KMJ

Case Series

Renal transplantation in marrow dysfunction: A case series

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Abstract: This abstract presents a case series of renal transplants in three patients with aplastic anemia, a rare hematological disorder characterized by bone marrow failure and pancytopenia. We conducted a retrospective analysis of these patients, focusing on their demographic data, clinical characteristics, transplant procedures, and post-transplant outcomes. Special attention was given to immunosuppression management and potential complications related to both conditions. Our literature review revealed only one previously published case report, highlighting the rarity of this clinical scenario. This case series aims to contribute insights into the unique challenges and considerations associated with renal transplantation in aplastic anemia patients. We discuss transplant outcomes, including graft function, patient survival, and complications. The study underscores the importance of a multidisciplinary approach in managing complex patients with both hematological and renal disorders and emphasizes the need for further research to establish evidence-based guidelines for such cases.

Keywords: Renal Transplant; bone marrow dysfunction; hematopoietic dysfunction; chronic kidney disease; hemodialysis

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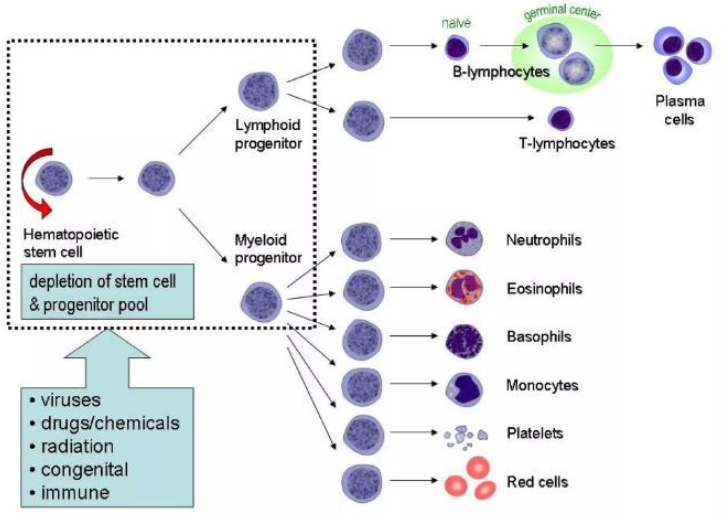
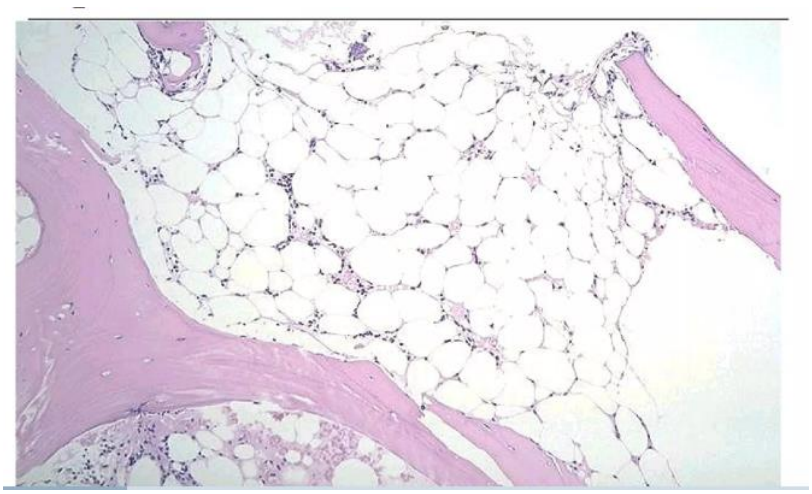
1. Introduction

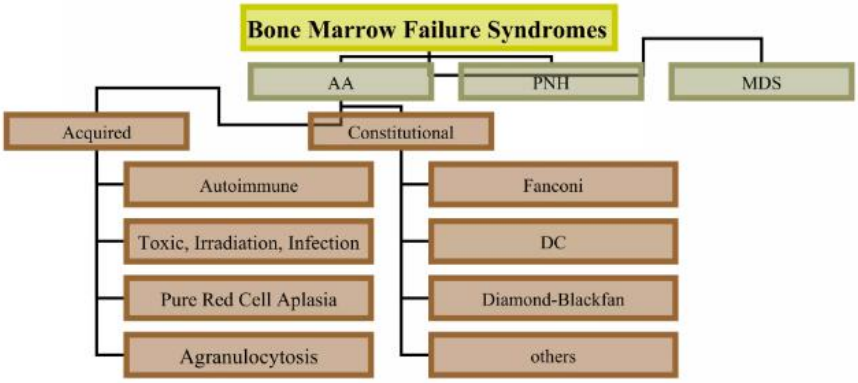
Bone marrow failure (BMF)

