Acquired Factor XIII Deficiency in Myeloid Malignancies: An Underrecognized Cause of Severe Hemorrhagic Complications

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Introduction

Factor XIII deficiency (FXIIID) could be inherited or acquired and manifest with spontaneous or delayed life-threatening hemorrhage. Acquired FXIIID is an uncommon but potentially life-threatening bleeding disorder that may complicate myeloid malignancies.

Aim

To describe the clinical characteristics, bleeding manifestations,laboratory findings, management, and outcomes of acquired factor XIII deficiency in patients with myeloid malignancies, highlighting early recognition and effective replacement therapy.

Methods

We describe eight patients with myeloid malignancies who developed acquired FXIIID. Clinical features, bleeding manifestations, laboratory findings, treatments, and characteristics were reviewed.

Table (1) summary of 8 cases with FXIII deficiency

	P 1	P2	P 3	P 4	P 5	P 6	P 7	P 8
Age/years	60	24	36	72	70	60		63
Sex	Male	Male	Female	Male	Female	Female	Female	Female
Diagnosis	AML transformed from CMML	AML	AML	AML transformed from CMML	AML transformed from MDS	CMML	AML	MDS
FXIII activity at diagnosis iu/ml (0.70-1.20)	0.15	0.40	0.10	0.15	0.13	0.40	0.3	0.40
Time from primary diagnosis disease to FXIII	One month	2 years (day 60+post HSCT)	Same time	Same time	Same time	Same time	Same time	Same time
Presentation	massive right subscapular hematoma	Acute subdural hematoma, hemorrhagic cystitis	subdural hemorrhage	Intramuscular hematoma	Intramuscular hematoma	retroperitoneal hematoma, central line bleeding	massive GI bleeding	Upper GI bleeding
Associated risk of bleeding	Sever thrombocytopenia	Sever thrombocytopenia virus HC	hypofibrogeneamia	Sever thrombocytopenia	hypofibrogeneamia thrombocytopenia	thrombocytopenia	Non	hypofibrogeneamia
Treatment	FXIII concentrate and platelet transfusion	FXIII concentrate and platelet transfusion	cryoprecipitate and tranexamic acid	FXIII concentrate and platelet transfusion	cryoprecipitate and tranexamic acid	cryoprecipitate and tranexamic acid	FXIII concentrate	FXIII concentrate
Molecular /cytogenetics	RUNX1 ,ASXL1, STAG2	RUNX1, U2AF mutation	TP53 mutation and KMT2A-MLL	T53 Mutation SRSF2, NRAS TET2	TP53,5q31 RUNX1, SF3B1 MLL (11q23)	SRSF2, ETV6		7q-,5q-, TP53

Results

A report of 8 cases of acquired FXIIID, among them 5 female and 3 male patients, with a median age of 61 years (range, 24–72 years). Three presented with de novo AML, whereas three developed AML secondary to CMML or MDS. One case was diagnosed with CMML and another with MDS. High-risk molecular and cytogenetic abnormalities included TP53 (n=4), RUNX1 (n=3), and SRSF2 and MLL/KMT2A rearrangements (n=2 each).

Acquired FXIIID occurred either as an early manifestation of the disease or during its progression. The median FXIII levels in patients was 0.22 IU/mL (reference range, 0.70–1.20 IU/mL). Thrombocytopenia was seen in seven patients, whereas three cases had concomitant hypofibrinogenemia.

Bleeding presentations were severe and heterogeneous: massive gastrointestinal bleeding (n=3), intracranial hemorrhage (n=2), and intramuscular hematomas (n=2), associated with hemorrhagic cystitis and central line–related bleeding in 2 cases. These are classic FXIIID bleeding patterns, deep tissue and serosal bleeds rather than mucosal or superficial bleeding.

Correction of bleeding complications was successful in all patients with FXIII substitution by FXIII concentrate (15 µg/kg) administered once or twice weekly, then every 4 weeks according to severity and site of bleeding, targeting FXIII >70% in 5 patients and cryoprecipitate with tranexamic acid in 3 patients. FXIII levels improved in patients who achieved remission from leukemia.

Discussion/Conclusion

Screening for FXIII at diagnosis of myeloid neoplasms could help to avoid severe bleeding during diagnostic or therapeutic interventions in patients at risk. Our cases illustrate that acquired FXIIID should be considered for patient of myeloid neoplasm with bleeding when routine coagulation studies are unrevealing. Early consideration of FXIIID and prompt replacement therapy are essential to reduce morbidity and improve outcomes.

Summary

We retrospectively analyzed eight patients with myeloid malignancies complicated by acquired factor XIII deficiency. Severe bleeding occurred despite normal routine coagulation tests. Factor XIII replacement or cryoprecipitate effectively controlled hemorrhage, while leukemia remission restored factor XIII levels. Early diagnosis and treatment are essential to prevent life-threatening bleeding.

References

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