ISSN: 2576-2842

Research Article

Journal of Gynecology & Reproductive Medicine

Congenital Syphilis and Medulloblastoma in A Paediatric Patient

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Submitted: 2024, Mar 20; **Accepted:** 2024, Apr 22; **Published:** 2024, Apr 30

Citation: Santiago-Reynoso J, García-González, O. G., Gaytan-Fernández, G. J., Zamarripa, S., Pérez-Villaseñor, M. (2024). Congenital Syphilis and Medulloblastoma in A Paediatric Patient. *J Gynecol Reprod Med, 8*(1), 01-07.

Abstract

Syphilis is a sexually transmitted disease in adults and is transferred intrauterine from mother to child. Syphilis has resurfaced worldwide with increasing numbers of cases being reported. This study shows a paediatric patient at the same time showed with a diagnosis of congenital syphilis (CS) and a diagnosis of medulloblastoma (MB). The patient is of interest as it has a diagnosis of intermediate risk medulloblastoma together with congenital syphilis. The patient's symptomatology corresponded with the effects of medulloblastoma (cervical pain, gait disturbance with latero-pulsion, headache, vomiting and irritability), although syphilis was confirmed on CCF (Cytochemistry Cephalorachid Fluid) biopsy and serum VDRL testing (Venereal Disease Research Laboratory), with few overt effects of syphilis, suggesting asymptomatic syphilis. The medulloblastoma was identified by cranial tomography, and treated surgically, followed by radiotherapy and follow-up chemotherapy. No matches are reported in the literature as in the case presented.

Keywords: Medulloblastoma, Congenital Syphilis, VDRL, Treponema Pallidum, Cytochemistry Cephalorachid Fluid

Introduction

Syphilis is a sexually transmitted infection caused by Treponema pallidum, with transplacental transmission and direct contact with the infectious injury. T. pallidum is capable of invading the nervous system within days after primary infection. Subsequent neurosyphilis may be symptomatic or asymptomatic, between the 1st and 2nd year after primary infection is identified as early, or late if it includes symptoms such as general paresis and tabes dorsalis. [1,2].

Maternal syphilis (MS) and congenital syphilis (CS) in Latin America and the Caribbean is a growing public health problem [3,4]. The prevalence of syphilis in pregnant women ranges from 0.1 to 7.0%, thus estimating 1.7 CS cases per-1000 live births in 2015. In Mexico between 2013 and 2017, CS cases increased from 43 to 121 respectively. Recently in the US, the US Centers for Disease Control and Prevention recorded 2148 cases of syphilis, 48.5% of which were concentrated in Texas and California, with a disproportionate burden in the black (746 cases) and Hispanic/Latino (637 cases) populations with the SC increasing (20.6 to 71.9) by 3.5 percent [5-9]. Presumed triggers include social factors where public health care and infrastructure does not cover the entire population, other conditions such as human behaviour, environmental changes, racial groups, economic status, adaptation and microbial changes which favour the increase in syphilis cases [10]. The CDC in the US estimated 7 million new cases of syphilis in 2024 [7]. In Mexico, social migration is also a factor in the increase of syphilis, especially in border areas, and should be taken up again as a public health problem of a disease that has resurfaced [10]. Herrera-Ortiz et al. focused on the prevalence of syphilis in pregnant women, reporting 0.26 and 2.3% [11]. In addition, infected infants (SC) with untreated infection may present with late clinical symptoms (>2 years), including the triad: interstitial keratitis, sensorineural hearing loss and notched central incisors (Hutchinson's teeth). Other late signs of CS include failure to thrive, arched (sabre) shins, painless swelling of the knees (Clutton's joints), frontal bossing, mulberry molars (multiple rudimentary, rounded enamel cusps affecting the first permanent

molars) and saddle nose (collapsed nasal bridge); in this light it is important to be prepared to monitor and detect cases from late manifestations. Paediatric and adult cases of syphilis may overlap with other conditions.

Medulloblastoma (MB) is the most common malignant tumour of the central nervous system (CNS) in the paediatric age group, with prevalence in males (1.5:1) under the age of 10 years [9, 12]. It is unknown whether environmental factors are causative for medulloblastoma, but it is recognised that hereditary factors represent the proven cause. Thus germline pathological variants of the APC, BRCA2, PALB2, PTCH1, SUFY and TP53 genes explain 5.9% of MB. In 1022 patients, they had no cancer predisposition syndrome, but MB was associated with basal cell nevus syndromes (Goorlin-Gotz syndrome); Turcott-type 2, Li-Fraumeni, neurofibromatosis type 1 and 2, Fanconi anaemia and Nijmegen [13-15]. Also, for MB it is related to the presence of JC virus (human neurotropic polyomavirus).

This paper reports the case of Congenital Syphilis (CS) as a finding during MB diagnostic tests, coinciding an infectious disease and the detection of medulloblastoma. The most recent statistics in Mexico for congenital and acquired syphilis cases in 2022 and 2023 are reported to be increasing.