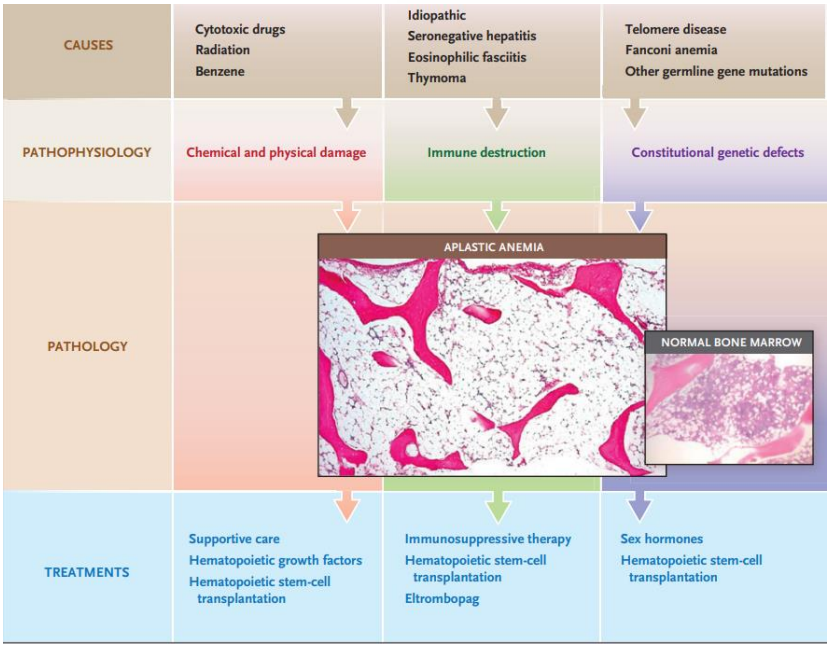
Decreased production of one or more major hematopoietic lineages leads to diminished or absent hematopoietic precursors in the bone marrow and attendant cytopenias.



