

# Pseudotumor Cerebri Associated with Cod Liver Oil Use: Case Report

## Balık Yağı Kullanımına Bağlı Psödötümör Serebri

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**ABSTRACT** Pseudotumor cerebri is a condition defined by elevated intracranial pressure without any clinical, laboratory, or radiographic evidence of responsible infection, vascular abnormality, space occupying lesion, or hydrocephalus. Excessive vitamin A is one of the commonly known etiologies. A 6-year-old female patient was diagnosed with pseudotumor cerebri due to regular intake of dietary cod liver oil in recent months, provided by her family for lack of appetite. We learned that our patient had received cod liver oil once a day and on some days, several times a day, total daily dose of 10-20ml (10ml=4000IU Vitamin A) for the last few months. Vitamin A level was higher than the normal range. The patient did not responded well to acetazolamide treatment previously, but responded well to the withdrawal of dietary cod liver oil. This case has been reported to draw attention on potential health problems that could result from dietary fish oil and/or excessive vitamin intake for lack of appetite or other health reasons.

**Key Words:** Cod liver oil; pseudotumor cerebri; child; intracranial hypertension; hypervitaminosis A

**ÖZET** Psödötümör serebri klinik, laboratuvar ve nöroradyolojik tetkiklerde kafa içi basınç artışına yol açacak herhangi bir patoloji saptanmadan hidrosefali, vasküler anomali, yer kaplayan oluşum, infeksiyon olmadan intrakranial basıncın artması olarak tanımlanır. A vitamini fazlalığı sık bilinen nedenlerinden biridir. Olgumuz 6 yaşındaki kız hastaya psödötümör serebri teşhisi kondu. Öyküsü derinleştirildiğinde son aylarda ailesi tarafından iştahsızlık nedeni ile balık yağı kullanımı olduğu fark edildi. Hastamızın son birkaç aydır bazı günler bir kez bazı günler birkaç kez 10-20 mL (10ml=4000IU Vitamin A) balık yağı aldığını öğrendik. Bakılan kan vitamin A düzeyi normalden yüksek bulundu. Daha önce asetazolamid tedavisine iyi yanıt vermeyen hasta diyetten balık yağı çıkarılmasına dramatik olarak cevap verdi. Bu olgu özellikle iştahsızlık ve diğer nedenlerle yanlış kullanılan balık yağı, vitaminlerin yol açabileceği sorunlara dikkat çekmek için sunuldu.

**Anahtar Kelimeler:** Kod karaciğer yağı; psödötümör serebri; çocuk; intrakranial hipertansiyon; hipervitaminoz A

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**P**seudotumor cerebri (idiopathic intracranial hypertension, benign intracranial hypertension) is a condition defined by elevated intracranial pressure without any clinical, laboratory, or neuroradiographic evidence of responsible infection, vascular abnormality, space occupying lesion, or hydrocephalus.<sup>1,2</sup> The diagnostic criteria of this syndrome are the modified Dandy criteria developed by Smith in 1985. The diagnostic symptoms are signs and findings of increased intracranial pressure (headache, vomiting, temporary visual loss, diplopia, papillary edema), absence of focal neurolog-

ical findings, normal findings of cerebrospinal fluid (CSF) except increased intracranial pressure, and symmetrically normal ventricles in imaging studies. Less frequently, there may be cervical, upper back, and shoulder pain, and meningeal irritation findings (photophobia, nausea, vomiting).<sup>1,2</sup>

Infections (particularly otitis media), hematological diseases (hemolytic and iron deficiency anemia), drug use (tetracycline), metabolic disorders (excess or deficient vitamin A), oral contraceptive use, hypo or hyperthyroidism, prolonged use or rapid withdrawal of corticosteroids, growth hormone therapy, and/or obesity may be the underlying reason(s).<sup>3</sup> In this report, a pediatric case of pseudotumor cerebri associated with hypervitaminosis due to prolonged usage of cod liver oil and multivitamin intake for lack of appetite is presented.

## CASE REPORT

A 6-year-old female patient admitted to the emergency department with fever, vomiting, and cervical pain. In the initial physical examination at the emergency department, no specific findings had been determined. But, fundoscopic examination was not performed. The laboratory studies revealed WBC count: 22 000/mm<sup>3</sup>, CRP: 10.2 mg/dL, ESR: 64 mm/s, and in the CSF evaluation, the leukocyte count was 10/mm<sup>3</sup>; protein level, 15 mg/dL; and glucose level, 59 mg/dL. CSF pressure was not measured at emergency department. The patient was then hospitalized in the pediatric infection ward with a diagnosis of aseptic meningitis. The ceftriaxone treatment that had started earlier was completed to 7 days and the patient was discharged after her acute phase reactant values reduced.

