INTRODUCTION

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

Intracranial hypertension commonly presents with headache, transient visual obscurations, and pulsatile tinnitus,\textsuperscript{1} while the most frequent signs are papilledema, visual field defect, and sixth nerve palsy.\textsuperscript{7,8} IIH is associated with many systemic illnesses such as Addison disease, hypoparathyroidism, and anemia, as well as, medications like corticosteroids, vitamin A (V.A), and tetracyclines.\textsuperscript{9-16} Besides that, IIH risk factors include obesity and family history.\textsuperscript{7-9} To our knowledge, this is the fifth case of the coexistence of uveitis and IIH among children, and the only one with no obvious risk factors for IIH.

CASE PRESENTATION

A 14-year-old girl with juvenile idiopathic arthritis (JIA)-associated uveitis who also had optic disc edema, was later diagnosed with Idiopathic intracranial hypertension (IIH). To our knowledge, this is the fifth case of the coexistence of uveitis and IIH among children, and the only one with no obvious risk factors for IIH.

KEYWORDS

idiopathic intracranial hypertension, juvenile idiopathic arthritis, pseudotumor cerebri, uveitis

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Abstract
A 14-year-old girl with juvenile idiopathic arthritis (JIA)-associated uveitis who also developed IIH without any apparent risk factor.
On physical examination, her blood pressure was 120/80 mm Hg, pulse was 105 beats per minute and regular, respiratory rate was 23 cycles per minute, the temperature was 38.5°C, and body mass index was 20 kg/m². She had red eyes, tenderness in the right elbow and both ankles, as well as a swan-neck deformity in the fifth finger in both hands (Figure 1). 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 the anterior surface of the lens, cells (3+) in both anterior chambers with few cells in the anterior vitreous, which demonstrated anterior uveitis. She also had grade 1 optic disk edema bilaterally. The macula, peripheral retina, 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. The 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. She was treated with prednisolone 0.5 mg/kg/day, which led to an improvement in fever, eyes redness, and articular manifestations within 3 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 blurred vision. Ophthalmic examination showed normal visual acuity with grade 3 optic disk edema in both eyes with no flare in the anterior chamber and vitreous. Vital signs were all normal. Brain computed tomography (CT) was normal and lumbar puncture disclosed a slightly 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 showed mild optic nerve tortuosity, posterior globe flattening (Figure 2), and prominent subarachnoid space around the optic nerves (Figure 3), while magnetic resonance venography (MRV) was normal. Based on revised diagnostic criteria, the patient was diagnosed with IIH and was put on acetazolamide 500 mg/day then the dose increased up to 750 mg daily. Three weeks later, the papilledema and the headache had resolved and acetazolamide and prednisolone were tapered off. After 2-year of follow-up, she was still doing well on a 2.5 mg methotrexate maintenance dose weekly.

**FIGURE 1** The left-hand shows mild swan-neck deformity in the fifth finger

**FIGURE 2** Brain magnetic resonance imaging showing mild optic nerve tortuosity (yellow arrow) and posterior globe flattening (blue arrow)
3 | DISCUSSION

We presented the case of a girl with arthritis, uveitis, and optic disk edema, who was later diagnosed with IIH. Uveitis is an intraocular inflammation that can be idiopathic or associated with underlying systemic diseases. Therefore, thorough investigations were done leading to the diagnosis of JIA-associated uveitis after excluding other systemic etiologies. Since optic disk 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, 18 days later the patient developed a headache and she was diagnosed with IIH which should be the cause of optic disk edema. Even though IIH is typically symptomatic in her age group, she had an atypical presentation at first similar to younger children who are frequently asymptomatic.18,23 Subsequently, the absence of headache and other symptoms apparently was not enough to exclude the diagnosis of IIH, especially when optic disk edema did not improve after the treatment of uveitis.

Our patient had two presumed risk factors for IIH. One of them is corticosteroids which were given for three consecutive days, 26 days before the diagnosis of IIH, as well as for 14 days as a treatment for uveitis without tapering-off. However, the risk of IIH in the case of corticosteroids 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 several cases, with a notice that in these reports, tetracycline was often combined with other assumed risk factors.14-16 IIH frequently develops within a few weeks to months after treatment initiation and sometimes cessation of the drug is enough for recovery.14-16 Our patient was treated with doxycycline for just 5 days before the first admission and 23 days before developing the headache, therefore, doxycycline cannot also be considered associated with IIH in our case.

To our knowledge, four juvenile 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.