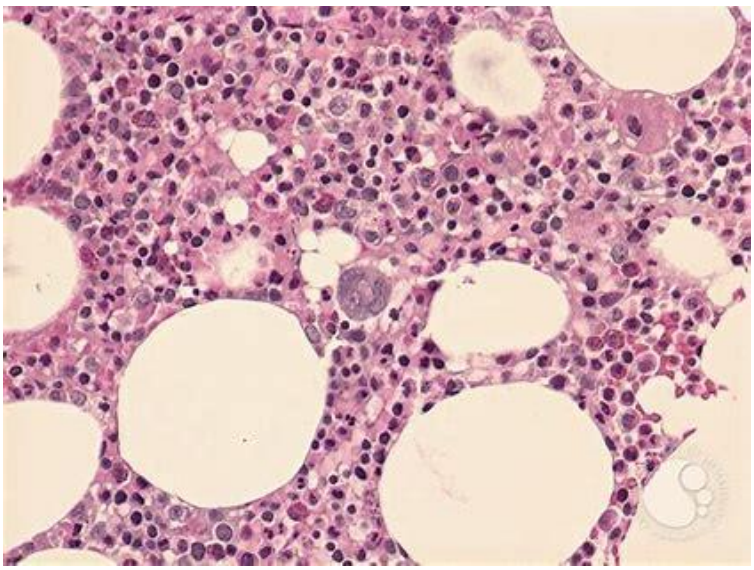


Bone Marrow Failure Syndromes

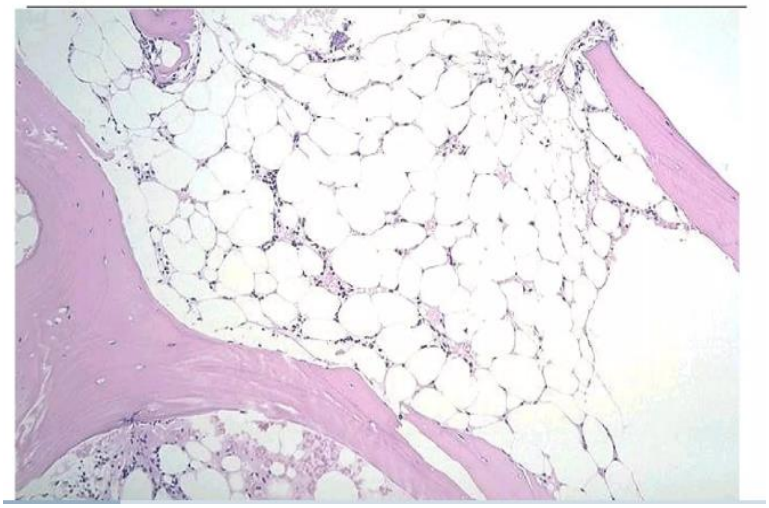




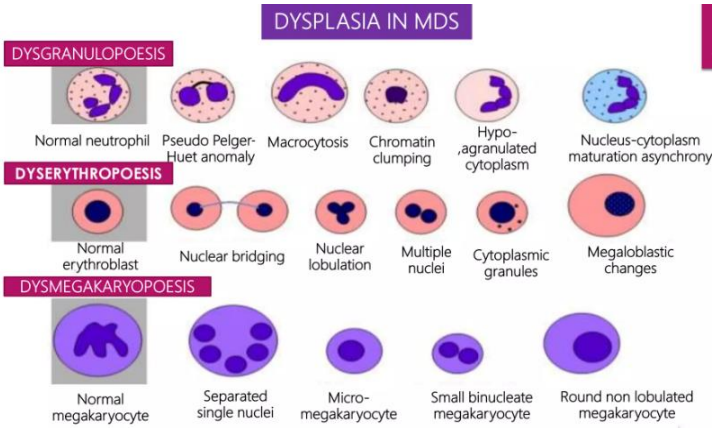
Normal BM



Aplastic BM



Dysplasia in MDS



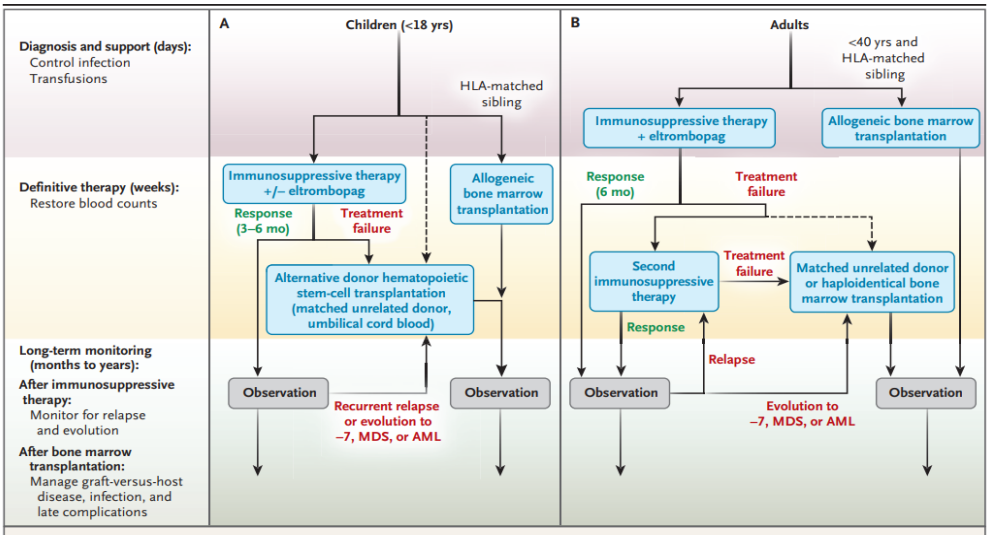
CYTOGENETIC ABNORMALITIES AND THEIR ASSOCIATIONS IN MDS	
Cytogenetic abnormality	Associated with
Del 5q	Good prognosis in elderly patients with thrombocytosis and macrocytic anemia
Del 7q	Differentiates hypocellular MDS from aplastic anemia
Monosomy 7	Pediatric MDS-25% cases demonstrate it,JMML (MDS/MPN)
Del 11q	Intermediate risk
Del 17p	Dysgranulopoesis ,pseudo-Pelger-Huet anomaly with small vacuolated neutrophils and TP53 mutation,and poor response to therapy
Monosomy 5	MDS-EB
Del 12p	CMML
Trisomy 8	MDS-RS & CMML
11q23	Secondary/therapy related MDS

