

Coexistence of Pseudotumor Cerebri and Chiari Malformation Type 1

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Abstract: *Objective:* To identify different radiological markers for the diagnosis of the coexistence of pseudotumor cerebri and Chiari malformation type 1. *Method:* Patients who were clinically suspected to have Chiari malformation type 1 and were referred to the Department of Radiology between 2007 and 2020, and whose diagnosis was radiologically confirmed through magnetic resonance imaging (MRI), were retrospectively evaluated. A total of 49 Chiari malformation type 1 patients with both cervical and cerebral examinations and 49 control subjects of the same age and gender without a diagnosis of Chiari malformation type 1 were included in the study. In Chiari malformation type 1 diagnosed patients, the presence of pseudotumor cerebri, the presence of syringomyelia in cervical spinal MRI images, and the distance of cerebellar tonsils and obex according to McRae line were evaluated in millimeters. *Result:* In Chiari malformation type 1 clinically and radiologically diagnosed cases, the cerebellar tonsils and obex were located lower in patients with a radiological diagnosis of pseudotumor cerebri compared to those without, and the rate of accompanying syringomyelia appeared to be higher. However, no statistically significant difference was observed between the two groups. *Conclusion:* The coexistence of pseudotumor cerebri and Chiari malformation type 1 is more common than previously estimated. Different treatment protocols in the coexistence of pseudotumor cerebri and Chiari malformation type 1 emphasize the importance of making this diagnosis. Further radiological imaging studies are needed to identify different radiological markers for the diagnosis of the coexistence of pseudotumor cerebri and Chiari malformation type 1.

Keywords: Pseudotumor cerebri; Chiari malformation type 1; Coexistence; Radiological markers

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1. Introduction

Chiari malformation type 1 (CM1) originates from embryonic developmental abnormalities of the brainstem and cerebellum, characterized by the displacement of cerebellar tonsils 5 mm or more caudally from the foramen magnum. This definition is purely radiological, and in the literature, patients with CM1 clinical features and cerebellar tonsillar displacement exceeding 3 mm from the foramen magnum are also observed ^[1,2]. The prevalence of CM1 is reported to be approximately 1% in the population ^[3]. CM1 is the mildest form of

Chiari malformations. While it is more common in females, it typically manifests symptoms in the third and fourth decades of life, hence it is also referred to as the adult form of Chiari malformations. Despite numerous hypotheses, its etiology remains unclear. Some of these hypotheses include primary mesodermal insufficiency, hypoplasia of the basal part of the occipital bone, or a small posterior cranial fossa (PCF) due to platybasia^[4-6].

Headache is the most common symptom in CM1. In CM1, the classic type of headache is a suboccipital headache or neck pain triggered or worsened by Valsalva-like maneuvers (such as coughing or straining)^[7]. Approximately 14% to 21% of CM1 patients are asymptomatic and are incidentally diagnosed through imaging methods^[8,9].

The compression of cerebellar tonsils, brainstem, and upper cervical spine at the foramen magnum can lead to symptoms of lower cranial nerve paralysis, such as limb weakness, dysphagia, and dysphonia. In CM1, the dynamics of cerebrospinal fluid (CSF) flow can be disrupted, and approximately 20%–72% of CM1 cases can lead to the development of syringomyelia in the cervical region due to CSF flow disturbance ^[10,11]. Syringomyelia is the most commonly associated disorder with CM1. Syringomyelia refers to the formation of CSF cavities within the spinal cord ^[12]. Syringomyelia, due to spinal cord compression, causes paresthesia, hyperesthesia, or anesthesia in a classic shawl-like pattern that does not involve a specific dermatome in the neck and shoulders. The widening of the central canal leads to dissociation loss of pain and temperature sensation, but light touch and proprioception are initially preserved. Weakness, non-radicular pain, and spasticity can also be observed primarily in the upper extremities. Untreated chronic syringomyelia can cause scoliosis and myelopathy in 18%–42% of CM1 patients ^[7,13,14].

