม่สามารถตรวจพบ อาการนำที่สำคัญของผู้ป่วยคือ เลือดออกง่ายตามผิวหนังและซีด ผู้ป่วย 65 ราย ได้รับการรักษาด้วยเทสโตสเตอโรน โปรปีโอเนท (Testosterone propionate) แต่มีเพียง 19 ราย ที่ได้รับยาเกินหกเดือน และสามารถนำมาศึกษาผลของยารักษาได้ ในจำนวนนี้มีเพียง 1 ราย (ร้อยละ 5.26) ที่มีผลเลือดกลับมาอยู่ในระดับปกติ หลังจากรับประทานยาประมาณ 18 เดือน ผู้ป่วย 13 ราย เสียชีวิต สาเหตุการตายที่สำคัญคือ โรคติดเชื้อและเลือดตกในสมอง (*ศรีนครินทร์เวชสาร* 2529 ; 1 : 1 - 5)

We present an analysis of 125 patients with the diagnosis of aplastic anemia seeking care from the Department of Medicine, Srinagarind Hospital during the last 4 years. Only 78 of 125 cases fulfilled the predefined eligibility criteria and were included in the study.

68 patients (87.2 percent) were classified as "severe aplastic anemia". Our study did not allow any convincing inference about possible etiologic factors. The most common leading symptoms were bleeding tendency and pallor. Only one out of 19 cases (5.26 percent) who received testosterone propionate for more than six months showed complete response. Septicemia and intracranial bleeding were the two most common causes of 13 deaths.

INTRODUCTION

Aplastic anemia is characterized by persistent pancytopenia in peripheral blood smear with lymphocytosis and moderately to markedly hypocellular bone marrow. In adults, the etiologies are usually acquired. Drugs, chemical toxins, radiation have all been reported to cause aplastic anemia [1,2]. Eighty percent of the population in Thailand are farmers. They are highly exposed to such chemical toxins and insecticides. In addition, drugs are freely purchased without prescription and used for symptomatic "pain" relief. Consequently, there may be many factors

leading to the development of aplastic anemia in any individual patient. In only a few cases, a correctable etiologic factor can possibly be identified.

Although, many methods have been developed in western countries for treatment of aplastic anemia, androgenic hormone especially testosterone with or without steroid is widely used in Thailand. However there is no convincing evidence of its efficacy in adult patients.[3] The disease is rather prevalent, the diagnosis and treatment of aplastic anemia are usually carried out in most general hospitals using simple equipments, medications and supportive therapy. This paper presents a detailed study of aplastic anemia in Srinagarind Hospital during the last 4 years.

PATIENTS AND METHODS

During January 1980 to February 1985, 125 patients were diagnosed as having aplastic anemia at the Department of Medicine, Srinagarind Hospital, KhonKaen University. Only 78 patients were eligible for entry to our study while others were not included because of insufficient data from the medical records. The criteria for diagnosis of aplastic anemia are classified as follows :

1) severe aplastic anemia is based on the presence of pancytopenia in the peripheral blood and marked hypocellular bone marrow,

2) mild aplastic anemia is characterized by pancytopenia with normal or hypercellular bone marrow, erythroid hyperplasia with some megaloblastoid change, and abscence of megakaryocyte. Pancytopenia in peripheral blood included decrease all level of haemoglobin, white blood counts and platelet counts with lymphocytosis on differential counts.

65 patients were treated with testosterone propionate 1 - 1.5 mg/day sublingually in divided dose, and in 27 of these patients, prednisolone was also given on an occasional basis of serious bleeding tendency. Results of the treatment were evaluated only in patients who had regular follow up for more than 6 months. The definition of treatment outcomes include :

i) complete response or "cure" was labelled when all the blood counts returned to within normal values (Hematocrit $>$ 30 Vol %, Hemoglobin $>$ 10 mg %, white blood count $\geq$ 5,000 cu.mm., Platelets count $>$ 200,000 cu.mm.

ii) partial response was labelled if the haemoglobin is normal but other blood counts are subnormal and

iii) no response was labelled when there was no improvement in any blood counts.