Prognosis of aplastic anaemia depends

1. Severity of disease based on absolute neutrophil count
   a. Non severe: >500
   b. Severe: 200-500
   c. More severe: <200
2. Age at diagnosis and start of treatment.
   a. Older the age and delay in treatment
3. Cause of aplastic anemia.
   a. Cytogenetic abnormalities

Severity of AA

- 2 of 3 peripheral blood count criteria
2. ANC < 500 /µL
3. Plat count< 20 000 /µL
4. Retics (Automated) < 60 000 /µL



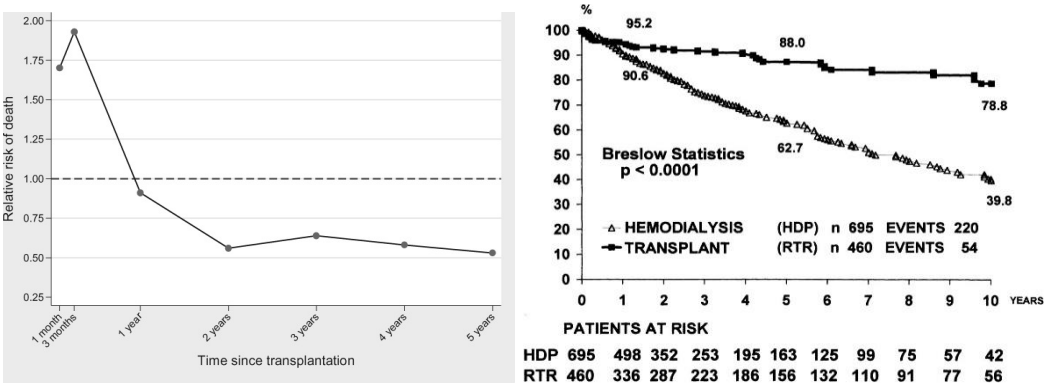
Prognosis

With current BMT regimen, most patients with severe aplastic anemia have a 60-70% long-term survival rate

Patients with severe aplastic anemia who receive antithymocytic globulin (ATG) or antilymphocyte globulin (ALG) but do not receive BMT have a 41%r response rate and a 1-year survival rate of 55.4%. Adding androgens increases response rates to 70%, with a 1-year survival rate of 76%.

Cyclosporine therapy at 200-400 mg/dl (Maintain serum trough levels at 100-250 nb/ml) has a reported 85% hematologic remission rate.

Survival of dialysis vs transplant



2. Case Presentation

2.1. Case 1

A 37-year-old male patient came with the following complaints. ESRD (End-Stage Renal Disease) on HD NKD (no kidney disease). Underwent live related renal transplant - Aug 2016, elsewhere mother donor. On steroid, free protocol then noted a Progressive graft dysfunction. Incisional hernia in 2020 for that Mesh hernioplasty done followed by HD started 2021 December.

On routine evaluation on 23-11-2021

1. Hb: 5.8 g/dl; TLC: 2900; DC: N - 65.3%; L: 24.2%; M: 7.4%; E: 2.4%
2. Platelet: 143000
3. Vitamin B12 and folate levels were normal.

Bone marrow aspiration 23-11-21

1. Marrow is hypocellular.
2. Cellularity in hypocellular area -15%. Megakaryocytes- nil erythroid and myeloid series –unremarkable.No increase inreticulin fibres.NO granuloma,immature precursors.
3. Chromosome analysis: 46 XY.

