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ORIGINAL ARTICLE

Rare manifestation of orbital hematoma in hemophilia B: A case report

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ABSTRACT

Introduction: Severe Hemophilia B is a blood coagulation disorder with the most common clinical manifestation is bleeding manifestation in major joint. Failure in early detection of hemophilia will lead to patients presenting with complications, possibly the life-threatening one. In this article, we present a case of 5-year-old boy with severe hemophilia B with rare bleeding manifestation of unilateral orbital hematoma. By reporting this case, we aim to increase the awareness so as to accelerate the diagnosis and management of hemophilia B. **Case Presentation:** A 5-year-old boy came to the emergency ward with complaints of a swollen and bluish right eye socket since a week prior to admission. Patient also experienced other symptoms such as frequent joint pain, prolonged bleeding after injury, and bruises (hematoma) on the trunk, elbows, and knees. Coagulation tests showed prolonged APTT with normal PT and INR. Due to resource-limited setting, sample referral was needed to perform factor VIII and IX examination, and FFP transfusion was given to the patients during the admission. Factor VIII and IX results were available after patient had been discharged, with a low-level activity of factor IX, which was <1%. Patient was diagnosed as severe hemophilia B, and was referred to tertiary health-care facility from outpatient department for comprehensive management. **Conclusion:** Despite of the most common location of bleeding manifestation in Hemophilia B, other bleeding manifestation such as orbital hematoma should also be considered as Hemophilia B manifestation. Early diagnosis and prompt treatment will give a better prognosis for patient with hemophilia.

Keywords: Hemophilia B, rare manifestation, bleeding manifestation, orbital hematoma

Introduction

Hemophilia B is a blood coagulation disorder due to the deficiency of factor IX in the body.[1] The factor IX deficiency is a result of mutation in the F9 gene which located in the long arm of X chromosome.[2] This mutation could be inherited through the X chromosome or spontaneous de novo mutation. Hemophilia B is an X-linked recessive disease that usually affects male. The estimated prevalence of hemophilia B is 3.8 per 100.000 males, with 1.1 per 100.000 being severe hemophilia B.[3,4]

The normal range of factor IX activity is approximately 50-150%, and the severity of hemophilia B is determined based on the deficiency of this factor IX. Hemophilia B can be classified as mild (6-40%), moderate (1-5%), and severe (<1%).[5] Severe hemophilia B is usually diagnosed before the age of 2 years old.[3] In untreated severe hemophilia B, the most common clinical manifestation to be seen is bleeding

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manifestation (either spontaneously or post-trauma) in major joint such as elbow, knee, or ankle. Intracranial hemorrhage or other internal organ hemorrhage can also occur and can be life-threatening.[6,7]

Typical bleeding manifestation in hemophilia are hemarthrosis (bleeding in joint) and hematoma (bleeding in muscle/soft tissue). Recurrent hemarthrosis and hemophilic arthropathy are the main morbidities in hemophilia. These conditions can lead to immobility and disability, thus reducing the productivity and quality of life as well as other psychosocial problems. Progressive joint breakdown usually starts in the second to third decade of life.[6,8] Failure in early detection of hemophilia will lead to patients presenting with these complications, or even present with life-threatening complications such as hemorrhage intracranial.[6,8,9]

Orbital hematoma is a condition where blood accumulates in the orbital region, and can occur spontaneously, traumatically or iatrogenically.[10] Spontaneous orbital hematoma is a rare condition, especially the one due to blood coagulation disorders.[11] By addressing the clinical manifestations of hemophilia, especially the rare manifestation of orbital hematoma, the duration of the decision whether to continue coagulation factor testing can be shortened so that early diagnosis and comprehensive treatment can be achieved.

In this article, we present a case of 5-year-old boy with severe hemophilia B, whose clinical bleeding manifestation was rarely reported, located in unilateral orbital hematoma. By reporting this case of hemophilia B with rare clinical manifestations, we aim to increase the awareness so as to accelerate the diagnosis and management of hemophilia B.

Case Presentation

A 5-year-old boy came to the emergency ward with complaints of a swollen and bluish right eye socket since a week prior to admission. The patient also experienced frequent joint pain in the knee and elbow joints in the past 1 month, and worsened in the last 1 day. In the past week, bruises (hematoma) also appeared on the trunk, elbows, and knees. From history taking there was prolonged bleeding after injury. There was no history of trauma, fever or any other symptoms. Patient has a history of similar experiences since 3 years old but only sought treatment now. Patient had an older brother who had similar symptom, but had passed away. At the time of arrival to the emergency room, the patient's vital signs were stable with BP 100/50 mmHg, pulse 97 beats per minute, respiratory rate 24 beats per minute, and temperature 37^0C.