Supportive care consisted of occasional blood component transfusions for symptomatic severe anemia and bleeding tendency. Causes of death and mortality rate were analysed from both the patients record and by contact with their families through mail questionnaires, and community follow up.

For statistical analysis the Fisher's exact probability test, and life table analysis were performed in an attempt to determine the clinical outcomes during 2 years of follow up after the diagnosis.

RESULTS

There were 78 patients, 45 males and 33 females. The male to female ratio was 1.39. Mean age of onset was 34 years (range 15 - 79 years), fifty percent of the patients were below 30 years. Table I showed the distribution of the patients present residency area. Forty - one percent lived in Khon Kaen. Most of them are farmers (Table II). Only 11.82 percent had the history of previous exposure to insecticides and 13.56 percent frequently used drugs as self - treatment of ailments. The medication used included various analgesics which were difficult to identify. Among the presenting symptoms (Table III), bleeding tendency was the most common complaint. The average duration of their symptoms before seeking treatment was about 5 months. Twenty

patients had been previously diagnosed and treated in other hospitals but with no improvement. Their bleeding sites were shown in Table IV, bleeding per gum and skin were commonly seen.

Table I Present Address

	Number	(Percent)
Khon Kaen	33	(42.30)
Udornthani	12	(15.38)
Mahasarakam	8	(10.25)
Karasin	7	(8.97)
Roi-et	7	(8.97)
Sakonakon	4	(5.13)
Others	7	(8.97)
N	78	(100.00)

Table II Occupation

	Number	(Percent)
Farmer	53	(67.96)
Government officer	7	(8.97)
Merchant	3	(3.84)
Others	15	(19.23)
N	78	(100.00)

Table III Presenting symptoms

	Frequency	(Percent)
Bleeding tendency	37	(39.74)
Pallor	18	(23.08)
Fever	14	(17.95)
Wasting and malaise	11	(14.10)
Dizziness	4	(5.13)
N	78	(100.00)

Table IV Bleeding Sites

Location	Frequency	(Percent)
Gum	15	(29.42)
Skin	14	(27.45)
Skin + gum	7	(13.73)
Hypermenorrhagia	6	(11.76)
Epistaxis	5	(9.80)
Skin + Epistaxis	4	(7.84)
Total	51	(100.00)

Table V Haematologic profile at Initial Visit

	Mean	Range
Hct	12.97 Vol %	3 - 30 Vol %
Hb	2.72 gm %	1.6 - 8.6 gm %
Wbc	3,001/cu mm	1,000 - 4,900/cu mm
Platelet	32,540/cu mm	2,000 - 98,000/cu mm

LABORATORY DATA

Table V showed the mean and range of hematologic data. These were taken initially at the first visit. Regarding the results of bone marrow analysis, 68 patients (87.18 percent) were classified as severe aplastic anemia while the rest were considered mild form. Only 3 of 14 cases tested for hemosiderin in urine showed positive results.

THERAPEUTIC DATA

65 patients were treated with testosterone, 27 of them were also treated with steroid occasionally. An average patient received 9.68 unit of packed red cells for severe anemia and 6.08 units of platelets for bleeding tendency during follow up average 4.1 months. Hepatitis B viral infection complicated 5 of 13 (38.46 percent) patients who developed hepatitis clinically.

Table VI summarized the results of therapy. 19 patients recieved testosterone regularly for more than 6 months. However, only one patient had complete response. The initial CBC of this case was not significantly different from that of those patients who died (Table VII). All but one dead patients but one were not responsive to androgenic hormone. This case responded partially before developing staphylococcal septicemia leading to eventual death. The causes of death could be identified in 8 patients, namely intracranial bleeding in 2 and sepsis in 6 patients. Among the dead, the average life span was 9.92 months after clinical diagnosis (range 1-26 months). Figure I Showed that the surviral time for 95 percent of the patients were about 72 percent.

