Case report

Hemorrhagic retinal detachment in acute promyelocytic leukemia

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ABSTRACT

A 14-year-old male had unilateral visual loss, blood-stained rhinorrhea, and generalized bruises with fever. Ocular echography of the right eye revealed unilateral hemorrhagic retinal detachment with internal echogenicity, and therefore, a hemorrhagic retinal detachment (oculus dexter). Peripheral blood smear tests revealed pancytopenia with 78\% leukemic cells. Bone marrow sampling and genetic analysis established the diagnosis of acute promyelocytic leukemia. Hemorrhagic retinal detachment can be a presentation of acute promyelocytic leukemia, and thrombocytopenia and disseminated intravascular coagulation may be the etiologies. The combined bleeding diathesis is a challenging status for surgical management with poor visual prognosis.

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1. Introduction

Leukemias are a group of hematologic malignancies that involve multiple organ systems. Ocular involvement is not uncommon in acute leukemia, having been reported to occur in up to 90\% of patients.\textsuperscript{1} The retina is more commonly involved in leukemia than other ocular tissues.\textsuperscript{2} Reddy and Jackson reported that 49\% of patients with acute lymphoblastic leukemia had retinopathy at diagnosis.\textsuperscript{3} Typical retinal involvement of leukemia are round or flame-shaped hemorrhages with white component, intraretinal hemorrhages, and cotton wool spots, comprising what is called leukemic retinopathy.\textsuperscript{1} Although exudative retinal detachment has only been reported in several cases of myeloproliferative and lymphoproliferative disorders,\textsuperscript{4–15} association with massive subretinal hemorrhage, also known as hemorrhagic retinal detachment, appears to be a rare ocular manifestation of acute leukemia.

Herein, we describe a case of unilateral hemorrhagic retinal detachment, concurrent with systemic manifestations and hematological abnormalities as the initial presentation of acute promyelocytic leukemia.

2. Case report

This 14-year-old boy was brought to our hospital with a 2-week history of progressive generalized bruises, decreased right eye vision for 3 days, and a fever episode. Other associated symptoms were weakness, nausea, cough, and blood-stained rhinorrhea. There was no body weight loss, headache, chills, nor night sweating, and he had no history of any systemic disease, ocular trauma, or surgery. Visual acuity was light sensation in the right eye and 20/30 in the left eye. Results of laboratory investigations showed pancytopenia with low platelet count (13,000/\textmu L). Leukemic cells with 31\% blast and 11\% promyelocytes were also identified. Clotting screen showed prolonged prothrombin time of 15.2 seconds, elevated D-dimer values (>10,000 ng/ml fibrinogen equivalent units) and
hypofibrinogenemia (178 mg/dL) suggested acute disseminated intravascular coagulation status. Serum biochemistry showed elevated C-reactive protein (433.6 mg/dL) levels, whereas urate, renal function, and liver function were within normal limits.

Based on the hematological abnormalities, the patient was referred to hematological analysis. Platelet transfusion was given immediately to correct the coagulopathy, and empirical antibiotics treatment was administered. Because of the suspected acute promyelocytic leukemia with disseminated intravascular coagulation, chemotherapy with oral all-trans retinoic acid (ATRA) was prescribed. Further analysis of the bone marrow aspirate showed a hypercellular infiltrative marrow with markedly suppressed normal cell elements. Approximately 80% of the total nucleated cells were hypergranular myeloid precursors (leukemic promyelocytes) and fewer (10%) were blasts. Some of the leukemic cells had lobulated nucleus, and some had Auer rods, with Faggot cells seen occasionally. The myeloperoxidase reaction was strongly positive. The bone marrow specimen was sent for cytogenetic analysis and translocation between chromosomes 15 and 17, t(15;17) (q22;q21), was detected. A standard reverse transcriptase polymerase chain reaction of the patient’s bone marrow sample was performed and the L-form PML-RAR-a fusion gene was identified. The diagnosis of acute promyelocytic leukemia was then confirmed.

