










Case Report

## An 8-year-old Girl with Intracranial Hemorrhage due to Acquired Factor XIII Deficiency as a Rare Complication of IgA Vasculitis: Case Report

### *IgA Vaskülitinin Nadir Bir Komplikasyonu Olarak İntrakranial Kanama ve Faktör XIII Eksikliği Görülen 8 Yaş Kız Hasta : Olgu Sunumu*

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#### ABSTRACT

IgA vasculitis (IgAV) is a complex immune-mediated vasculitis characterized by the involvement of small vessels, typically presenting in childhood. Patients often present with clinical findings, such as palpable purpura, gastrointestinal symptoms, renal involvement, and arthralgia. Rarely, central nervous system's vessels may also be involved, leading to intracranial hemorrhage. An 8-year-old girl admitted to the pediatrics department with a preliminary diagnosis of IgAV developed severe headaches, leading to cranial CT and MRI, which revealed intracranial hemorrhage (ICH). The patient was administered intravenous methylprednisolone at a dosage of 30 mg/kg/day for five days. Due to low Factor XIII and VIII levels, fresh frozen plasma was administered at 15 ml/kg. The patient showed clinical improvement and a significant reduction in ICH, leading to her discharge on the 21st day of hospitalization. According to our current knowledge in the literature, this case is the 6th case in children diagnosed with IgAV presenting with ICH, and the 2nd case presenting with ICH with low factor XIII levels. Mortality can be prevented if the rare complications of IgAV are recognised in time and with appropriate treatment modalities.

**Keywords:** Child, IgA vasculitis, Factor XIII deficiency, intracranial hemorrhage.

#### ÖZET

İgA vaskülit (İgAV) genellikle çocukluk çağında ortaya çıkan, küçük damarların tutulumuyla karakterize kompleks bir immün aracılı vaskülitir. Hastalar sıklıkla palpable purpura, gastrointestinal bulgular, böbrek tutulumu ve artralji gibi klinik bulgular ile başvururlar. İgA vaskülit komplikasyonlarından nadir olarak görülen Merkezi Sinir Sistemi'nin damarları da tutulabilir ve bunun sonucunda nadir de olsa intrakranial kanama gelişebilir. İgAV ön tanısıyla Çocuk Servisine yatırılan 8 yaş kız hastanın klinik seyrinde şiddetli baş ağrılarının gelişmesi sebebiyle çekilen Beyin BT ve Beyin MR görüntülemesinde İntrakranial Kanama (İKK) izlendi. Hastaya metilprednisolon 30 mg/kg/gün intravenöz 5 gün uygulandı. Faktör düzeylerinden XIII ve VIII düzeylerinin de düşük olması nedeniyle 15 ml/kg'dan taze donmuş plazma da

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uygulandı. Klinik izlemde iyileşme ve İKK'da bariz gerileme olan hastamız yatışının 21. Gününde taburcu edildi. Bu vaka literatürde bugünkü bilgilerimize göre çocuklarda kanama ile seyreden 6. Vaka ve faktör XIII düzeylerinin düşük olduğu 2. Vakadır. IgAV'nun nadir görülen komplikasyonları zamanında fark edilirse ve uygun tedavi modaliteleri ile mortalite önlenebilir.

**Keywords:** Çocuk, IgA vaskülit, Faktör XIII eksikliği, intrakraniyal kanama

## INTRODUCTION

IgA vasculitis, also known as Henoch-Schönlein purpura (HSP), is a small-vessel vasculitis and the most common form of systemic vasculitis in children. The reported incidence is approximately 10–20 cases per 100,000 individuals, according to the literature. Nearly 90% of cases occur in the pediatric age group, and unlike other systemic vasculitides, it generally has a self-limiting prognosis. Diagnosis of IgAV is made when palpable purpura is accompanied by joint pain, abdominal pain, proteinuria, or hematuria or if there is evidence of IgA deposition in biopsy samples (1-5). The presence of one or more additional symptoms alongside palpable purpura is sufficient for diagnosis. Although the disease is predominantly self-limiting, IgA vasculitis can lead to severe complications in some cases. Severe complications may involve renal issues, such as hematuria, proteinuria, nephrotic syndrome, or chronic kidney disease, gastrointestinal complications, such as intussusception, bowel ischemia, or perforation; and rare but life-threatening conditions, such as pulmonary hemorrhage, myocardial involvement, seizures, or intracranial hemorrhage (1-5). This case report aims to contribute to the literature by presenting a pediatric patient with IgA vasculitis who developed intracranial hemorrhage and was successfully treated with methylprednisolone and fresh frozen plasma.

