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POSTER ABSTRACTS

508.BONE MARROW FAILURE: ACQUIRED

Pathogenetic Subtypes of Pure Red Cell Aplasia and Therapeutic Management Strategies : A Single Centre Experience in the United Kingdom of 75 Patients over 10 Years

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Introduction

Pure red cell aplasia (PRCA) is a syndrome characterised by a severe anemia, reticulocytopenia and severe depletion of erythroid precursors in an otherwise unremarkable bone marrow. PRCA arises congenitally in Diamond-Blackfan Anemia and usually presents in childhood. Acquired PRCA can occur at any age, can be transient due to infections such as from parvovirus B19, or more chronic, secondary to autoimmune conditions, malignancies especially thymoma, erythropoiesis stimulating agents, , pregnancy and ABO incompatible hematopoetic stem cell transplantation. PRCA is also known to arise from drug and toxin exposure. Haematological malignancy/clonal disorders for e.g. CLL, MGUS, T-LGLs have well known associations with PRCA. PRCA can also be a feature of myelodysplastic syndrome and can herald evolution to aplastic anemia. Despite the heterogeneity in aetiology, the mainstay of treatment remains immunosuppression with steroids and/or ciclosporin. Here, we report our single centre experience of a large cohort of 75 patients with PRCA, referred to our centre over a 10 year period.

Methods

Patients with pure red cell aplasia referred to the Department of Hematological Medicine at King's College Hospital were identified by interrogation of the Electronic Patient Record (EPR) and pathology systems. The search terms used were a clinical or pathological diagnosis of 'pure red cell aplasia' or 'PRCA'. Our hospital receives diagnostic samples from the South East of England, therefore data was collected only for patients with clinical information available. Patients (n=33) who developed PRCA post-allogeneic stem cell transplant were excluded.

Results

A total of 75 patients with both a pathological diagnosis of PRCA and available clinical information were identified, 31 (41.3%) were female. Median age was 51 years (range 9 - 84). The majority of patients had underlying conditions known to be associated with PRCA. Of the haematological conditions, PRCA was most seen in association with MDS (Table 1).

Of the 75 patients in our cohort, 82% (61/75) required treatment for PRCA and 57% (43/75) required two or more lines of therapy. In total 25.3% (19/75) patients received corticosteroids as first line therapy. Of those, 75% showed a response, with 50% achieved a complete response. The response rate was less favourable (57%) in those patients in whom ciclosporin was used as first line therapy. Most common second line therapy was Ciclosporin (22.3%) followed by Cyclophosphamide (4%), Sirolimus (2.7%) and Anti-Thymocyte Globulin (1.33%).

Of the cohort with an underlying MDS, 52% (11/21) responded to treatment, compared to 65% of those with idiopathic PRCA, likely reflective of the recalcitrant nature of PRCA in MDS. Other therapies received were IVIG, erythropoietin and disease-directed therapy,e.g lenalidomide for MDS with 5q- and thymectomy.

Median follow of patients were 42 months.The overall survival of PRCA since last follow up was 50% for the cohort as a whole and 63% for those without an associated malignancy or clonal disorder.

D iscussion

In this large single centre experience of PRCA, we describe a lower incidence of idiopathic PRCA, lower median age despite a large proportion of MDS and increased incidence in male as compared to published literature. Response to initial therapy was seen in the majority of idiopathic PRCA patients, however response was lower in patients with an underlying malignancy. Of note we identified STAT3 mutations in two patients, highlighting the role of molecular testing and keeping a broad differential diagnosis when presented with this rare condition.

Disclosures Kulasekararaj: *Achillion:* Consultancy; *Novartis:* Consultancy, Honoraria, Membership on an entity's Board of Directors or advisory committees; *Amgen:* Honoraria, Membership on an entity's Board of Directors or advisory committees; *Alexion, AstraZeneca Rare Disease:* Consultancy, Honoraria, Membership on an entity's Board of Directors or advisory committees; *Akari Therapeutics:* Consultancy; *Samsung:* Consultancy; *BioCryst:* Consultancy; *Celgene/BMS:* Consultancy, Honoraria, Membership on an entity's Board of Directors or advisory committees; *F. Hoffmann-La Roche Ltd:* Consultancy, Membership on an entity's Board of Directors or advisory committees.

Table1: Secondary causes of PRCA in our cohort of patients

Underlying Cause of PRCA	Frequency % (number/75)
Idiopathic	10.7% (8)
Constitutional	8% (6)
MDS – RCMD	10% (8)
RAEB1/2	13% (10)
5q-	4% (3)
MLD	6% (5)
SLD	1% (1)
MDS/MPN	5% (4)
Unclassified	5% (4)
Other haematological malignancies	
T-LGL	8% (6)
MGUS	2.7% (2)
CLL	1.3% (1)
Thymoma	13.3% (10)
Infections	
Parvovirus	2.7% (2)
HIV	4% (3)
CMV	2.7% (2)
Other	
Goods Syndrome	2.7% (2)
Anti-EPO antibodies	2.7% (2)
STAT3 mutation	2.7% (2)

*2 of 8 patients with T-LGL had a low level *STAT3* mutation. MDS- myelodysplastic syndrome, RCMD – refractory cytopenia with multilineage dysplasia, RAEB – refractory anemia with excess blasts, MLD – multilineage dysplasia, SLD – single lineage dysplasia, MPN – myeloproliferative neoplasm, T-LGL- T-large granular leukemia, MGUS- monoclonal gammopathy of undetermined significance, CLL- Chronic Lymphocytic Leukemia, EPO- Erythropoietin

Figure 1

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