Idiopathic Intracranial Hypertension in a Girl with Juvenile Idiopathic Arthritis-Associated Uveitis: a case report

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Case report

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Abstract

Background Idiopathic intracranial hypertension (IIH) is a rare disorder of elevated pressure of cerebrospinal fluid (CSF) with no evident cause. It has several associated conditions and medications and it may present asymptomatically. Case presentation We here present the case of a 14-year-old girl with juvenile idiopathic arthritis (JIA)-associated uveitis who also had papilledema. She was diagnosed later with IIH as she developed headaches. To the best of our knowledge, this is the fifth case to have uveitis and IIH among children and the only one with no obvious risk factors for IIH, as all were excluded including corticosteroids, tetracyclines and weight gain Conclusions our case suggests to suspect IIH in children when optic disc edema accompany uveitis even in asymptomatic patients, considering that papilledema doesn't resolve despite uveitis recovery in this case.

Background:

Idiopathic intracranial hypertension (IIH), also called pseudotumor cerebri, is a disorder of elevated pressure of cerebrospinal fluid (CSF) with no evident cause (i.e. normal neuroimaging and CSF tests) (1,2). IIH is a rare condition with an incidence of 0.1- 0.9 per 100,000 population; it predominantly affects obese women of childbearing age; a significantly smaller percentage occur in children (3–6).

IIH commonly presents with headache, transient visual obscurations and pulsatile tinnitus (1), while the most frequent signs are papilledema, visual field defect and sixth nerve palsy (7,8). IIH is associated with many systemic illnesses and medications like corticosteroids, vitamin A (V.A), tetracyclines (9–16). Besides that, risk factors include obesity and family history (7–9). To our best knowledge, IIH association with uveitis has been reported, in only four children so far (17–19). In this report, we discuss the case of a girl diagnosed with juvenile idiopathic arthritis (JIA)-associated uveitis developed IIH without any apparent risk factor.

Case Presentation:

A 14-year-old girl presented to our hospital with a two-day complaint of bilateral painful red eyes with mild blurred vision preceded by a month of persistent low back pain that did not improve on rest. She also had a two-year history of recurrent inflammatory arthritis and a half-hour morning stiffness with no obvious swelling. Moreover, the joint pain had become continuous and more intense ten days before presenting to our center with fever peaks several times a day. She had been treated with prednisolone 20 mg daily for just three days, then with gentamicin, doxycycline and rifampicin for five days to no avail. She had no relevant past medical, travel or family history.

On physical examination, her blood pressure was 120/80 mm Hg, pulse was 105 bpm and regular, respiratory rate was 23 bpm, temperature was 38.5c°, and body mass index was 20 kg/m2. She had red eyes, tenderness in the right elbow and both ankles, as well as boutonniere deformity in the fifth finger in both hands. The rest of the physical examination was normal.

On ophthalmic examination, her distance visual acuity without correction was 20/20 in both eyes. Slit-lamp examination revealed bilateral precipitates on the endothelium of cornea and anterior surface of lens, cells (3+) in both anterior chambers with flare in anterior chamber and vitreous, which demonstrated anterior uveitis. She also had grade one papilledema bilaterally. The macula and vessels in each eye were normal. Intraocular Pressure (IOP) was normal.

Laboratory investigations revealed a blood leukocyte count of 12.4 K/mm3 with 85% neutrophils, a hemoglobin concentration of 12.2 g/dL, and a platelet count of 340 K/mm3. Erythrocyte sedimentation rate (ESR) was 50 mm at the end of the first hour and C-reactive protein (CRP) was 4.6 mg/L. Liver function tests, creatinine, urea, urinalysis and microscopy were within normal limits. Antinuclear antibody (ANA), rheumatoid factor (RF), HIV antibodies, VDRL, HBsAg, anti-HCV, Brucella IgG Ab, Brucella IgM Ab, and blood culture were all negative. Tuberculin test was negative after 48 -72 hours. X-ray of the hands showed malalignment with joint space narrowing in the proximal interphalangeal joints of the fifth fingers in both hands. Chest, pelvis and lumbosacral spine X-ray images were within normal limits. Echocardiogram was normal with no evidence of endocarditis.

After ruling out infectious causes, malignancies, and other systemic autoimmune diseases, the patient was diagnosed with enthesitis-related JIA based on the International League of Associations for Rheumatology (ILAR) classification criteria (20). She was treated with prednisolone 0.5 mg/kg/day, which led to improvement in fever, eyes redness and articular manifestations within three days. On discharge, we added methotrexate 10 mg once a week. Seven days later, she returned for follow-up with a new complaint of generalized, persistent, tension headache that improved partially on analgesics, accompanied by severe blurred vision and decreased visual acuity. Ophthalmic examination exhibited three grade papilledema in both eyes with no flare in the anterior chamber and vitreous. Vital signs at the second presentation were all normal. Brain computed tomography (CT) was normal and lumbar puncture disclosed an increased opening pressure of 300 mm H2O. CSF analysis revealed no cells, a CSF protein of 40 mg/dL (normal up to 45 mg/dL), and a CSF glucose of 56 mg/dL with serum glucose of 79 mg/dL. Total blood leukocyte count was 10.4 K/mm3 with a differential count of neutrophil 86%. ESR was 20 mm at the end of the first hour. All other laboratory studies were normal. Magnetic resonance imaging (MRI) of the brain with magnetic resonance venography (MRV) were normal. Based on Revised diagnostic criteria the patient was diagnosed with IIH and started on acetazolamide 500 mg/day increased up to 750 mg daily (2). Three weeks later, the papilledema had resolved and then she was kept on the same dose of acetazolamide for one month. After that, acetazolamide and prednisolone were tapered off over one year. Currently, she is doing well on a 2.5 mg methotrexate maintenance dose weekly.