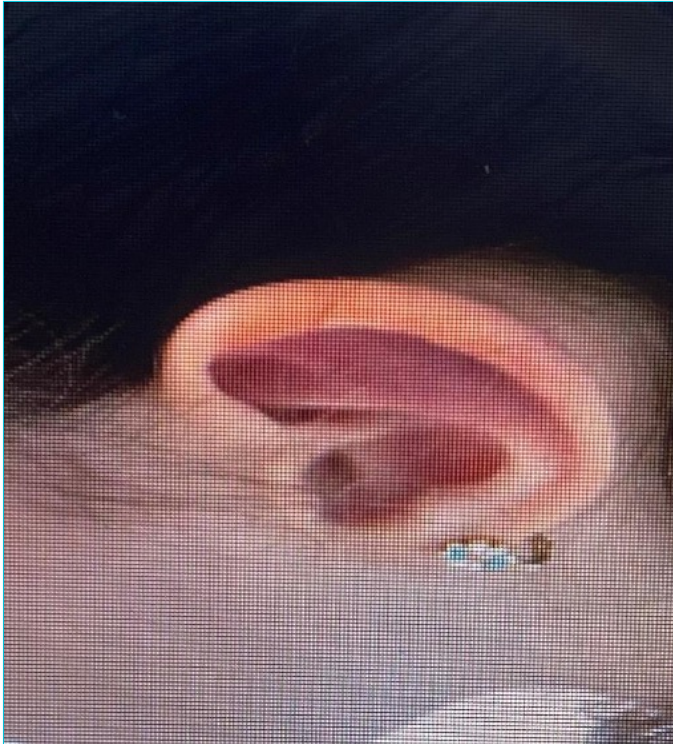
## CASE REPORT

An 8-year-old girl with no prior medical history presented to the pediatric emergency department with a two-week history of swelling and pain in the fingers of both hands, accompanied by abdominal pain that had persisted for the past week. Upon evaluation, the patient developed palpable purpura and petechiae on her legs and feet, which did not blanch on pressure, leading to an initial diagnosis of IgA vasculitis (Figure 1). No feature in the patient's past or family history would explain factor XIII deficiency. There was no consanguinity between the mother and father. The patient had no history of chronic disease, medication use, or trauma.

During admission, vital signs were recorded as follows: body temperature 36.7°C, blood pressure 95/65 mmHg, heart rate 85 bpm. Laboratory results showed a C-reactive protein of 34 mg/dL, WBC  $17.88 \times 10^3/\mu\text{L}$ , PLT  $393 \times 10^3/\mu\text{L}$ , and normal coagulation parameters. Abdominal examination revealed tenderness and guarding. Complete urine analysis was found to be normal. The abdominal X-ray and ultrasound findings were unremarkable. However, due to persistent severe abdominal pain impacting oral intake and the detection of occult blood in the stool, treatment with methylprednisolone at a dose of 2 mg/kg/day was initiated. Acetaminophen was prescribed for joint pain at a dosage of 10 mg/kg, divided into four daily doses. Twelve hours later, ecchymotic lesions appeared on the auricle and the area behind the ear (Figure 2).



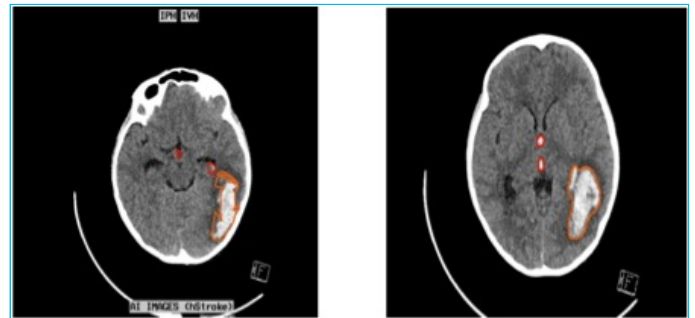
**Figure 1.** Petechiae and purpura lesions observed on the left foot.