Diagnosis

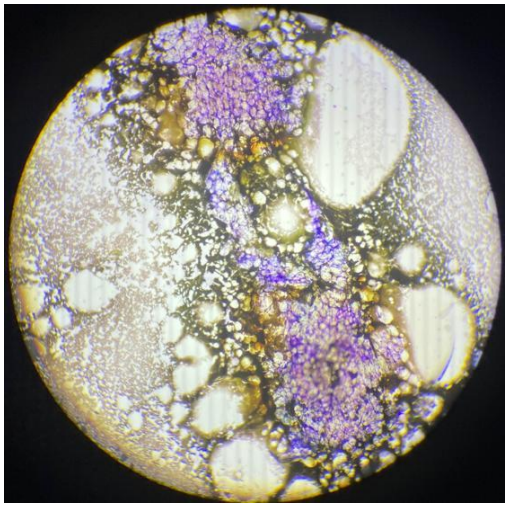
Non-severe Aplastic anaemia

Prognosis: Good

1. No cytogenetic abnormalities
2. Non severe aplastic anaemia
3. No dysplasia or immature precursors

Treatment given

Drug	Dose	Frequency
Danazol	100 mg	1-0-1
Eltrombopag	100 mg	1-0-0



Attained clinical response as evidenced by;

Discussion

Points in favour of renal transplant

1) Non-severe aplastic anemia with good long-term prognosis
2) Consistent improvement in Blood counts.
3) Non-requirement of transfusion, infections or bleeding diathesis
4) Proceeded with renal transplant as patient and family members are keen in renal transplant, as he was not doing well with dialysis.

Donor spouse: 29/f B+
HLA: Haplomatch; DSA: Negative; PRA: Negative; CM: Negative.

Pre OP counts

Hb: 9.6; TLC: 4400; N: 60 %; Platelets: 2.63 lakhs

Renal transplant on 15-8-2022
Induction: ATLG (Anti-T-Lymphocyte Globulin)
Immunosuppression: Tacrolimus (TAC)/Mycophenolate mofeti (MMF)/Steroids

1) L lap donor nephrectomy
2) Single renal vessels
3) Left renal bed

Therapeutic dilemmas

Induction agent

ATLG vs Basiliximab

1) ATG is set to be an immunosuppressive agent in treating aplastic anemia.
2) ATLG quite similar to ATG given in view of cost constraints

Maintenance immunosuppression

1) Tacrolimus/MMF/steroids vs Tacrolimus/Everolimus/steroids
2) In view of stable counts, High-risk transplant decided to go with Tac/mmf/steroids. Outcome was good.

Discharge

Danzol was stopped and Eltrombopag continued for 1-month post-transplant.

1) Hb:9.6; TLC: 6700; Platelet - 2.63
2) Sr. creatinine: 0.96

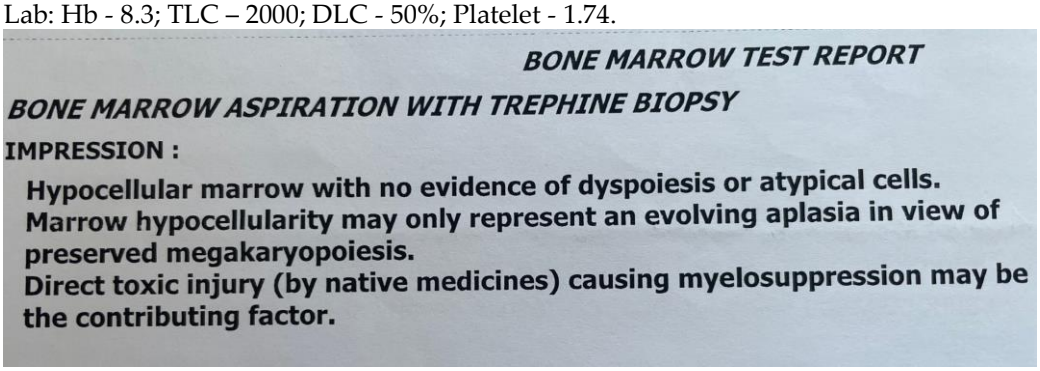
Last, follow up

1) Hb :13.5 TLC 7200 Plat : 1.9 lakhs
2) Sr. creatinine - 0.86

2.2. Case 2

A 42-year-old male patient came with the following complaints, CKD diagnosed 2020 and HD was inducted in Jan 2020, elsewhere. Started on transplant work up elsewhere.

Lab: Hb - 8.3; TLC – 2000; DLC - 50%; Platelet - 1.74.