According to the modified Dandy criteria, pseudotumor cerebri (PTC) is a syndrome characterized by an increase in intracranial pressure (ICP) with normal CSF content and the absence of focal neurologic findings, except for isolated sixth cranial nerve palsy ^[15]. PTC is classified into two types: idiopathic intracranial hypertension (IIH) and secondary PTC syndrome associated with specific causes such as venous sinus thrombosis ^[16]. The incidence of idiopathic intracranial hypertension is 19/100,000 ^[17,18]. Patients with idiopathic intracranial hypertension most commonly present with headache, which is seen in 68%–98% of cases. Other clinical features include pain, pulsatile tinnitus, and visual disturbances that can lead to blindness ^[17,19].

Idiopathic intracranial hypertension, despite being a clinical diagnosis based on high opening pressure (>20 cm H_2O in non-obese patients, > 25 cm H_2O in obese patients with a body mass index of 30 or higher) in conjunction with normal CSF content, has associated supportive neuroimaging findings described. These imaging findings include flattening of the posterior sclera, tortuosity of the optic nerve sheath, empty sella syndrome, dilated Meckel's cave, and constriction of transverse venous sinuses. Neuroimaging methods can assist in clinical diagnosis or support, especially for clinicians unfamiliar with the diagnosis ^[20,21].

The goal of this study is to identify different radiological markers for the diagnosis of the coexistence of PTC and CM1.

2. Materials and methods

In this study, 49 CM1 patients (age range 20–59 years with an average of 37.82 ± 10.53 years, 44 females, and 5 males) with both cervical and cerebral MRI examinations and a confirmed diagnosis through magnetic resonance imaging (MRI) who were referred from the Department of Neurosurgery to the Department of Radiology with a clinical pre-diagnosis of CM1 between 2007 and 2020 were included. Additionally, 49 control subjects of the same age and gender without a diagnosis of CM1 were also included. The magnetic resonance images were retrospectively evaluated. Ethical approval was obtained from the Mersin University Ethics Committee (no. 2022/60) before the measurements began.

The CM1 patient and control groups were scanned using a 1.5 Tesla (T) General Electric (Milwaukee, Wisconsin, U.S.A.) Excite II device and a 1.5 T Siemens (Erlangen, Germany) Magneton Area device with a 16-channel head and neck coil. The axial and sagittal slice thicknesses for cervical MRI examinations were set to 3 mm. The presence of PTC was radiologically evaluated from cerebral MRI images, including findings such as empty sella syndrome, expansion in Meckel's cave, tortuosity of the optic nerve sheath, widening of the CSF space adjacent to the optic nerve, and flattening of the posterior sclera (**Figure 1**) ^[20,21]. The presence of syringomyelia was assessed from cervical spinal MRI images, and the distances in mm of the cerebellar tonsils and obex were measured according to the McRae line (a line extending from Basion to Opistion; **Figure 2**) ^[22].



Figure 1. Radiological assessment of pseudotumor cerebri (PTC) presence from cerebral MRI images. (a) Expansion in Meckel's cave; (b) tortuosity of the optic nerve sheath (white arrow) and widening of cerebrospinal fluid space adjacent to the optic nerve (black arrow); and (c, d) empty sella syndrome.



Figure 2. The presence of syringomyelia (arrow), (a) the distance of obex (a marker for the cervicomedullary junction, where the fourth ventricle becomes the central canal in the cervical spinal cord) measured in mm according to the McRae line (a line extending from Basion to Opistion), and (b) the distance of the cerebellar tonsils were assessed from cervical spinal MRI images. Measurements performed above the McRae line were evaluated as negative values, while measurements performed below were considered positive.

Measurements performed above the McRae line were evaluated as negative values, while measurements performed below were considered positive. Patients in the CM1 group had no intracranial space-occupying pathology that could affect the measurements. In the control group, there were no congenital or systemic diseases related to the craniovertebral junction that could affect the measurements. Patients diagnosed with CM1 clinically and radiologically were categorized into two groups, similar to those with PTC and those without PTC, based on tonsillar herniation exceeding 5 mm. The Shapiro-Wilk test was used to check whether the measurements had a normal distribution, which was confirmed. Descriptive statistics provided mean and standard deviation for continuous variables and number and percentage for categorical variables. Student *t*-test was used to compare the means between the two groups. Analysis of variance (ANOVA) was applied for comparisons of more than two groups. For pairwise comparisons between groups, the Dunnet test was preferred for comparisons against the control group, and the Tukey test was used for all other comparisons. Receiver operating curve (ROC) analysis was used to evaluate the success of the parameters in distinguishing cases with syringomyelia from cases without syringomyelia. Descriptive statistics included the area under the curve, sensitivity and specificity values, and confidence intervals. A significance level of P < 0.05 was considered statistically significant.