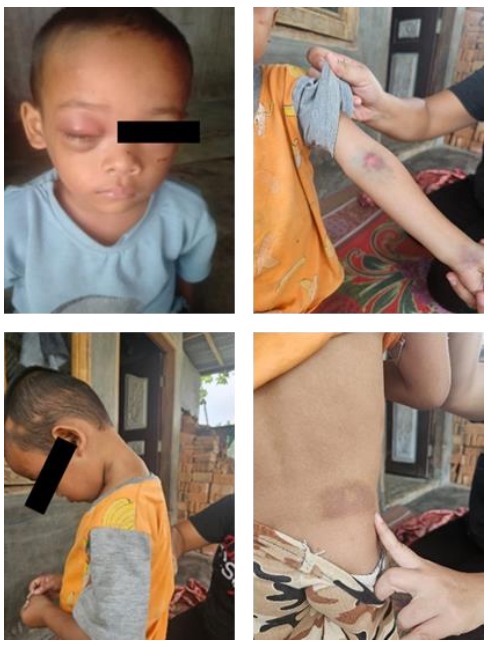

Figure 1. Bleeding manifestations in patient: (a) orbital hematoma, (b) elbow hematoma, (c) nape hematoma, and (d) waist hematoma

On physical examination, there was an orbital hematoma accompanied by edema in the right eye, starting from the upper eyelid to the infraorbital region. The edema made it difficult for the patient to open his right eye. Visual acuity examination was difficult to perform due to the swelling, but the patient stated

that there was no visual impairment. There was also a hematoma with a diameter of 3-4 cm on the arm crease. Hematoma also appeared at the waist area with a size of about 5 cm. Nape and knee also appeared to have hematoma.

The patient was malnourished, with weight 13.3 kg (< 5th percentile of CDC growth charts), height 104 cm (between 10th to 25th percentile of CDC growth charts), and BMI 13.3 kg/m2 (< 5th percentile of CDC growth charts).

Laboratory results revealed Hb level of 11.9 g/dL, thrombocytosis of 504,000/uL, normal range of PT (14.2; normal range: 11-18), prolonged APTT (125.5; normal range 27-42), and normal INR (0.93; normal range: 0.85-1.15). In the emergency ward, patient was decided to be hospitalized, and diagnostic assessment was continued by performing factor VIII and IX examination. The testing for the coagulation factor is not available in the hospital, hence referral of patient's blood sample needed to be done to a higher facility, which will take around 1 week after the sample collection.

During the hospitalization, the patient received 6 units of FFP transfusion immediately without waiting for the coagulation factor test results, with the administration of 2 bags per day for 3 days. After the FFP transfusion was completed, the patient's clinical condition improved and was discharged. The patient was asked to come back to outpatient department 1 week after discharged to discuss about the coagulation factor results.

Figure 2. Clinical improvement of the orbital hematoma on the patient upon discharge

Several days after the patient had been discharged, Factor VIII and IX results were available, with the factor VIII activity was found to be 87.2% and factor IX activity was <1%. Based on these results, patient was diagnosed as severe hemophilia B. Patient then visited the outpatient department as instructed, and education regarding the hemophilia B was given to the patient's mother. As the factor IX replacement therapy was not available in the hospital, patient needed to be referred to the tertiary health-care facility for comprehensive management.

Discussion

Bleeding manifestations in hemophilia usually occur after minor trauma or spontaneous bleeding.[9] There is a direct correlation between the deficiency of coagulation factors and the severity of clinical manifestations in patients.[12] Bleeding in mild hemophilia is rarely due to spontaneous bleeding and often occurs after severe trauma or surgery. In moderate hemophilia, bleeding usually occurs after trauma, tooth

extraction, or surgery. Only about 25% of moderate hemophilia cases experience recurrent joint bleeding, which can delay diagnosis. In severe hemophilia, bleeding usually occurs spontaneously.[9]

Orbital hematoma is most commonly associated with trauma or surgery.[10] On the other hand, spontaneous orbital hematoma is rarely occured.[11] Spontaneous orbital hematoma can result from vascular malformations, malignancy, blood coagulation disorders, inflammatory conditions (orbital myositis and amyloidosis), paroxysmal cough in pertussis, and blue rubber bleb nervus syndrome. Considering that the conditions that can cause spontaneous orbital hematoma can be life-threatening, determining the etiology of the hematoma needs to be done thoroughly.[13]