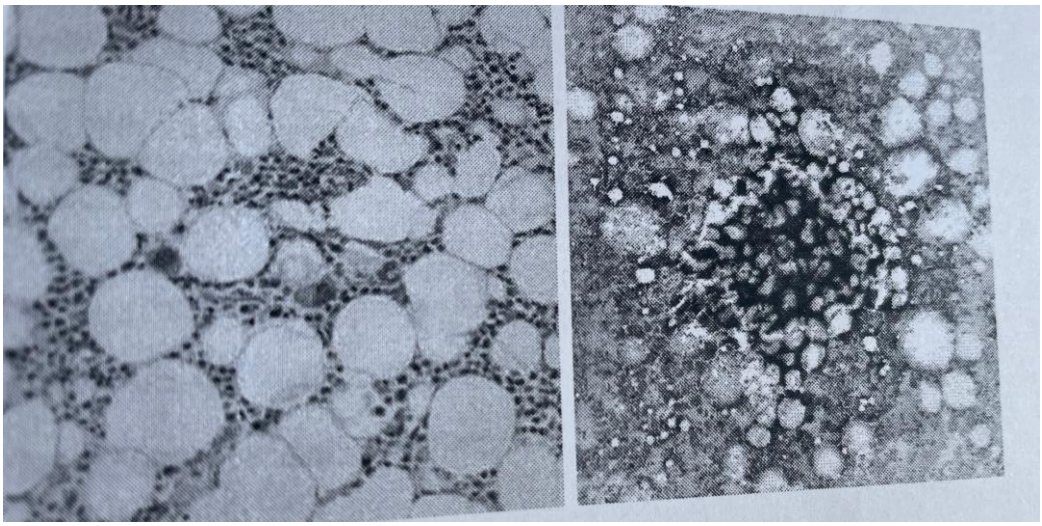


BONE MARROW TEST REPORT

BONE MARROW ASPIRATION WITH TREPHINE BIOPSY

IMPRESSION :

Hypocellular marrow with no evidence of dyspoiesis or atypical cells.
Marrow hypocellularity may only represent an evolving aplasia in view of preserved megakaryopoiesis.
Direct toxic injury (by native medicines) causing myelosuppression may be the contributing factor.



Cytogenetics: No abnormality detected

Started on Danazol/Eltrombopag/Erythropoietin.

Date	Hb	TLC	N %	Platelets
10-10-21	9.6	3200	62	1.74
21-12-21	9.8	2800	65	1.9
5-4-22	7.9	3100	64	2.25

Proceeded for renal transplant

Due to stable ANC (Absolute Neutrophil Count)

1. Non requirement of blood transfusion,
2. Absence of infection and bleeding diathesis
3. Normal cytogenetics which all portends favourable prognosis

Donor: Paternal aunty - 67 years
HLA: 3/6 match
CDC CM: Negative
Screening PRA Class II - Weak positive
PRA by SAB Class I is 19% (Max MFI 1200)
Class II - 0%

Renal transplant on 8-9-22

Induction: not given due to low normal counts for fear of infection

Immunosuppression: TAC/MMF/Steroids.

Date	Hb	TLC	PMN	Platelet
9-9-22	8.9	14700	72%	3.61
13-9-22	8.2	12700	68%	2.78
27-10-22	11.2	6100	74.9%	1.56
26-8-23	15.3	7400	73.2%	2,01

Discharge: Sr. creatinine - 1.4
Follow up 20-8-23: 1.49 - urine routine; Normal BP - 120/80