**Figure 2.** Ecchymotic lesions on the left auricle and behind the ear.

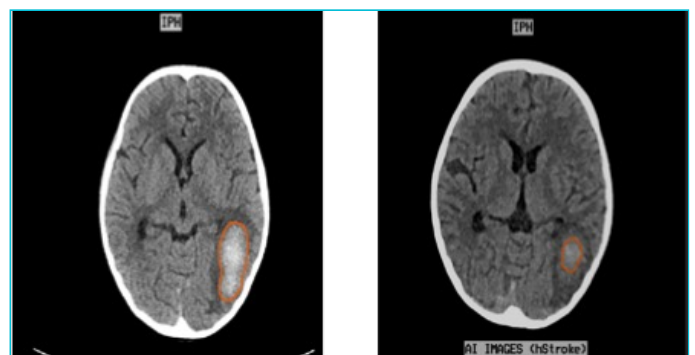
At approximately 10 hours after admission, the patient experienced increasingly severe headaches, leading to the performance of a cranial CT scan, followed by a cranial MRI. The cranial CT revealed a 5x2.5 cm hemorrhagic area surrounded by edematous changes at the level of the left temporoparietal lobes. Additionally, hemorrhagic areas consistent with subarachnoid hemorrhage were identified in both lateral ventricles (predominantly on the left), as well as in the third and fourth ventricles, with near-complete layering (Figures 3 and 4). The cranial MRI revealed a hypointense nodular area measuring approximately 6.7x3.3 cm in the T2-weighted sequences at the left temporo-occipital region. No evidence of restricted diffusion was observed in the cerebral or cerebellar hemispheres on diffusion-weighted imaging (DWI) or Apparent diffusion coefficient (ADC) mapping. Due to the persistence of the patient's headache, the patient was admitted to the pediatric intensive care unit for close monitoring and further management. Consultations with pediatric neurology, neurosurgery, and pediatric hematology were conducted. Based on the recommendations, methylprednisolone at a dose of 30 mg/kg was administered intravenously for five days. Prophylactic levetiracetam at 20 mg/kg/day was also initiated intravenously. During follow-up, the Glasgow Coma Scale (GCS) score was evalu-

ated as 15, and no urgent surgical intervention was deemed necessary. Ophthalmologic examination revealed no papilledema. The patient's vital signs and blood pressure remained within normal ranges.



**Figure 3 and 4.** Clearly illustrate the intracranial hemorrhage foci in the marked regions.

The skin biopsy report indicated leukocytoclastic vasculitis, interpreted as consistent with IgA vasculitis. Peripheral blood smear evaluation was unremarkable. Factor VIII and Factor XIII levels were reported as 5% (reference range: 70–150) and 15% (reference range: 70–140), respectively, consistent with deficiencies of Factor VIII and Factor XIII. The patient received 5 mg of intravenous vitamin K alongside Fresh Frozen Plasma (FFP) at a dose of 15 mg/kg. During follow-up, control imaging demonstrated resorption of the intracranial hemorrhage, and clinical findings, including headache, showed significant improvement (Figures 5 and 6). Oral methylprednisolone, initiated at an anti-inflammatory dose, was tapered gradually. Factor VIII and Factor XIII levels normalized to 114% (70–150) and 69% (70–140), respectively. The patient, exhibiting no clinical symptoms or findings, was discharged with instructions to attend outpatient follow-up appointments.



**Figure 5 and 6.** The intracranial hemorrhage areas on CT scans are clearly shown to have significantly regressed following pulse steroid therapy and fresh frozen plasma, as indicated in the marked regions.

At the patient's outpatient follow-up visit in the first month post-discharge, a repeat cranial CT scan revealed no evidence of the intracranial hemorrhage area (Figure 7). Furthermore, no complications were observed during the six-month follow-up period. At the end of six months, pT, Aptt and other hematological tests were normal. The genetic test results regarding ble-

eding or factor deficiency were interpreted as normal. E 148Q variant was detected as heterozygous in familial Mediterranean fever gene analysis. Our patient continues to be followed up regularly by the pediatric neurology, pediatric hematology and pediatric nephrology departments.

**Table 1.** Laboratory Tests of the Patient with IgA Vasculitis

Hospitalisation Tests	Discharge Tests
WBC: 13.73x 10 <sup>3</sup> /uL	13.8x10 <sup>3</sup> /uL
HgB:12.9 g/dL	11.9 g/dL
PLT: 385 x10 <sup>3</sup> /uL	356 x10 <sup>3</sup> /uL
PT:12.6	13.5
Aptt: 43 sec	30 sec
INR:1.22	1.18
Factor VIII: 5%	114%
Factor XIII: 15%	69%
Factor IX: 214%	130%
Factor XI: 209%	150%
Protein C activity: 150%	-
Protein S activity: 119	-
D Dimer: 8.65 mg/L	1 mg/L
Von Willebrand Factor antibody: 149%	
Von Willebrand Factor activity: 72%	-
Anti Thrombin 3: 123	
CRP: 20 mg/L	3.3 mg/L
WBC: White Blood Count, HgB: Hemoglobin, PLT: Platelet, PT: Prothrombin Time, APTT: Activated Partial Thromboplastin Time, CRP: C-Reactive Protein	





**Figure 7.** At the outpatient follow-up visit (1st month post-discharge), complete resolution of the hemorrhagic foci is observed.