One week later, the patient came to the emergency department with cervical pain and vomiting. At that time, the laboratory studies revealed; WBC count of 11 000/mm<sup>3</sup>, CRP level of 4.3 mg/dL, and ESR of 40 mm/s. The patient was then re-hospitalized. In the follow-up, the patient had no fever or vomiting, and the cranial CT findings were normal. Collagen tissue disease was suspected due to recurrent meningeal irritation but tests (anti-nuclear antibodies, anti-neutrophil cytoplasmic antibody, anti-double-stranded DNA) were within normal

limits. The cervical vertebra graphy and spinal MRI of the patient were also normal. On the 15<sup>th</sup> day of her re-hospitalization, the patient was referred to pediatric neurology department with the complaints of diplopia and severe headache. Neurologic examination revealed papillary edema. The CSF findings were also normal except a pressure of 300 mmH<sub>2</sub>O in lumbar puncture. The patient was diagnosed as pseudotumor cerebri, and thus, acetazolamide was started at a dose of 20 mg/kg/day. However, the complaints of the patient persisted. Then, another lumbar puncture was performed for therapeutic and control purposes, and the CSF pressure was found to be 400 mmH<sub>2</sub>O. The results of the MRI, MR venography, ACTH/Cortisol (morning), parathyroid hormone, iron profile, and vitamin D evaluations, conducted in order to determine the etiology, were normal. After a detailed history, it was noted that her mother was giving the patient dietary cod liver oil in recent months prior to her presentation to increase her appetite. The blood vitamin D level of the patient was found to be normal, but vitamin A level was 56 mg/dl (reference values: 26-46 mg/dl), which was higher than the normal range. The fish oil was immediately withdrawn from her diet. The symptoms of the patient dramatically regressed after the withdrawal of fish oil with low-dose steroid therapy (dexamethasone, 0.01 mg/kg per day- 5 day) and the CSF pressure was normal after 3 weeks.

## DISCUSSION

Pseudotumor cerebri, commonly known as idiopathic intracranial hypertension (IIH), is most frequently seen in obese female adolescents.<sup>4</sup> There were reports of IIH associated with hypervitaminosis in patients taking synthetic retinol derivatives for treatment of acne and promyelocytic leukaemia, and also as a result of excessive consumption of liver and carrot, ginseng tea and medications containing vitamin A.<sup>5-9</sup> In this article, we presented a case of idiopathic intracranial hypertension associated with hypervitaminosis A due to excessive cod liver oil consumption.

The pathogenesis of idiopathic intracranial hypertension associated with vitamin A hypervitaminosis has not been clearly defined to date.

Theoretically, it develops with increased CSF secretion in the coroid plexuses or diminished absorption of CSF in the arachnoid villi.<sup>9</sup> Warner et al,<sup>10</sup> followed by Fishman et al,<sup>11</sup> have proposed that vitamin A associated IHH is related to aquaporin genes. Aquaporin 1 is expressed by the coroid plexus cells. In rat models, aquaporin genes were shown to increase CSF production and thus, intracranial pressure.<sup>9</sup>

Cod liver oil contains high amounts of vitamin A, D, and omega 3 fatty acids. It may be useful in the treatment of rheumatologic diseases and rickets. Vitamin A is essential for bone growth, night vision, cellular growth, testicular and ovarian functions, and immune system.<sup>13</sup> The daily recommended dose of vitamin A intake is 2300-3000 IU (FDA recommendation for children of 4-8 years of age: 1320 IU).<sup>9,14</sup> Minadex® syrup, which is actually cod liver oil (Abdi Ibrahim, Istanbul, Turkey), contains 10 ml=4000IU of Vitamin A. Our patient had received this product once a day and on some days, several times a day, total daily dose of 4000-8000 IU for the last few months. The patient also had a history of suspected aseptic meningitis nearly a month ago. This indefinite infection either may have triggered IHH development or would be one of the first symptoms of IHH. Upon withdrawal of dietary cod

liver oil containing vitamin A, the condition of the patient dramatically improved.

American Pediatrics Academy does not recommend regular intake of multivitamins in children over one year of age, except in the presence of certain conditions such as chronic diseases, eating disorders, malabsorption, and hepatic disorder. Nevertheless, in a study conducted in the USA, the rate of multivitamin usage among preschoolers was found to be 46%.<sup>15</sup> Likewise, it was determined that mothers of children with lack of appetite in particular had a tendency to supplement the diet of their children with iron and multivitamins. Similarly, our patient was given multivitamin preparations containing cod liver oil despite being in a normal percentiles for weight and height range for her age (25-50 percentile) upon doctors' recommendation and influence of close relations.

By presenting this patient, we aimed to draw attention to an important side effect of excessive and unnecessary vitamin intake. Considering the serious side effects of IHH such as increased intracranial pressure to the extent of requiring a cranial shunt insertion and papillary edema that may lead to visual loss, pediatricians in particular should warn the families against misuse of vitamin containing drugs.

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