Discussion And Conclusion:

We presented the case of a girl with arthritis, uveitis, and optic disc edema, which was diagnosed later with IIH. Uveitis is an intraocular inflammation which could be idiopathic or associated with underlying systemic diseases. Therefore, we started a thorough investigation that eventually excluded other systemic etiologies and she was diagnosed with JIA associated uveitis. Since optic disc edema may be found in patients with uveitis and resolves after the treatment of uveitis (21,22), we initially opted to only monitor it. However, in this case, the optic disc edema was actually due to IIH evident by the headaches the patient

developed seven days later. Even though the patient was from an age group which is typically symptomatic, she had an atypical presentation at first similar to younger children who are frequently asymptomatic (i.e. had optic disc edema with no headaches) (18,23). Subsequently, the absence of headache apparently was not enough to exclude the diagnosis of IIH, especially when papilledema did not improve after the treatment of uveitis.

Our patient had two presumed risk factors for IIH. One of them is steroids which were given for three consecutive days 25 days before the diagnosis of IIH, as well as for seven days as a treatment for uveitis without tapering-off. However, the risk of IIH in case of steroids is seen when they are tapered after long term use which does not apply to our case (6,14). The other risk factor is doxycycline, one of the tetracyclines that have been associated with IIH in a number of cases, with a notice that in these reports, tetracycline was often combined with other assumed risk factors (14–16). IIH frequently develops within few weeks to months after treatment initiation and sometimes cessation of these drugs is enough for recovery. Our patient was treated with doxycycline for just five days prior to the first admission, therefore, doxycycline cannot also be considered associated with IIH in our case.

To our knowledge, four children cases were reported to date as having uveitis and IIH (table 1-A); three of them had anterior uveitis similar to our case and one had panuveitis. Only one of the cases had JIA-associated uveitis similar to our report.

Further search revealed four other cases of reported IIH complicated JIA without uveitis (table 1-B). One of them was a girl had treated with methotrexate without steroid for one year before being diagnosed with IIH. Methotrexate was considered a suspected cause, so it was stopped and the patient was given acetazolamide leading to improvement of the symptoms a week later. Unlike our patient who was kept on methotrexate after the diagnosis of IIH and improved nevertheless.

All former cases had IIH with possible predisposing drugs and/or conditions in contrast to our patient who did not have any known ones. As treatment of pediatric patients is empiric due to the lack of enough clinical trials, most cases, including ours, were treated with acetazolamide in addition to the opposition of the predisposing factors if present.

In conclusion, IIH has a possible association with uveitis including JIA-associated uveitis as well as JIA without uveitis. It is a curable condition especially if it is diagnosed early. We suggest to suspect IIH when optic disc edema is found with uveitis even in asymptomatic patients.

List Of Abbreviations:

Idiopathic intracranial hypertension (IIH)

Cerebrospinal fluid (CSF)

Juvenile idiopathic arthritis (JIA)

Vitamin A (V.A)

Intraocular Pressure (IOP)

Erythrocyte sedimentation rate (ESR)

C-reactive protein (CRP) Antinuclear antibody (ANA)

Rheumatoid factor (RF)

The International League of Associations for Rheumatology (ILAR)

Computed tomography (CT)

Magnetic resonance imaging (MRI)

Magnetic resonance venography (MRV)

Declarations:

Ethics approval and consent to participate: Not applicable

Consent for publication: The informed consent has been obtained.

Availability of data and material: The medical records of our patient are saved in the archive in our center.

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Authors' Contribution:

AA: Did the literature search and drafted the discussion; HA: Drafted the case presentation; IH: Drafted the introduction and edited the paper for submission; MA and all authors reviewed the article and approved the last version of it.

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Tables:

Table 1. Pediatric cases of Idiopathic Intracranial Hypertension (IIH) with Juvenile Idiopathic Arthritis (JIA) and/or Uveitis

	Cases	Age/ Sex	IIH	Uveitis	JIA	Associated conditions	Associated drugs	Treatment*
Section A: With uveitis	**Margalit** (17)	Girl 11-year	Present symptomatic	Panuveitis	-	Weight gain	-	Acetazolamide, weight reduction
	Buscher (19)	Boy 11-year	Present asymptomatic	Anterior uveitis	-	Weight gain	Cyclosporine	Acetazolamide, prednisone, MMF†
	Curragh first case (18)	Girl 8-year	Present asymptomatic	Anterior uveitis	Oligoarticular JIA	-	Steroids	Furosemide‡
	Curragh second case (18)	Boy 5-year	Present asymptomatic	Anterior uveitis	-	-	Steroids	Acetazolamide
Section B: Without uveitis	**Burstzyn** (24)	Child Unknown	Present symptomatic	-	Systemic JIA	-	Steroids	Lumbar puncture, acetazolamide, ONSF§
	Bhettay (25)	Child Unknown	Present unknown	-	Undefined JIA	-	V.A	V.A cessation
	Wanigasinghe (23)	Boy 5-year	Present symptomatic	-	Systemic JIA	-	Steroids , V.A	Acetazolamide, furosemide
	Incecik (26)	Girl 9-year	Present symptomatic	-	Undefined JIA	-	Methotrexate	Acetazolamide, methotrexate cessation
Section C:	**Our case**	Girl 14-year	Present symptomatic¶	Anterior uveitis	Enthesitis-related JIA	-	-	Acetazolamide

* Treatment of IIH and associated disease; † Mycophenolate mofetil; ‡ Acetazolamide was commenced but not tolerated; § Unilateral optic nerve sheath fenestration; Without withdrawal; ¶ Asymptomatic at first.

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