PURE RED CELL APLASIA IN THAILAND : REPORT OF TWENTY FOUR CASES

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INTRODUCTION

Pure red cell aplasia (PRCA) is characterized by a normochromic, normocytic anemia with reticulocytopenia, and generally, a normal white blood cell and platelet count. The bone marrow usually is normocellular with normal granulopoiesis and megakaryocytopoiesis, but is virtually devoid of erythroblast (Jacobs *et al.*, 1959; Di Giacomo *et al.*, 1966). Varied etiologic factors have been associated with or causally related to the onset of PRCA. Approximately half the patients with PRCA have thymomas (Jacobs *et al.*, 1959; Schmid *et al.*, 1965; Di Giacomo *et al.*, 1966; Hirst *et al.*, 1967). Others are associated with drugs (Swineford *et al.*, 1958; Ozer *et al.*, 1960; Brittingham *et al.*, 1964; Goodman *et al.*, 1964; Recker *et al.*, 1969; Ibrahim *et al.*, 1969; Jurgensen *et al.*, 1970), infections (Chernoff *et al.*, 1951; Gasser, 1957) carcinoma (Entwistle *et al.*, 1964; Mitchell *et al.*, 1971) and immunologic disorders (Doughaday, 1968; Cassileth *et al.*, 1973). The purpose of this paper is to report 24 cases of PRCA seen at the Ramathibodi Hospital, Bangkok, Thailand.

MATERIALS AND METHODS

Twenty-four cases of PRCA were seen at the Ramathibodi Hospital, Bangkok during the period from January 1971 to February 1985. Criteria for the diagnosis of PRCA include: (1) normochromic, normocytic anemia; (2) corrected reticulocyte count less than 0.5%; (3) a normocellular bone marrow with selective virtual absence of the erythroid precursors, in the presence of essentially unaltered granulopoiesis and adequate number of megakaryocytes. Routine clinical charts and laboratory findings were recorded, and the haematological studies carried out were according to conventional methods.

RESULTS

The age, sex and hematological data of the 24 cases are summarized in Table 1. There were 4 males and 20 females, age ranging from 15 to 73. Table 2 summarizes the underlying causes of PRCA in these patients. Only two cases were found to have no underlying diseases, therefore considered as acquired primary type. Of the 21 cases with secondary PRCA, ten were associated with infections, mostly gram negative organisms. Systemic lupus erythematosus was associated in 3 cases; autoimmune hemolytic anemia in two, thymoma, thyroid carcinoma, protein calorie malnutrition, rheumatoid arthritis non-Hodgkin lymphoma, and Sheehan's syndrome, in one each. Three of the 24 patients died, two from uncontrolled gram negative infection, the other from uncontrolled SLE and subsequently systemic fungal infection. One of the primary PRCA responded to prednisolone and cyclophosphamide and went into complete remission while the other did not respond to the same immunosuppressive therapy and required periodic blood transfusion. The patient associated with thymoma, the PRCA did not respond to thymectomy but did so after the administration of prednisolone. Two of the 3 cases associated with SLE, PRCA recovered after prednisolone

Table 1

Age, sex and hematological data of cases of PRCA.

No.	Sex	Age (yr)	Hb. gm%	Hct. %	Retic. %	WBc /c.mm	Platelet /c.mm	Underlying conditions
1.	F	73	2.7	12	0.1	5,350	340,000	No underlying disease, not respond to prednisolone and cyclophosphamide
2.	F	15	4.1	11	0.9	4,100	220,000	No underlying disease, responded to prednisolone and cyclophophamide
3.	F	55	4.8	14	0.1	9,400	350,000	Thymoma, after thymectomy PRCA persisted, responded to prednisolone
4.	F	44	6.9	23	0.1	9,600	188,000	SLE, responded to prednisolone.
5.	F	29	6.4	22	ND	6,500	220,000	SLE, subsequently died from infection
6.	F	50	7.3	24	ND	7,200	310,000	SLE, improved after prednisolone
7.	F	55	5	16	0.3	7,600	260,000	Sheehan's syndrome responded to prednisolone
8.	F	73	7.9	24	0.9	20,100	338,000	Cancer thyroid, untreated
9.	M	46	6.7	23	0.2	14,900	350,000	Cholangiocarcinoma, melioidosis, not improved
10.	M	32	7.6	25	ND	7,300	310,000	Aspergillosis improved with treatment
11.	F	27	5.2	13	0.3	5,700	198,000	*E. coli* sepsis, PRCA resolved after infection was treated
12.	F	34	7.4	23	0.7	7,700	518,000	Actinomycosis, BM recovered after infection was treated.
13.	F	24	6.5	21	0	13,050	154,000	*Klebsiella* and *Pseudomonas* peritonitis, died
14.	F	42	8.2	26	0	3,000	220,000	Amoebic colitis with superimposed *Pseudomonas* septicemia, died
15.	F	43	7.2	22	ND	13,500	345,000	*Pseudomonas* septicemia, improved with treatment
16.	F	17	8.5	25	1	6,900	376,000	Miliary tuberculosis, anemia resolved after treatment of tuberculosis
17.	F	58	5.1	16	ND	18,000	250,000	*Hemophilus* influenza pneumonia, infection not well controlled, anemia persisted
18.	F	55	6.7	20	0.3	11,700	210,000	Protein calorie malnutrition
19.	F	40	6	18	0.4	6,800	300,000	Chronic pyelonephritis, improved after antibiotics
20.	F	39	4.8	13	0.2	8,910	312,000	AIHA, responded to prednisolone
21.	M	73		11	0.6	4,250	300,000	Dilantin, anemia resolved after discontinuation of dilantin
22.	F	44	6.6	23	1	6,000	372,000	Rhematoid arthritis
23.	F	54	6.5	23	0.3	5,400	210,000	Non-Hodgkin lymphoma
24.	M	63	9.0	25	0.8	13,200	adequate	Autoimmune hemolytic anemia, responded to prednisolone