A further search revealed four other cases of reported IIH complicated with JIA without uveitis (Table 1-B). One of them was a girl who had been treated with methotrexate without steroid for 1 year before being diagnosed with IIH. Methotrexate was considered a suspected cause, so it was stopped and the patient was given acetazolamide, leading to the improvement in symptoms a week later. On the contrary, our patient 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 certain ones (Table 1). As treatment of pediatric patients with IIH is empiric due to the lack of enough clinical trials, most cases, including ours, were treated with acetazolamide in addition to opposing predisposing factors when present.

This case report has a potential limitation. There is a possibility that IIH and uveitis were unrelated entities. However, IIH should be suspected in cases of uveitis complicated with optic disk edema, as prompt diagnosis and treatment can prevent vision loss.

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**TABLE 1** Pediatric cases of Idiopathic Intracranial Hypertension with Juvenile Idiopathic Arthritis and/or Uveitis

| Section A: With uveitis          | Cases          | Age/Sex | IIH       | Uveitis     | JIA           | Associated conditions | Associated drugs | Treatmenta                  |
|--------------------------------|----------------|---------|-----------|-------------|---------------|------------------------|------------------|---------------------------|
| Margalit17                     | Girl 11-y      | Present symptomatic | Panuveitis | —           | Weight gain         | —                      | Acetazolamide, weight reduction |
| Buscher19                      | Boy 11-y       | Present asymptomatic | Anterior uveitis | —           | Weight gain         | Cyclosporine          | Acetazolamide, prednisone, MMFb |
| Curragh first case18           | Girl 8-y       | Present asymptomatic | Anterior uveitis | Oligoarticular JIA | —                      | Steroids              | Furosemidec               |
| Curragh second case18          | Boy 5-y        | Present asymptomatic | Anterior uveitis | —           | —                      | Steroids              | Acetazolamide          |

| Section B: Without uveitis     | Cases          | Age/Sex | IIH       | Uveitis     | JIA           | Associated conditions | Associated drugs | Treatmenta                  |
|--------------------------------|----------------|---------|-----------|-------------|---------------|------------------------|------------------|---------------------------|
| Burstzyn24                     | Child unknown  | Present symptomatic | —           | Systemic JIA | —                      | Steroids              | Lumbar puncture, acetazolamide, ONSFd |
| Bhettay25                      | Child unknown  | Present unknown | —           | Undefined JIA | —                      | V.A                   | V.A cessation          |
| Waniaginghe23                  | Boy 5-y        | Present symptomatic | —           | Systemic JIA | —                      | Steroids 5, V.A       | Acetazolamide, furosemide |
| Incecik26                      | Girl 9-y       | Present symptomatic | —           | Undefined JIA | —                      | Methotrexate          | Acetazolamide, methotrexate cessation |

| Section C: Our case            | Cases          | Age/Sex | IIH       | Uveitis     | JIA           | Associated conditions | Associated drugs | Treatmenta                  |
|--------------------------------|----------------|---------|-----------|-------------|---------------|------------------------|------------------|---------------------------|
|                                 | Girl 14-y      | Present symptomatic | Anterior uveitis | Enthesitis-related JIA | —                      | —                      | Acetazolamide          |

aTreatment of IIH and associated disease.

bMycophenolate mofetil.

cAcetazolamide was commenced but not tolerated.

dUnilateral optic nerve sheath fenestration.

5Without withdrawal.

fAsymptomatic at first.
CONFLICT OF INTEREST
None declared.

AUTHOR CONTRIBUTIONS
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.

CONSENT FOR PUBLICATION
Informed consent has been obtained.

DATA AVAILABILITY STATEMENT
The medical records of our patient are saved in the archive in our center.