The reporting of this rare manifestation of orbital hematoma provides insight into the bleeding manifestations that can occur in hemophilia B. The most common locations of bleeding manifestations in hemophilia B are hemarthrosis in the knees, elbows, and ankles[9,12] and hematomas in the forearms, lower legs, buttocks, and iliopsoas muscle.[14,15] Manifestations of hematoma in the eye region are rarely reported. A meta-analysis in 2014 showed that only 19% (24/124) of cases of non-traumatic orbital hemorrhage were due to inherent bleeding disorders in reported cases over the past 30 years, and only 0.8% (1/124) were due to hemophilia.[16] A retrospective study conducted in India revealed that only 3.63% (4/110) of hemophilia patients experienced periorbital hemorrhage.[17] Some other bleeding sites in hemophilia that have been reported include the lateral chest wall, intraperitoneal bleeding, gums, and nasal mucosa.[17–19] Considering the possibility of bleeding manifestations outside the common locations, clinicians need to increase awareness of this.

Severe hereditary hemophilia is most often diagnosed in early life.[9] As a baby with severe hereditary hemophilia grows older, physical activity increases, thus muscular hematoma can be caused by light trauma or occur spontaneously.[15,20] Recurrent hemarthrosis in the same joint will cause inflammation of the synovial tissue, leading to progressive damage and hemophilic arthropathy.[21] Hemophilic arthropathy can cause joint remodeling, chronic pain, decreased quality of life, and may require joint replacement.[21,22] Delayed diagnosis and delayed treatment also increase the risk of life-threatening conditions such as intracranial hemorrhage.[9,23]

The history of the patient's deceased brother with similar symptoms should have provided a clue about the patient's condition. However, it seems that information about blood coagulation diseases was not conveyed to the patient's parents, hence the patient only sought treatment at the age of 5 years although the symptoms leading to the suspicion of hemophilia B had occurred previously in the patient. Severe hemophilia is usually diagnosed at an age below 2 years, in which case, this patient has a risk of presenting with complications.[3] Fortunately, there was no significant complications found during the admission. Some literature states that hemophilia B has fewer bleeding episodes than hemophilia A.[15,24,25] which explains why complications or life-threatening manifestations had not appeared by the age of 5 years in this case. In contrast, a 2014 cohort study suggested that hemophilia A and B have a similar bleeding phenotype.[26]

In patients with suspected hemophilia, blood coagulation tests such as PT and APTT should be conducted. Patients with normal PT and prolonged APTT lead to a suspected diagnosis of hemophilia B; therefore, coagulation factor tests need to be performed to determine the definitive diagnosis. This coagulation factor test can also determine the classification of the hemophilia patient.[15]

Factor replacement therapy is the main therapy in the management of hemophilia cases.[27] In this presenting case, the results of factor VIII and factor IX tests were not yet available during the patient's admission to the hospital, and based on clinical considerations, the patient was still given FFP first before the results came out. As FFP contains all of the coagulation factor, FFP can be used to increase the coagulation factor level in patients without waiting for the test results.[3] According to guidelines published by the World Federation of Hemophilia (WFH), FFP is not recommended due to concerns about the quality of the transfusion and the safety of transfusion-transmitted diseases.[3] However, in resource-limited settings, FFP that have been screened for the transfusion-transmitted disease can be considered.[3,8,28] Factor replacement therapy can be given to patients without waiting for the coagulation factor results, based on the patient's clinical condition.[8,27,28]

Factor replacement therapy should be given to patients with hemophilia so that the levels of coagulation factors in the body reach the desired target, which will reduce bleeding episodes and prevent complications.[3,9] The administration of prophylaxis in patients with hemophilia can also help patients with hemophilia have a good quality of life that is similar to the non-hemophilic population.[3] With improved management of hemophilia, life expectancy in patients with hemophilia is getting better and better, which is 56.8 years.[29] In contrast, in untreated severe hemophilia, it is estimated that 1-2 out of 100 patients die each

year.[30] This shows the importance of diagnosing hemophilia early, and conducting comprehensive management for better patient survival.

Conclusion

Despite of the most common location of bleeding manifestation in Hemophilia B, other bleeding manifestation such as orbital hematome should also be considered as Hemophilia B manifestation. Early diagnosis and prompt treatment will give a better prognosis for patient with hemophilia.

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