

## A Case of Acute Promyelocytic Leukemia With Retinal and Intracranial Hemorrhage in an Adolescent Girl

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### Case Study

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#### ABSTRACT

A 13 year old girl presented to our emergency department with a 4 day history of fever, headache, and confusion. An emergency computed tomography (CT) scan of the brain revealed multiple intracranial hemorrhages and a right retinal hemorrhage. Her laboratory test showed pancytopenia, as well as severe coagulopathy. Therefore, APL was suspected, a peripheral blood smear revealed abnormal hypergranular promyelocytes with Auer rods, and the diagnosis was confirmed by fluorescence in situ hybridization and cytogenetic analyses. The patient was initially managed with transfusions of platelet concentrate, red blood cells, fresh frozen plasma, antibiotics, osmotic diuresis, mechanical ventilation, and remission induction therapy by all-trans retinoic acid (ATRA). After that, the patient achieved molecular remission on the 50<sup>th</sup> day. Currently, at one year after diagnosis, the patient is without paralysis, and although she has some visual field defects. If pediatricians and emergency physicians suspect a diagnosis of APL, it is important to start appropriate treatment promptly. This case demonstrates that visual field defects may persist after remission.

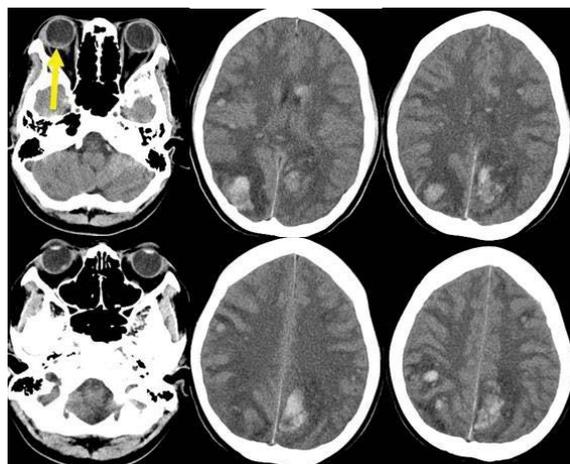
### INTRODUCTION

Acute promyelocytic leukemia (APL) is a distinct subtype of acute myeloid leukemia (AML). Disseminated intravascular coagulation (DIC) is a well-known complication of APL that progresses to life-threatening hemorrhage. However, APL is currently considered to be a high curable disease if appropriate treatment is started in time. Therefore, prompt diagnosis is crucial. Here, we report a case of APL presenting with retinal and intracranial hemorrhage in an adolescent girl.

### CASE DESCRIPTION

A 13 year old girl with an unremarkable medical history presented to our emergency department with a 4 day history of fever, headache, and confusion. On arrival, her Glasgow Coma Scale (GCS) score was 9 (Eyes 1, Verbal 3, and Motor 5) and her vital signs were stable. Physical examination revealed anisocoria, pallor and petechiae, but no other apparent neurological deficits. An emergency computed tomography (CT) scan of the brain revealed multiple intracranial hemorrhages and a right retinal hemorrhage (**Figure 1**).

\*Axial CT images show dominant multiple intracranial hemorrhage of the bilateral occipital lobe, as well as right retinal hemorrhage (↑)



**Figure 1.** Retinal and intracranial hemorrhage on CT.

There was no evidence of abdominal or thoracic hemorrhage. Her laboratory test showed pancytopenia with a total white cell count of  $1.0 \times 10^9/L$  (blasts 33.5%, neutrophils 21.5%, lymphocytes 45.0%), hemoglobin 43 g/L and platelets  $6.0 \times 10^9/L$ , as well as severe coagulopathy (prothrombin time 17.3 s, activated partial thromboplastin time 44 s, fibrinogen 1.0 g/L and fibrinogen degradation products  $1.3 \times 10^5$  g/L). Therefore, APL was suspected and she was admitted for further management. A peripheral blood smear revealed abnormal hypergranular promyelocytes with Auer rods. The diagnosis was confirmed by fluorescence in situ hybridization and cytogenetic analyses which revealed the presence of the PML-RARA fusion gene and the typical APL karyotype t(15;17)(q22;q12) with no apparent abnormalities.

The patient was initially managed with transfusions of platelet concentrate, red blood cells, fresh frozen plasma, antibiotics, osmotic diuresis and mechanical ventilation, because the patient was sedated, her performance status could not be assessed and her remission induction therapy regimen was all-trans retinoic acid (ATRA) 45 mg/m<sup>2</sup>/day orally and arsenic trioxide (ATO) 0.15 mg/kg/day intravenously until molecular remission. Conservative therapy was sufficient to manage the intracranial hemorrhage and brain edema of the patient. Although the CT scan revealed only a right, bilateral retinal hemorrhages were noted on funduscopy, worse on the right than on the left side.

She was weaned off mechanical ventilation on the 11<sup>th</sup> day, and her GCS gradually improved. And the patient was blind in her right eye and only perceived light in her left eye. After that, the patient achieved molecular remission on the 50<sup>th</sup> day, which she maintained throughout 9 months of follow-up. Currently, at one year after diagnosis, the patient is without paralysis, and although she has some visual field defects, her eyesight is gradually improving without any further medical intervention. She is attending school and studying for her high school examinations.

### DISCUSSION

APL is a distinct subtype of AML characterized by a specific t(15;17) chromosomal translocation forming the PML-RARA chimeric gene that drives abnormal promyelocyte proliferation [1]. APL is considered a medical emergency, as it often presents with significant coagulopathy that can progress to life-threatening hemorrhage. Fortunately, APL is rare in children and accounts for 10-15% of AML cases in Japan. It is estimated that approximately 10 patients per year develop pediatric APL in Japan. The current standard of induction therapy with ATRA and anthracycline-based chemotherapy has a 95% complete remission rate [2]. Despite the success rate of treatment, early death due to severe hemorrhage remains a leading cause of treatment failure, and is reported to occur in 6.5% of adult patients in Japan [3]. Unfortunately, the incidence of severe hemorrhage prior to APL diagnosis is unknown, but there has been at least one confirmed report of an unexpected death due to cerebral hemorrhage in a 15 year old boy with undiagnosed APL [4]. Therefore, since there are not many cases of childhood APL, pediatricians and emergency physicians should be mindful of APL as a possible differential diagnosis in cases of pancytopenia, intracranial hemorrhage, and DIC. If pediatricians suspect a diagnosis of APL, it is important to start appropriate treatment promptly.

### CONCLUSION

In this case, APL was complicated by DIC, which led to intracranial and retinal hemorrhage. This presentation was reported in one adult patient in 2015, but the clinical case and prognosis were not described [5]. In the current report, we describe the clinical course of a pediatric patient with APL complicated by retinal and intracranial hemorrhage, which was successfully treated with ATRA and ATO. This case demonstrates that visual field defects may persist after remission.

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### AUTHOR'S CONTRIBUTIONS

Dr.Satoru Kutsuna contributed to the drafting and writing of this manuscript. Satoru Kutsuna, Tadamitsu Uesato, Yuki Genma and Yoichi Okoshi were responsible for patient care and data collection. Hiroshi Yoshino and Kunimasa Yan undertook critical revision of the manuscript. Each author contributed to read, edit, and approved the final manuscript.

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