3. Result

In the PTC (-) CM1 group, the number of females was 34 (89.5%), and males were 4 (10.5%). In the PTC (+) CM1 group, there were 10 females (90.9%) and 1 male (9.1%), while in the control group, there were 44 females (89.8%) and 5 males (10.5%). The distribution of males and females in the groups was homogeneous (P = 0.990). Female patients predominated in both PTC (+) and (-) CM1 groups. The average age in the PTC (+) CM1 group was 46.27 ± 8.51 years, and in the PTC (-) CM1 group, it was 35.37 ± 9.84 years (**Table 1**).

 Table 1. The mean age of patients according to groups and mean cerebellar tonsillar and obex distances relative to the McRae line (mean ± standard deviation)

	Group			
	Control $(n = 49)$	PTC (+) CM1 (<i>n</i> = 11)	PTC (-) CM1 (<i>n</i> = 38)	<i>P</i> -value
Cerebellar tonsillar distance relative to McRae line (mm)	-1.20 ± 2.42	$8.05\pm3.07\texttt{*}$	$7.98\pm3.30\texttt{*}$	< 0.001
Obex distance relative to McRae line (mm)	$\textbf{-7.47} \pm 1.83$	$0.59\pm 6.31 \texttt{*}$	$-1.12 \pm 5.20*$	< 0.001
Age (years)	37.82 ± 10.53	$46.27 \pm 8.51*$	35.37 ± 9.84	0.009

*Statistical difference compared to the normal group. Abbreviation: PTC, pseudotumor cerebri; CM1, Chiari malformation type 1.

In this study, PTC was present in 11 out of 49 CM1 cases (22.45%). In the PTC (-) CM1 group, nine (23.7%) had syringomyelia, while in the PTC (+) CM1 group, five (45.5%) had syringomyelia. There were no cases of syringomyelia in the control group (0%). The rate of syringomyelia in both PTC (+) and (-) CM1 groups was higher than in the control group (P < 0.05). Although the rate of syringomyelia was higher in PTC (+) CM1 patients, there was no statistically significant difference between the two groups (P > 0.05).

In this study, the position of the cerebellar tonsils in control patients was above the McRae line $(-1.20 \pm 2.42 \text{ mm})$. For PTC (+) and (-) CM1 patients, the position of cerebellar tonsils and obex according to the McRae line was significantly lower than that of the control group (P < 0.001) (**Table 1**). While PTC (+) CM1 patients had

cerebellar tonsils and obex positioned lower than PTC (-) CM1 patients, there was no statistically significant difference in the distance of cerebellar tonsils and obex according to the McRae line between PTC (+) and (-) CM1 patients (P = 0.997, 0.437, respectively).

In patients with syringomyelia, the distance of cerebellar tonsillar and obex according to the McRae line was significantly lower than in the group without syringomyelia (P < 0.001, 0.004, respectively) (**Table 2**). In this study, ROC analysis was performed to evaluate the value of the distance of cerebellar tonsils and obex according to the McRae line in patients with and without syringomyelia. According to the McRae line, the distance of cerebellar tonsils in patients without syringomyelia had a cut-off value of ≤ 2.6 mm and the obex distance had a cut-off value of ≤ -5.5 mm (**Table 3**). There was no statistically significant difference in distinguishing between patients with and without syringomyelia in terms of the distance of obex according to the McRae line (P = 0.1185).

 Table 2. Cerebellar tonsillar and obex distances relative to the McRae line between groups with and without syringomyelia (mean ± standard deviation)

	Group		
	Syringomyelia (+) (<i>n</i> = 14)	Syringomyelia (-) (<i>n</i> = 84)	- P-value
Cerebellar tonsillar distance relative to McRae line (mm)	9.41 ± 4.09	2.39 ± 4.95	< 0.001
Obex distance relative to McRae line (mm)	-0.39 ± 5.11	$\textbf{-4.72} \pm 5.07$	0.004

 Table 3. ROC analysis of cerebellar tonsillar and obex distance values relative to the McRae line between cases with and without syringomyelia

Parameter	ROC [CI]	Р	Cut-off	Sensitivity	95% CI	Specificity	95% CI
Obex distance relative to McRae line (mm)	0.762 [0.666–0.843]	0.0001	≤-5.5	58.33	47.1–69.0	92.86	66.1–99.8
Cerebellar tonsillar distance relative to McRae line (mm)	0.835 [0.747–0.903]	< 0.0001	≤2.6	58.33	11.3–29.1	100.00	76.8–100.0

Abbreviation: CI, confidence interval.

