A STUDY OF SERUM IMMUNOGLOBULIN LEVELS IN ADULT ACUTE MYELOID LEUKEMIA PATIENTS RECEIVING STANDARD INDUCTION CHEMOTHERAPY

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Introduction

Acute myeloid leukemia (AML) is a heterogenous malignant disease caused by an impaired differentiation of hematopoietic stem cells into myeloid cells leading to accumulation of immature blast cells in the bone marrow (BM), the peripheral blood (PB) and rarely other organs. AML accounts for 80% of adult acute leukemia and is primarily a disease of older adults with an annual incidence rate of 20.1 per 100,000 population in those aged above 65 years.

Induction chemotherapy with anthracycline and cytarabine, is the mainstay for treatment of AML; all trans retinoic acid (ATRA) or arsenic trioxide (ATO) are added in Acute Promyelocytic Leukemia cases (APL). However, induction chemotherapy also induces more prolonged neutropenia in AML patients, favoring infectious complications and deaths. Immunoglobulins (Ig) are produced by B-cells in response to bacteria, viruses, fungi, parasites, cellular antigens, chemicals, and synthetic substances. Decreased serum immunoglobulin levels are associated with lower survival rate in septic patients.

Aim of the Work

To evaluate the effect of induction chemotherapy on immunoglobulin levels and to correlate IgA, IgG and IgM levels with the demographic, clinical and laboratory parameters and the patients' response to induction chemotherapy.

Subjects and Methods

The study was performed on 40 newly-diagnosed adult AML patients admitted to the Hematology unit, Internal Medicine Department, Alexandria Main University Hospital between September 2022 and May 2023. 20 healthy adult age- and sex-matched controls were also enrolled for comparison.

All studied patients except AML M3 cases received standard induction regimen, (3+7 protocol): daunorubicin of 45-60 mg per m^2 for 3 days with continuous IV infusion of cytarabine of 100-200 mg per m^2 for 7 days.AML M3 cases, were given (ATRA) at 45 mg per m^2 in 2 divided doses daily with daunorubicin 45- 60 mg per m^2 for 3 days and when required for high-risk patients: cytarabine 100 mg per m^2 for 7 days was added.

Serum IgA, IgG and IgM levels were measured in patients and controls using Enzyme-Linked Immunosorbent Assay (ELISA) technique. Patients' samples were taken before and following standard induction chemotherapy at the onset of the first febrile episode or at the nadir of aplasia.

Results

Table 1: Serum Ig levels in AML cases (at presentation, at febrile neutropenia or aplasia) and in controls

Serum Ig	Cases		Controls (n=20)
	Pretreatment (n=40)	At febrile neutropenia or aplasia (n=36[#])	
IgA (mg/dl)			
Min. – Max.	10.0 – 615.0	41.0 – 542.0	94.0 – 316.0
Mean ± SD.	258.85 ± 107.08	204.42 ± 101.65	215.25 ± 74.20
Median (IQR)	248.50 (211.0–300.50)	193.0 (146.0–240.0)	224.50 (138.50–282.50)
Sig. bet. groups	$^{Z}p_1<0.001^*$, $^{U}p_2=0.196$, $^{U}p_3=0.478$		
IgG (mg/dl)			
Min. – Max.	749.0 – 2773.0	596.0 – 2172.0	979.0 – 1644.0
Mean ± SD.	1554.20 ± 462.44	1130.11 ± 343.32	1259.40 ± 183.96
Median (IQR)	1506.0 (1253.50–1779.50)	1027.50 (897.50–1264.50)	1225.0 (1108.50–1426.50)
Sig. bet. groups	$^{Z}p_1<0.001^*$, $^{U}p_2=0.005^*$, $^{U}p_3=0.013^*$		
IgM (mg/dl)			
Min. – Max.	56.0 – 496.0	41.0 – 354.0	51.0 – 266.0
Mean ± SD.	161.67 ± 92.36	119.03 ± 76.85	112.10 ± 57.03
Median (IQR)	137.0 (117.50–177.50)	93.0 (68.50–139.50)	90.0 (72.0–131.50)
Sig. bet. groups	$^{Z}p_1<0.001^*$, $^{U}p_2=0.006^*$, $^{U}p_3=0.932$		

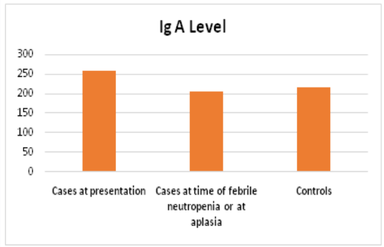

Figure 1: Serum IgA levels in AML cases (at presentation, at FN or aplasia) and in controls. Significant difference was noted only between cases at presentation and at FN or aplasia. (p<0.001)

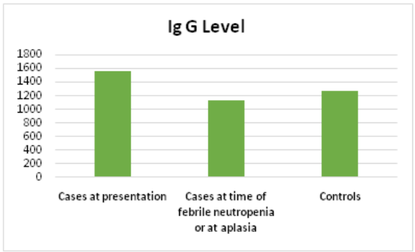

Figure 2: Serum IgG levels in AML cases (at presentation, at FN or aplasia) and in controls. Significant differences were noted between all 3 groups. (p<0.05)

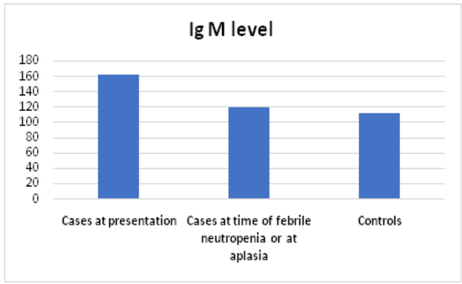

Figure 3: Serum IgM levels in AML cases (at presentation, at FN or aplasia) and in controls. Significant differences were noted between cases at presentation (p<0.001) and at FN or aplasia and between cases at presentation and controls (p=0.006).

Conclusion

- AML patients present with significantly higher serum IgG and IgM level compared to normal individuals and endogenous levels of IgA, IgG and IgM significantly decrease in de-novo AML patients following induction chemotherapy.
- Serum IgG level following induction chemotherapy in AML patients is lower at time of febrile neutropenia or aplasia compared to controls.
- Serum immunoglobulin levels do not correlate with blood count, FAB subtypes, increased susceptibility to infections, percentage of BM blasts response to induction chemotherapy, treatment outcome and survival in AML patients.

Recommendations

-Relying on the levels of serum immunoglobulin either before or during a febrile period as guidance for therapeutic administration of IVIG is not recommended.

-Development of therapeutic strategies for IVIG administration in clinical trials for febrile neutropenic adult AML patients who are not responsive to anti-infectious agents after induction chemotherapy is recommended.