therapy. Cases of PRCA associated with infections, anemia usually resolved if the infections were successfully treated.

Table 2

Causes of PRCA in 24 cases.

Primary	2
Secondary	22
Infection	10
Systemic lupus ertyhematosus	3
Thymoma	1
Autoimmune hemolytic anemia	2
Carcinoma of thyroid	1
Sheehan's syndrome	1
Protein calorie malnutrition	1
Dilantin	1
Rheumatoid arthritis	1
Non-Hodgkin lymphoma	1

DISCUSSION

Pure red cell aplasia was indicated by the moderate to severe anemia, reticulocytopenia, no changes in the white blood cells and platelets, together with a marked reduction of erythropoietic activity in the bone marrow showing normal white blood cell and platelet precursors. PRCA has been reported to be associated with a wide variety of situations and Krantz has proposed a practical classification for PRCA (Krantz *et al.*, 1977). PRCA with thymoma has been reported as often as primary acquired PRCA (Jacobs *et al.*, 1959; Schmid *et al.*, 1965; Di Giacomo *et al.*, 1966; Hirst *et al.*, 1967). Removal of the thymoma is followed by remission of the anemia in 29% of these cases. Chronic acquired secondary PRCA has been noted with systemic lupus erythematosus, rheumatoid arthritis, autoimmune hemolytic anemia, severe renal failure, severe nutritional deficiency and neoplasm (Foy *et al.*, 1961; Entwistle *et al.*, 1964; Pasternack *et al.*, 1967; Dougha-day, 1968; Mitchell *et al.*, 1971; Cassileth *et al.*, 1973; Krantz *et al.*, 1977). An acute and self limited cessation of red cell production can arise during the course of infections such as atypical pneumonia, mumps, viral hepatitis, meningococcemia, staphylococcemia and infectious mononucleosis (Chernoff *et al.*, 1951; Gasser, 1957). PRCA has also been reported after exposure to a wide variety of drugs (Swineford *et al.*, 1958; Ozer *et al.*, 1960; Brittingham *et al.*, 1964; Goodman *et al.*, 1964; Ibrahim *et al.*, 1966; Recker *et al.*, 1969; Jurgensen *et al.*, 1970). Most patients recovered quickly when the drugs were discontinued. There are usually no underlying diseases associated with chronic primary acquired PRCA. A number of these cases were found to have immunoglobulin inhibitor to erythroid precursors in the bone marrow. A few have inhibitor to erythropoietin. Still in some cases no serum inhibitor was found, thus unknown origin and pathogenesis.

In our studies, the majority of cases are secondary acquired form. Infection, mostly gram negative organism, is the leading cause in this group. In most of the patients PRCA improved after the infection was controlled. Three patients died from uncontrolled infection.

Infection is still a major health problem in Thailand. It is possible that PRCA associated with infection might be more common than we thought. Several cases came from the provinces and since these population have the tendency to have a lower base line hemoglobin level than an accepted WHO criteria, it is possible that these cases might have been thought to be nutritional anemia and treated as such. The majority of infections associated with PRCA reported in the literature were from gram positive organisms. Five out of 10 cases of our serics were due to gram negative organisms. To our knowledge, PRCA secondary to aspergillosis and actinomycosis have not been reported before.

Case 7 had Sheehan's syndrome and PRCA. It is not known whether PRCA is secondary to the endocrine abnormality or it is unrelated. PRCA resolved after prednisolone therapy. This could have been another case of acquired primary PRCA.

SUMMARY

Twenty four cases of pure red cell aplasia were reported. No underlying diseases were found in two cases. Of the 22 cases with secondary form, 10 were from infections, mostly gram negative organisms. Three cases had systemic lupus erythematosus, two had autoimmune hemolytic anemia. The following conditions were found in one each : thymoma, thyroid carcinoma, protein calorie malnutrition, rheumatoid arthritis, non-Hodgkin lymphoma and Sheehan's syndrome. Three patients died, two from uncontrolled infection, the other from uncontrolled SLE and subsequently systemic fungal infection. Only one of the 2 primary cases responded to immunosuppressive drugs. The majority of patients with underlying infections, PRCA resolved after the infections were treated. This is the first reported series of PRCA in Thailand.

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