

# SPONTANEOUS REMISSION IN APLASTIC ANAEMIA

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## Introduction

Drug induced aplastic anaemia carries a bad prognosis and a high mortality rate. We describe here a case of Phenylbutazone induced aplastic anaemia who has gone into spontaneous remission.

## Case History

Mr. G.E.S. 57 years, male, electrical fitter presented in January 1979 with two week history of epistaxis, haematuria and bruising. About two months before this episode he had seen his doctor because of pain in the left shoulder joint. The doctor prescribed delta-buta-zolidine three tablets daily, which he took for six weeks, but discontinued when he first noticed blood on the handkerchief after blowing his nose. The doctor had then changed his medication to prednisolone 15 mg daily and ampicillin 1gm daily for ten days. The patient had not suffered any serious illness in the past. He never had jaundice, did not take any medication regularly and denied handling any toxic chemicals. Clinical examination showed extensive purpuric rash over the extremities, abdomen and hard palate as well as conjunctival and fundal haemorrhages. He was afebrile and there was no evidence of infection. Systemic examination showed no significant abnormalities. Bone marrow aspirate and iliac crest triphine biopsy showed a very hypoplastic marrow.

Diagnosis of aplastic anaemia most probably phenyl butazone induced was made. Management was started with replacement therapy. He required frequent platelet transfusion due to increasing haemorrhage and concentrated red cell transfusion to correct the rapidly developing anaemia. Oxymethalone 150 mg daily was started one week after the diagnosis was made. However his pancytopenia continued; he required platelets and red cell transfusion once a week and often developed urinary tract infection. After being on oxymethalone for six months he had developed effusion of the knee and ankle joints and became

mildly jaundiced. Laboratory tests for auto antibodies were negative. Serum bilirubin which had been normal was elevated to 60  $\mu\text{mol/l}$ . Serum alkaline phosphatase, gamma G.T., ALT and AST were also raised. Oxymethalone was then discontinued; the blood count at that time was as follows:-

Hb 6.6g/dl; RBC  $2.30 \times 10^{12}/\text{l}$ ; PCV .203 WBC  $1.8 \times 10^9/\text{l}$ ; Platelets  $40 \times 10^9/\text{l}$ ; Reticulocytes less than 1%.

The weekly red cell and platelets transfusion were maintained but in the beginning of August 1979 we felt he was maintaining his haemoglobin better than in the past and he was less haemorrhagic. It was therefore decided to withhold further transfusions. On the 5th September 1979 his blood count showed:-

Hb 12.5 g/dl; RBC  $3.9 \times 10^{12}/\text{l}$ ; Retics 3.0%

WBC  $3.6 \times 10^9/\text{l}$ ; Platelets  $54 \times 10^9/\text{l}$ .

Bone marrow aspirated on 3-10-79 revealed a cellular sample showing active erythropoiesis and granulopoiesis with sufficient megakaryocytes and increased iron stores. Iliac crest triphine biopsy also showed areas of increased cellularity with many normal haemopoietic cells.

There has been significant clinical improvement, he felt well in himself, and was not haemorrhagic.

His last blood transfusion was on 9th August 1979. On 18th December 1979 his Hb was 14.9 g/dl; the

white cell count ( $3.6 \times 10^9/l$ ) and the platelet count ( $50 \times 10^9/l$ ) has stayed subnormal but he has not suffered from any complications due to this. He is now on no treatment.

### Comments

A significant number of cases of aplastic anaemia are caused by drugs. The disease may run an acute or chronic course with complete recovery rate of only 10% and five year mortality of about 70% (Williams et al., 1973).

**Table: Showing Some of the Haematological Results**

<i>Date</i>	16-1-79	11-6-79	5-9-79	18-12-79
Hb (G/dl)	12.5	6.9	12.5	14.9
WBC x $10^9/l$	1.5	1.8	3.6	3.2
Neutrophils	7%	33%	62%	51%
Lymphocytes	90%	66%	24%	38%
Platelets x $10^9/l$	5.0	40.0	54.0	55.0
RBC x $10^{12}/l$	3.88	2.30	3.90	4.44
Reticulocytes	0.5%	1%	3.0%	—
L.A.P. Score	300	(N=25-100)		
Hb-F	0.9%		3.6%	
Ham's Test	Negative		Negative	
Prothrombin Time	13 secs			
Control	13 secs			
Partial Thromboplastin time	37 secs			
Control	39 secs			

**Prognostic Index  $C=0.198395$  (see text)**

Characteristically phenyl butazone aplastic anaemia occurs after a prolonged course of treatment with total dose exceeding 50 g and while the drug was still being taken (Hale and de Gruchy, 1960; MC Carthy and Chalmers, 1961).

There is no rapid recovery of bone marrow function after withdrawal of the drug, suggesting either stem cells or stroma have been damaged (Benestad, 1979). A number of workers have attempted to

define prognostic factors in aplastic anaemia. In early studies the clinical condition of the patient was considered a useful guide. More recently, a rapid onset of disease and the presence of haemorrhagic manifestations (Lynch et al., 1975) have been associated with diminished survivals.

The criteria for severe aplastic anaemia used by the International Aplastic Anaemia Study Group (Williams et al., 1978) includes anaemia with reticulocytes <11.0%; granulocytes <500/mm<sup>3</sup>; Platelets <20,000/mm<sup>3</sup> and severely hypocellular (25% of normal) or moderately hypocellular (25-50%, of normal) bone marrow. Lynch et al have used computer assisted discriminant analysis to devise a prognostic formula. This has been based on the observation that survival fell sharply until about four months after the onset of symptoms. After that time survival fell less sharply, suggesting the possibility of two distinct populations. The prognostic index is called C (unitless). Although, there was considerable overlap of C values for the two population, patients at the extremes were clearly segregated. Patients with C values of above 0.041 uniformly died within four months, while those with C values of less than 0 uniformly survived. Using any of the above mentioned criteria, our patient had an extremely poor prognosis. Bone marrow transplantation had to be ruled out due to unavailability of a suitable donor and oral androgen therapy was started with oxymethalone. The results of a prospective study by the International Aplastic Anaemia Study group had failed to support a beneficial effect of androgens on the course of patients with severe aplastic anaemia. However, for want of an alternative approach, treatment with oral androgens was continued for six months. The treatment was discontinued because of absence of any encouraging haematological responses and increasing side effects. The patient, while he was only on a supportive programme of platelet and red cell transfusion, has gone into partial remission which has been maintained for four months without any further supportive measures. We feel this is most likely to be spontaneous remission.

## References

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