4. Discussion

In the literature, as in this study, CM1 is reported to be more common in females ^[4-6]. The findings in this study are consistent with the literature, which indicates that CM1 generally causes symptoms in the third and fourth decades ^[4-6].

In the treatment protocol for CM1, posterior fossa decompression is performed, while in the PTC treatment protocol, ventriculoperitoneal shunt therapy is applied. For the complete resolution of symptoms and prevention of recurrence in patients with PTC and CM1 coexistence, both treatment procedures should be performed together ^[23]. Therefore, the importance of diagnosing PTC and CM1 coexistence is significant.

Aiken and colleagues observed cerebellar herniation of more than 5 mm in 9 out of 43 IIH patients (21%)^[23]. Johnston *et al.* reported that 6% of IIH patients had radiological criteria for CM1 (cerebellar herniation of more than 5 mm)^[24]. Banik *et al.* found that more than 2 mm of cerebellar ectopia was present in 24% of IIH patients, while more than 5 mm of cerebellar herniation was observed in 11% of patients ^[25]. Fagan and colleagues described the coexistence of CM1 with IIH and the difficulty of its treatment, defining it as Chiari Pseudotumor

Cerebri Syndrome^[26]. The percentage of PTC-CM1 coexistence in this study is similar to the result found by Aiken and colleagues^[23].

The coexistence of CM1 with syringomyelia in the PTC (-) and (+) CM1 groups is consistent with the literature's reported rate of 20%–72% for syringomyelia in CM1 ^[27]. To date, there is no other study on the prevalence of syringomyelia in PTC and CM1 coexistence.

Huang *et al.* and Işik *et al.* found the position of cerebellar tonsils to be located 1 and 2.9 mm above the McRae line, respectively, which is consistent with this study ^[28,29]. Aiken and colleagues found the distance of obex according to the McRae line to be lower in IIH patients (P < 0.01) ^[23]. They even observed that similar to CM1 cases, the obex in IIH patients who exhibited herniation with a hook-like protrusion into the cervical canal was significantly lower than in the control group. Therefore, they suggested that obex distance could be a discriminating factor in distinguishing patients with PTC and CM1 from those with only PTC ^[23]. In this study, although PTC (+) CM1 patients had cerebellar tonsils and obex positioned lower than PTC (-) CM1 patients, there was no statistically significant difference in the distance of cerebellar tonsils and obex according to the McRae line between PTC (+) and (-) CM1 patients (P = 0.997, 0.437, respectively). Therefore, it is believed that investigating the distance of cerebellar tonsils and obex according to McRae line may not provide a significant contribution to the diagnosis of PTC coexistence in CM1 patients. Aiken and colleagues may have come to a different conclusion due to the small sample size of five patients with PTC-CM1 coexistence, which is much smaller than the 11 patients in this study.

Bogdanov and colleagues found the inferior herniation of cerebellar tonsils according to the McRae line to be approximately 7.6 ± 1.5 mm in CM1 cases with syringomyelia, which is similar to this study ^[30].

5. Conclusion

The coexistence of PTC and CM1 is more common than previously estimated. Different treatment protocols for PTC-CM1 coexistence highlight the importance of establishing the diagnosis. In PTC (+) CM1 patients, cerebellar tonsils and obex are located lower compared to PTC (-) CM1 patients, and the rate of syringomyelia appears to be higher. However, no statistically significant difference is observed between the two groups. The main limitation of this study is that the diagnosis of PTC is supported by radiological images rather than the gold standard, which is the opening CSF pressure ^[15]. Another limitation is that while this study investigates the coexistence of PTC on the basis of CM1 cases, in some studies that were compared to, PTC cases was investigated in the context of CM1 coexistence ^[23-25]. Therefore, a direct comparison of the studies may not be entirely appropriate. To identify different radiological markers for the diagnosis of PTC-CM1 coexistence, more radiological imaging studies are needed.

Disclosure statement

The authors declare no conflict of interest.

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