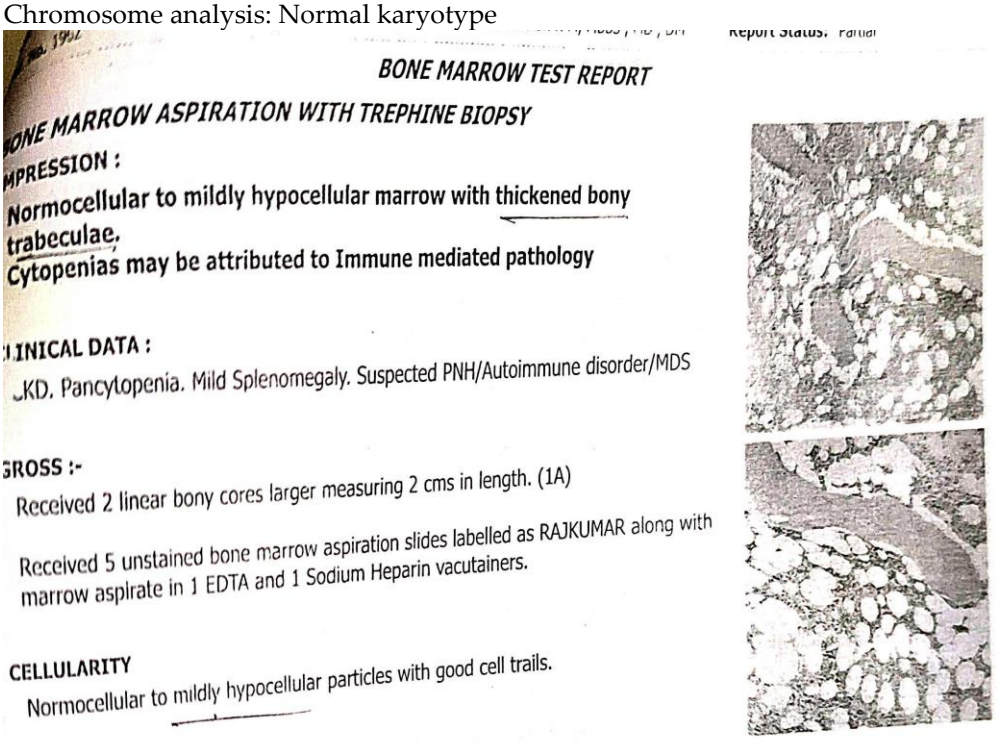
2.3. Case 3

A 29 years old Male 0+ patient came with the following complaints like Chronic IgA nephropathy-2017. June 2022- ESRD -HD inducted.

Transplant workup - mother donor-0+
Immunological workup – satisfactory. On April 2023 - Developed pancytopenia.
Lab: Hb -6.9 gm% TC 2400 Platelet - 1.16 lakhs

Bone Marrow Report

Chromosome analysis: Normal karyotype



BONE MARROW TEST REPORT

ONE MARROW ASPIRATION WITH TREPHINE BIOPSY

MPRESSION :

Normocellular to mildly hypocellular marrow with thickened bony trabeculae,
Cytopenias may be attributed to Immune mediated pathology

INICAL DATA :

KD. Pancytopenia. Mild Splenomegaly. Suspected PNH/Autoimmune disorder/MDS

GROSS :-

Received 2 linear bony cores larger measuring 2 cms in length. (1A)

Received 5 unstained bone marrow aspiration slides labelled as RAJKUMAR along with marrow asplrate in 1 EDTA and 1 Sodium Heparin vacutainers.

CELLULARITY

Normocellular to mildly hypocellular particles with good cell trails.

Then managed with Danazol and erythropoeitin.
Before the renal transplant in Jan 2024,
Lab: Hb - 9.7gm/dl, TLC - 3100, Platelet count - 1.81 lakhs.
Renal transplant on 20-1-24
Induction: Basiliximab
Immunosuppression: Tac/MMF/Steroids
Uneventful postoperative period.
Discharge

1. Sr. Creatinine: 1.2 mg/dl
2. Hb 10.2 gm/dl : TLC - 4500 Platelet - 1.6 lakhs

Follow up September 2024

1. Sr. Creatinine: 1.2 mg/dl
2. Hb 14.5 gm/dl; TLC – 7600; Platelet - 1.8 Lakhs

Determinants for safe renal transplant in aplastic anaemia

Favourable factors	Unfavourable factors
Non severe aplastic anaemia, Consistent response following treatment for a minimum 3 months, Normal cytogenetics.	Severe Aplastic anaemia requiring transfusions, Persistent platelet count < 1 lakh, Persistent neutropenia, Myelodysplasia, Abnormal cytogenetics, Inherited bone marrow failure syndromes.

Points learned from those 3 cases

1. Renal transplant can safely be done in non severe aplastic anemia.
2. Maintenance immunosuppression can safely maintain remission of aplastic anaemia.
3. Antimetabolites can safely be used without the danger of fall in counts.
4. Proper evaluation of aplastic anaemia can safely include and exclude the patients for renal transplant.