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CORRESPONDENCE

Corpus Callosum Bleed: A Rare Presentation of Acute Promyelocytic Leukemia

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Dear Editor,

Acute promyelocytic leukemia (APML), a curable subtype of acute myeloid leukemia (AML), is characterised by translocation t(15;17) (q24.1;q21.2) that forms PML-RARα fusion gene, and intricate life-threatening coagulopathy. Induction therapy with arsenic trioxide (ATO) and all-trans retinoic acid (ATRA) usually results in durable remission. This report illustrates the successful outcome in a high risk APML patient who had corpus callosum bleed at presentation.

A 13-year-old boy presented with headache, altered sensorium and gum bleed for 3 days. Examination revealed E3V4M5 status, sluggishly reacting pupils, right lower limb paresis (MRC grade 2/5), mute bilateral plantar reflexes and bilateral vitreous haemorrhages. Hemogram revealed hemoglobin 65 g/L, TLC 35 $\times$ 10^9/L, platelet count 8 $\times$ 10^9/L and 89% abnormal promyelocytes on peripheral smear. Coagulation screen revealed prolonged prothrombin time (19 s) and activated partial thromboplastin time (40 s), low fibrinogen (0.7 g/L) and elevated fibrin degradation products, suggesting diffuse intravascular coagulation (DIC). ATRA and ATO based induction therapy was started promptly. Thrombocytopenia and coagulopathy were managed aggressively by transfusion of platelets and fresh frozen plasma. Bone marrow was hypercellular with 95% abnormal promyelocytes and blasts; flow cytometry showed typical APML expression pattern (CD13+, CD33+, HLA-DR−, no aberrant expression markers) (Fig. 1). *PML-RARA* fusion gene was detected by qualitative RT-PCR; FLT3 was negative. Plain CT head showed hazy bulge in the region of splenium of corpus callosum and no evidence of haemorrhage. MRI brain axial images revealed ill-defined T2 hypointense and hyperintense patchy areas centred along corpus callosum—suggesting acute and subacute stages of bleed (Fig. 2). An organised haematoma was also apparent in the interpeduncular fossa. He developed severe differentiation syndrome and worsening of sensorium on day 5 of induction therapy which was managed with IV Dexamethasone, hydroxyurea and supportive care. Subsequently, he developed fungal pneumonia and type I respiratory failure which

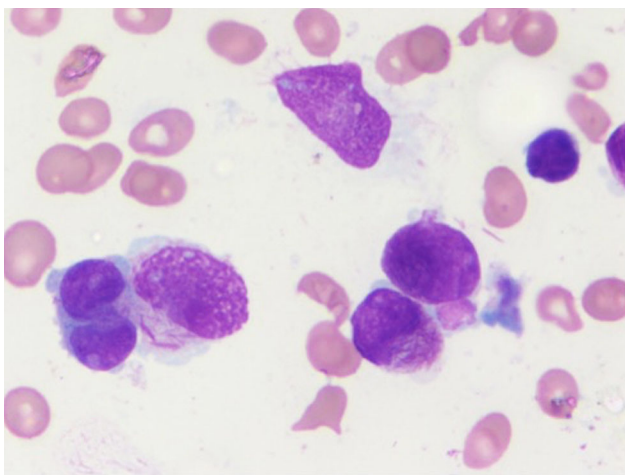

Fig. 1 Bone marrow aspirate smear showing promyelocytes with dense granulation and multiple Auer rods. (May Grun wald Giemsa Stain, × 100X)