The patient was enrolled into chemotherapy with the Taiwan Pediatric Oncology Group Acute Promyelocytic Leukemia 2001 protocol. He received three courses of induction chemotherapy with oral ATRA, intrathecal methotrexate, and intravenous idarubicin. Persistent severe thrombocytopenia deferred the ophthalmic surgery for hemorrhagic retinal detachment, until completing the third course of induction chemotherapy and platelet count improved to 158,000/µL without transfused platelet, which was 10 weeks after the initial presentation. Preoperative survey showed stationary subretinal and vitreous hemorrhage (Fig. 2B), and visual acuity of the right eye remained light perception. Encircling scleral buckling with external drainage of clotted subretinal hemorrhage without use of thrombolytic agent, three-port vitrectomy, fluid–gas exchange, silicon oil tamponade, and lensectomy were done. Severe proliferative vitreoretinopathy with organized blood clot obscuring the retina was noted intraoperatively. The operation was further complicated with unstoppable vitreous hemorrhage. The patient’s condition was followed up 4 weeks postoperatively, revealing stationary right eye visual acuity of light sensation. Molecular remission of acute promyelocytic leukemia was finally achieved after receiving arsenic trioxide chemotherapy. Further consolidation chemotherapy was then arranged.

3. Discussion

Hemorrhagic retinal detachment could be seen in acute promyelocytic leukemia as a complication of bleeding diathesis due to thrombocytopenia and disseminated intravascular coagulation status. The bleeding tendency may defer or/and complicate the operation and may lead to visual morbidities.

Retinal detachment in leukemia is rare, and has been reported in several cases of exudative retinal detachment with subretinal serous fluid accumulation. It may occur when the choroid layer is infiltrated by the neoplastic cells, which decreases blood flow through the choriocapillaris, resulting in ischemia of the overlying retinal pigment epithelium and disrupting intercellular tight junctions. We herein described a case of acute promyelocytic leukemia presenting with exudative retinal detachment with subretinal hemorrhage. Acute promyelocytic leukemia is characterized by its bleeding diathesis due to several processes including thrombocytopenia and disseminated intravascular coagulation. The subretinal hemorrhage may arise from spontaneous extravasation of red blood cells from choroidal circulation through disrupted tight junction of retinal pigment epithelium.

Fig. 1. Ocular fundus (oculus dexter) taken on the 2nd day after the first emergency department visit showed macula-off retinal detachment with vitreous hemorrhage.

Fig. 2. (A) Axial vertical view of ocular B-scan ultrasonography showing retinal detachment with subretinal, preretinal, and vitreous hemorrhage. (B) Persistent ultrasonography findings on the 46th day after the first emergency department visit.
Subretinal hemorrhage is most commonly associated with age-related macular degeneration, polypoidal choroidal vasculopathy, presumed ocular histoplasmosis, high myopia, retinal arterial macroaneurysm, and trauma. Published surgical series for the management of subretinal hemorrhage included vitrectomy and internal drainage with or without tissue plasminogen activator injection, penetrating endodiathermy coagulation, and argon laser retinal perforation. Several guidelines were proposed for the selection of surgical candidates who will likely be benefited from surgery, including a duration of subretinal hemorrhage less than 30 days, preferably less than 7 days. According to the guidelines of American Society of Hematology, platelet counts of at least 50,000/µL should be maintained in surgical procedures. We performed encircling scleral buckling, vitrectomy, and internal drainage of subretinal hemorrhage in this patient when his platelet counts increased to 158,000/µL after completing a third course of induction chemotherapy without transfused platelets. However, the operation was still complicated with intraoperative vitreous hemorrhage in addition to severe proliferative vitreoretinopathy and obscured retina by organized blood clots. Defect in platelet function in patients with leukemia or persistent deficiencies of clotting cascade due to coagulating factors consumption following acute disseminated intravascular coagulation may have contributed to the bleeding event. Therefore, it is critical to perform a thorough survey of hemostasis function preoperatively in leukemic patients undergoing surgery.

The prognosis of hemorrhagic retinal detachment is related to several factors, including the duration of retinal detachment, the presence of macular involvement, the thickness of the hemorrhagic fluid, and the etiologies of hemorrhagic retinal detachment. Another factor related to poor visual outcome is the retinal damage secondary to subretinal hemorrhage, which has been shown in animal model, and elucidated in three mechanisms: chemical toxicity, mechanical traction on the photoreceptor outer segments, and establishment of a diffusion barrier. The factors that contributed to poor visual outcome in our case include the longer duration of retinal detachment, which is 10 weeks after initial presentation, macular involvement, and the presence of proliferative vitreoretinopathy.

Hemorrhagic retinal detachment could be a presentation in acute promyelocytic leukemia. Prompt surgical evacuation of subretinal hemorrhage and achieving reattachment of the photoreceptor layer are important. Delayed interventions or intraoperative hemorrhagic complications due to bleeding diathesis may lead to visual morbidity.

References