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REFERENCES
1. Wall M. Idiopathic intracranial hypertension. Neurol Clin. 2010;28(3):593-617. https://doi.org/10.1016/j.ncl.2010.03.003
2. Friedman DI, Liu GT, Digre KB. Revised diagnostic criteria for the pseudotumor cerebri syndrome in adults and children. Neurology. 2013;81(13):1159-1165. https://doi.org/10.1212/WNL.0b013e318a55f17
3. Durcan FJ, Corbett JJ, Wall M. The incidence of pseudotumor cerebri. Population studies in Iowa and Louisiana. Arch Neurol. 1988;45(8):875-877.
4. Radhakrishnan K, Ahsikog JE, Cross SA, Kurland LT, O’Fallon WM. Idiopathic intracranial hypertension (pseudotumor cerebri). Descriptive epidemiology in Rochester, Minn, 1976 to 1990. Arch Neurol. 1993;50(1):78-80.
5. Kesler A, Gadoth N. Epidemiology of idiopathic intracranial hypertension in Israel. J Neuroophthalmol. 2001;21(1):12-14.
6. Rangwala LM, Liu GT. Pediatric idiopathic intracranial hypertension. Surv Ophthalmol. 2007;52(6):597-617. https://doi.org/10.1016/j.survophthalm.2007.08.018
7. Wall M, Kupersmith MJ, Kieburtz KD, et al. The idiopathic intracranial hypertension treatment trial: clinical profile at baseline. JAMA Neurol. 2014;71(6):693-701. https://doi.org/10.1001/jamaneurol.2014.133
8. Wall M, George D. Idiopathic intracranial hypertension. A prospective study of 50 patients. Brain. 1991;114(Pt 1A):pp. 155-180.
9. Giuseffi V, Wall M, Siegel PZ, Rojas PB. Symptoms and disease associations in idiopathic intracranial hypertension (pseudotumor cerebri): a case-control study. Neurology. 1991;41(2, Pt 1):239-244.
10. Ireland B, Corbett JJ, Wallace RB. The search for causes of idiopathic intracranial hypertension. A preliminary case-control study. Arch Neurol. 1990;47(3):315-320.
11. Bandyopadhyay S, Jacobson DM. Clinical features of late-onset pseudotumor cerebri fulfilling the modified dandy criteria. J Neuroophthalmol. 2002;22(1):9-11.
12. Liu GT, Kay MD, Bienfang DC, Schatz NJ. Pseudotumor cerebri associated with corticosteroid withdrawal in inflammatory bowel disease. Am J Ophthalmol. 1994;117(3):352-357.
13. Rickels MR, Nichols CW. Pseudotumor cerebri in patients with Cushing’s disease. Endocr Pract. 2004;10(6):492-496. https://doi.org/10.4158/EP.10.6.492
14. Friedman DI. Medication-induced intracranial hypertension in dermatology. Am J Clin Dermatol. 2005;6(1):29-37. https://doi.org/10.2165/00128071-200506010-00004
15. Kesler A, Goldhammer Y, Hadayer A, Pianka P. The outcome of pseudotumor cerebri induced by tetracycline therapy. Acta Neurol Scand. 2004;110(6):408-411. https://doi.org/10.1111/j.1600-0404.2004.00327.x
16. Gardner K, Cox T, Digre KB. Idiopathic intracranial hypertension associated with tetracycline use in fraternal twins: case reports and review. Neurology. 1995;45(1):6-10.
17. Margalit E, Sung JU, Do DV, Yohay K, Nguyen QD. Panuveitis in association with pseudotumor cerebri. J Child Neurol. 2005;20(3):234-236. https://doi.org/10.1177/08830738050200031601
18. Currah D, McLoone E. Pseudotumour cerebri syndrome in two children on systemic steroid therapy for uveitis. Ocul Immunol Inflamm. 2018;26(2):295-297. https://doi.org/10.1080/0927948.2016.1215474
19. Buscher R, Vij O, Hudee T, Hoyer PF, Vester U. Pseudotumor cerebri following cyclosporine A treatment in a boy with tubulointerstitial nephritis associated with uveitis. Pediatr Nephrol. 2004;19(5):558-560. https://doi.org/10.1007/s00467-004-1429-9
20. Petty RE, Southwood TR, Manners P, et al. International league of associations for rheumatology classification of juvenile idiopathic arthritis: second revision, Edmonton, 2001. J Rheumatol. 2004;31(2):390-392.
21. Savoie B, Yin D, Banik R. Uveitis with optic disc edema secondary to concomitant idiopathic intracranial hypertension. Spencer S Eccles Heal Sci Libr Univ Utah. 2013;194.
22. Thorne JE, Woreta F, Kedhar SR, Dunn JP, Jabs DA. Juvenile idiopathic arthritis-associated uveitis: incidence of ocular complications and visual acuity loss. Am J Ophthalmol. 2007;143(5):840-846.e2. https://doi.org/10.1016/j.ajo.2007.01.033
23. Wanigasinghe J, Lucas MN, Jayanethi S, Lamabadusuriya SP. Idiopathic intracranial hypertension in a child being treated for systemic onset juvenile idiopathic arthritis. Sri Lanka J Child Health. 2010;39(3):115. researchgate.net.
24. Burstyn L, Levin S, Rotenberg B, et al. Fulminant bilateral papilloedema during low-dose steroid taper in a child with systemic idiopathic arthritis treated with tocilizumab. Clin Exp Rheumatol. 2019;37(1):149-151.
25. Bhetty ME, Bakst CM. Hypervitaminosis A causing benign intracranial hypertension. A case report. S Afr Med J. 1988;74(11):584-585.
26. Incceci F, Ozcanayz DG, Yilmaz M. Methotrexate-induced pseudotumor cerebri in a patient with juvenile idiopathic arthritis. Acta Neurol Belg. 2019;119(1):141-142. https://doi.org/10.1007/s13760-018-0979-8

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