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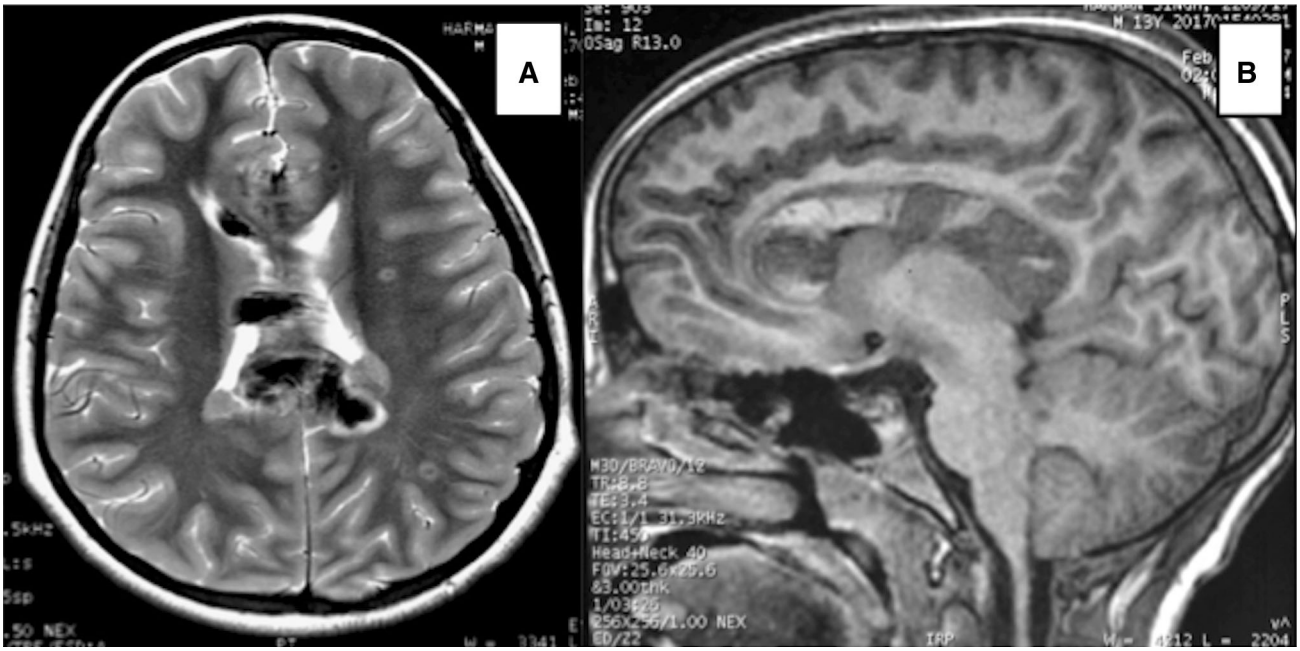

Fig. 2 **a** T2—weighted axial images at the level of septum pellucidum and body of bilateral lateral ventricles and corpus callosum show heterogeneous areas ill-defined patchy hypointense and hyperintense areas centered along corpus callosum—suggesting acute and subacute stages of bleed. There is mild surrounding edema predominantly seen along right frontal deep white matter. **b** T1—weighted mid sagittal images show patchy areas of hypointense, iso and hyperintense areas spanning the entire length of corpus callosum including genu and splenium—suggesting acute and subacute stages of bleed

were manged with mechanical ventilation and liposomal amphotericin. He achieved complete haematological response on day 32 and end of induction bone marrow was in complete remission. As the sensorium slowly improved, neurological dysfunction in the form of emotional lability, thoughtless object grasping and apraxia became evident. However, these features gradually resolved by 3 months.

The APML associated complex coagulopathy is contributed by—procoagulant molecules released from malignant promyelocytes and primary hyperfibrinolysis. The APML related early death rate has been significantly higher in 'real world setting' (17.3–29%) as compared to clinical trials (3.7%) [1–3]. Haemorrhage is the leading cause of early death and induction failure in APML followed by sepsis and differentiation syndrome. Intracranial haemorrhage, which generally portends a poor clinical outcome, accounted for 62% of the early 'haemorrhagic' deaths in one study [4]. High initial TLC, high peripheral blood blast count, poor performance status and low platelet count are robust predictors of early 'haemorrhagic' death. In contrast to detrimental effect of cytotoxic chemotherapy on coagulopathy, ATRA based therapy is known to rapidly improve coagulopathy by inducing cell differentiation [5].

Corpus callosum lesions manifest in the form of significant disruption in cognition and dexterity. Spontaneous corpus callosum bleed is an uncommon entity that results from ruptured peri-callosal aneurysms or vascular malformations, amyloid angiopathy, intra-tumoral haemorrhage, infectious encephalitis and high altitude exposure [6]. In the background of coagulopathy, hyperleucocytosis and severe thrombocytopenia also contributed to development of corpus callosum bleed in this patient. Apart from disease control, ATRA plus ATO based therapy also contributed to recovery by interrupting haematoma progression through rapid coagulopathy reversal. Agile transfusion support, physiotherapy and rehabilitation also played key role. In conclusion, outcome in APML patients with intracranial haemorrhage may be improved with ATRA plus ATO based therapy, aggressive transfusion support and exhaustive supportive care.

Compliance with Ethical Standards

Conflict of interest The author declares that they have no conflict on interest.

Informed Consent Informed signed written consent was taken from the patient involved.

Ethical Approval All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards.

Human and Animals Rights No animals were involved in the study.

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