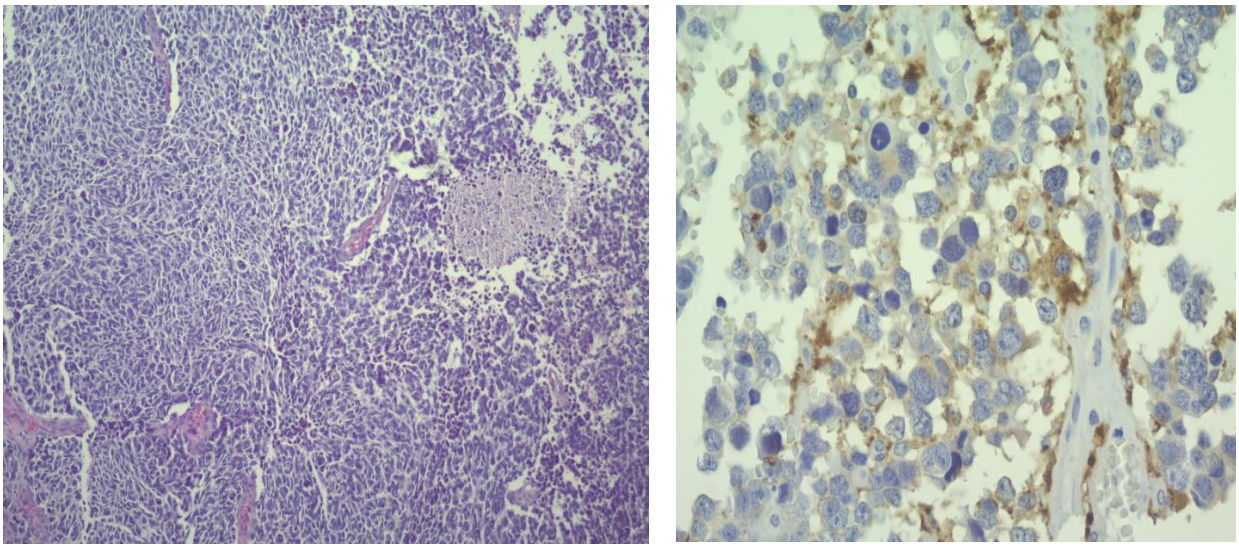
Clinical Case

A 3-year-old male patient of the fourth gestation, originally from and residing in the State of Zacatecas, presented with clinical symptoms of two weeks' evolution characterised by cervical pain, gait disturbance with latero-pulsion, headache, vomiting and irritability. From the physical examination, he responded neurologically to questioning with language expected for his age, symmetrical pupils of 2 mm, adequate response to light stimuli, gaze tracking and apparently adequate vision when identifying objects; mild cervical pain was confirmed. He moved all 4 limbs with preserved strength.

Simple CT scan of the skull showed triventricular ventriculomegaly and a tumour occupying the right cerebellar hemisphere that collapsed into the 4th ventricle. The lesion showed hypodense and apparently calcified areas.

Cranial MRI: The tumour was found to be approximately 6x5 cm in greatest diameter. Perilesional oedema, obliteration of the 4th ventricle causing triventricular dilatation, the lesion is heterogeneously reinforced with contrast.

Immunohistochemical pathology: showed weak Synaptophysin; GFP: Negative, S-100 Negative, Vimentin Negative. Positive for malignant neoplastic cells compatible with medulloblastoma with areas of anaplasia (**Figure 1**).



a) Confirmation of medulloblastoma with areas of anaplasia. Magnification 400x

b) Synaptophysin showed positive staining in the cytoplasm observed as dark brown areas. Magnification 400x

Figure 1: Immunohistochemical pathology.