## DISCUSSION

IgA vasculitis is the most prevalent vasculitis in childhood. Clinical diagnosis is based on the presence of non-thrombocytopenic palpable purpura, arthritis, and abdominal pain. Nephropathy is the most common complication. Hemorrhages generally occur in the respiratory, gastrointestinal, and urinary tracts. Neurological complications are rare but can be severe when present. Intracranial hemorrhage is an extremely rare complication of IgA. In patients presenting with symptoms, such as headache, dizziness, ataxia, seizures, irritability, mononeuropathy, intracranial hemorrhage, or acute motor-sensory axonal neuropathy, central nervous system involvement, should be considered, and cranial imaging should be performed. Factor XIII deficiency should also be suspected in cases of cerebral hemorrhage (6–9). In our case, persistent severe headaches unresponsive to analgesics raised suspicion of an intracranial complication, which was confirmed through imaging. Additionally, Factor VIII and Factor XIII deficiencies were detected during the acute phase, and treatment was initiated with fresh frozen plasma. Patients with intracranial hemorrhage should be evaluated for factor deficiencies. When reviewing the literature regarding this case, we identified only one similar case. In the case reported by Imai et al., investigations following intracranial hemorrhage revealed Factor XIII deficiency, and treatment with Factor XIII replacement was successful (10). Excessive consumption of FXIII may occur due to various factors, such as surgery, disseminated intravascular coagulation, inflammatory bowel disease, Henoch-Schonlein purpura, sepsis, leukemia, and th-

rombosis. In addition, liver disease and hyposynthesis from certain drugs, including valproic acid, chemotherapeutic agents, and tocilizumab, may also lead to FXIII deficiency (11). However, since our case had no history of factor XIII deficiency, no chronic disease, and no history of drug use, this deficiency was considered secondary to consumption due to IGAV. In our case, both Factor XIII and Factor VIII deficiencies were observed, and the patient was administered pulse steroid therapy and fresh frozen plasma. To our knowledge, this is the first reported case involving deficiencies in both factors. However, we believe that in our case this deficiency was acquired as a secondary effect of the IGAV. Another case in the literature involved a 5-year-old girl with intracranial hemorrhage, whose factor levels were not determined. She was successfully treated with dexamethasone and supportive care, though the administered dexamethasone dosage was not reported (9).

A study by Dalens et al. reported that in IgA vasculitis, the risk of complications increases when Factor XIII levels fall below 60% of normal (12). Similarly, our patient's Factor XIII level was 15%, significantly below this threshold. The mechanism underlying reduced Factor XIII activity in IgA vasculitis remains unclear. It has been hypothesized that Factor XIII may be degraded by proteases from infiltrating leukocytes or excessively consumed during fibrin formation around affected vessels (13). Routine coagulation tests, such as prothrombin time (PT), activated partial thromboplastin time (aPTT), and international normalized ratio (INR), while valuable for diagnosing numerous other factor deficiencies, are incapable of detecting FXIII deficiency due to its role in the process of fibrin formation (14). As a result, these tests often yield normal results in individuals with FXIII deficiency. In our case, PT and aPTT results were also normal.

Although IgA vasculitis is generally a self-limiting disease, rare cases with poor prognosis due to intracranial hemorrhage have been reported. In patients presenting with severe headaches unresponsive to analgesics, cranial imaging with computed tomography or cranial MRI should be performed, and factor levels should be assessed. In the presence of hemorrhage, pulse steroid therapy should be administered alongside antiepileptics. If factor deficiencies are identified, treatment with fresh frozen plasma should be initiated.

It should be kept in mind that IgA vasculitis, although typically self-limiting, can lead to rare and severe complications, such as intracranial hemorrhage, particularly in the presence of Factor XIII deficiency.

#### Patient Consent Form / Hasta Onam Formu

The parents' of this patient consent was obtained for this study.

#### Conflict of Interest / Çıkar Çatışması

The authors declared no conflicts of interest with respect to authorship and/or publication of the article.

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