Table VI Results of Therapy

		(Percent)
Complete response	1	1.28
No response	18	23.08
Death	13*	16.67
Loss to follow up	27	34.61
Referred to other hospitals	9**	11.54
Others	10**	12.82
Total	78	100.00

*** one of these patients had partial response before developing septic shock.**

**** all of these patients were treated below 6 months.**

Table VII Hematologic data of 13 dead patients and one responsive patient.

	Mean			
	Hct (gm%)	Hb (vol%)	Wbc(%PMN) (cu mm)	Plt (cu mm)
Complete response	17.0	5.5	2,500 (21)	
Death	16.5	5.29	2,696 (21.4)	36,727
P value	0.50	0.40	0.50	

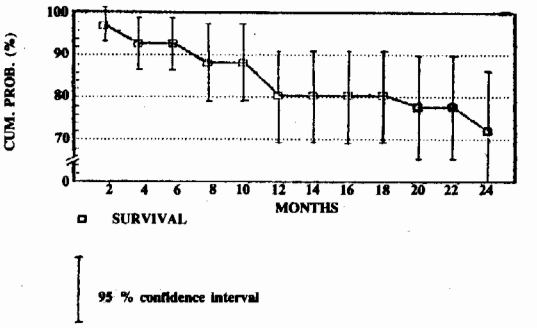

Figure I Life table analysis during 2 years follow up.

DISCUSSION

In Thailand, aplastic anemia is not uncommon. The exact incidence of the disease is unknown. In our study, 125 cases were diagnosed during the past 4 years. Similar to the previous reports [4, 5], men were slightly more affected than women. The present data do not allow any reliable conclusion about the etiologic factors of the disease in our locality.

Hemolytic anemia with complement - sensitive red cells typical of paroxysmal nocturnal hemoglobinuria could be found in 5 to 10 percent of all patients with aplastic anemia[6,7]. The percentage of hemolytic anemia with complement - sensitive red cells in Thai patients with aplastic anemia reported by Kruatrachue[8] was 15.5 percent. The high proportion of postitive hemosiderin test in our study (21.43 percent) may be due to the fact that the tests were carried out only in suspected cases.

According to a set of predefined criteria, most of our patients were classified as severe aplastic anemia. There is no statistically significant difference between the mean initial blood counts of those who responded to treatment and the fatal cases. This may be due to inadequate sample size. However, the observation was similar to the finding of Israngkul et al.[4].

According to most available reports, the results of testosterone propionate treatment in aplastic Thai adults were worse than children[3,4]. In our study, only one out of 19 cases who were treated for more than six months (5.26 percent) responded to testosterone. This patient was treated for about 18 months before his blood picture satisfied the criteria of "complete response". At the moment, the dose of testosterone in this patient is being tapered. In this case, it is difficult to conclude whether his improvement was due to the efficacy of treatment or due to spontaneous recovery.

Recently, another androgenic hormone, methenolone was reported to be associated with favourable response in adult Thai patients[9]. At present, this drug is not widely used and is rather expensive. It is appropriate to test its efficacy in a well designed study. If proven efficacious, reduction in medication cost may be possible if increase demand results in subsequent increase utilization.

Averaged blood component transfusion, packed red cells and platelet, were about 9 and 6 units respectively. Hepatitis B complicated more than one-third of our patients who developed clinical hepatitis after blood component transfusions.

Reported mean survivals of aplastic patients varied. In most studies, survival periods ranged from 6 months [12], 12 months [10] to 24 months [11]. Although most of our patients were classified as severe aplastic anemia, the survival at 2 years was 72 percent. The common causes of death in this series were semilar to the known causes of death in other studies : i.e. infection and intracranial bleeding [5].

CONCLUSION

We have studied the clinical course of patients with the diagnosis of aplastic anemia attending the medical services at Srinagarind Hospital. It is our belief that testosterone therapy has little or no benefit in adult aplastic anemia in our setting, though this drug is commonly used in most general hospital in Thailand.

ACKNOWLEDGEMENT

This paper was supported by a research grant of the Faculty of Medicine, Khon Kaen Foundation.

The authors are grateful for the data analysis and the statistical guidance given by the clinical epidemiology unit, Faculty of Medicine, Khon Kaen University.

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