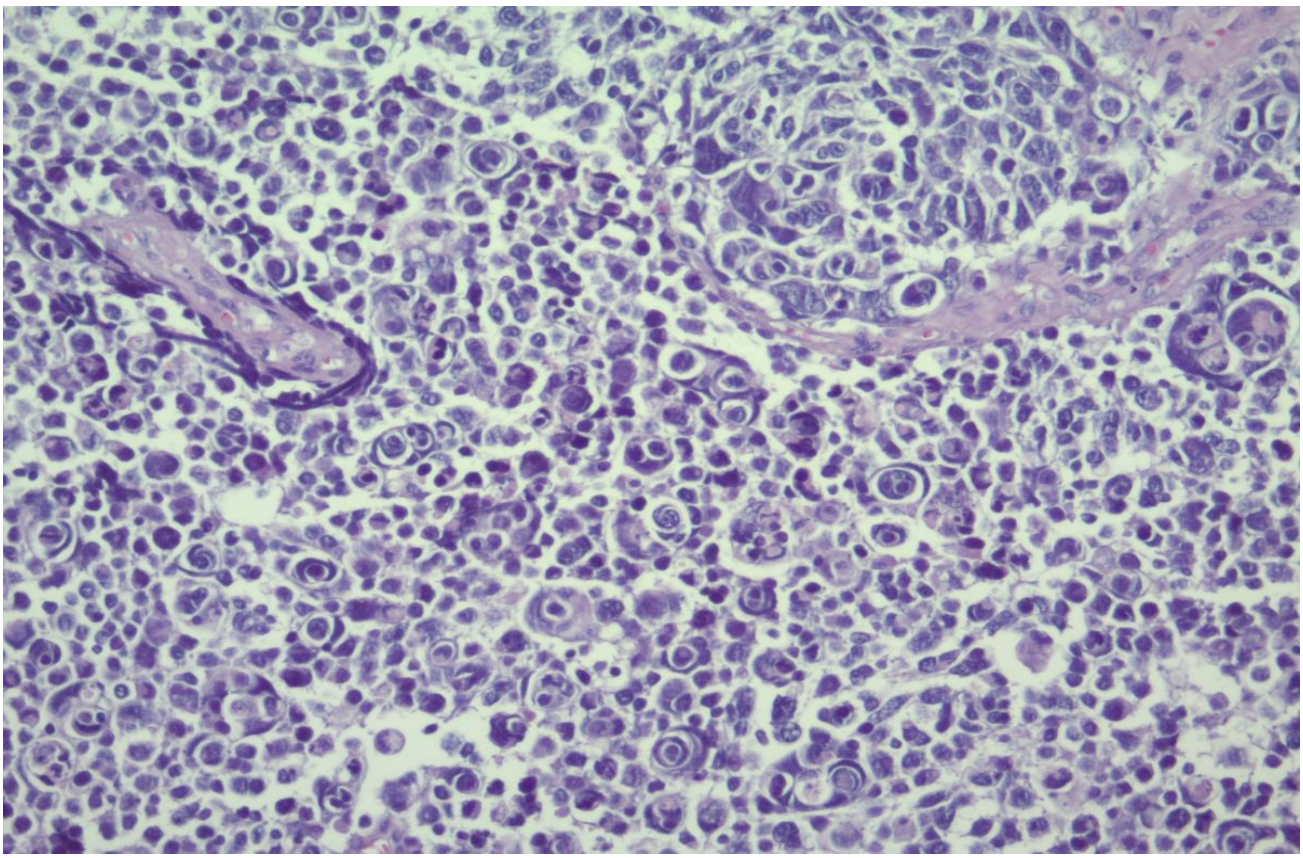


Figure 2: Enlarged view of the histopathology of meduloblastoma. Characteristic medulloblastoma with round or oval nuclei, hyperchromatic, prominent nucleoli, low cytoplasmic differentiation. Magnification 400x.

In the diagnostic approach protocol that led to the performance of lumbar puncture in search of malignant cells and cerebrospinal fluid cytochemistry (CSF). The characteristics were pH: 7.50, Colour: Red; Appearance: Turbid; Coagulability: Negative; Cell count (Leucocytes 1520/mL; Mononuclear 65%; Polymorphonuclear 35%; Erythrocytes 0.014x106 / mL; Glucose 55 mg/dL; Protein 600 mg/dL; VDRL Positive; Pandy's Test: Negative; Chlorides 115 mmo/L.

Anti-Treponema pallidum antibodies: Positive, VDRL 33.25 with a second positive VDRL determination 1:512. Anti-HIV (HIV) antibodies negative.

Test	Results
Cranial tomography	Triventricular ventriculomegaly + tumour in right cerebellar hemisphere
Cranial MRI	Positive tumour 6x5 cm
Immunohistochemical pathology	Synaptophysin: Weak GFP: Negative Vimentin: Negative Cells: (+) Medulloblastoma
Cytochemistry Cephalorachid Fluid	pH: 7.50 Colour: Red Appearance: Shady Coagulability: Negative Cell Counting: Leucocytes 1520/mL Mononuclear 65% Polymorphonuclear 35% Erythrocytes 0.014 x 10^6 /mL Glucose 55 mg/dL Protein 600 mg/dL VDRL: Positivo Pandy´s test: Negativo Chlorides: 115 mmol/L
Serum	VDRL: Positive
Antibodies	*Treponema pallidum*: Positive VDRL 33.25 anti-HIV Negative.

GFP = green fluorescent protein, VDRL = Venereal Disease Research Laboratory. venereal disease research laboratory. HIV= human immunodeficiency virus

Table 1: Analysis on biopsy specimen and cerebrospinal fluid in the infant

The child's mother reported positive serum VDRL with initiation and completion of antibiotic treatment as a fifth pregnancy at 6 months of development.

As shown, the tests of the MB approach and search for malignant cells, the cerebrospinal fluid was VDRL positive, as well as the serum VDRL positive. The treponemal test was confirmatory and based on a positive non-treponemal test (serum VDRL) + positive treponemal test + positive VDRL in CSF, the diagnosis was integrated as confirmed congenital neurosyphilis in addition to MB. Treatment was started with crystalline penicillin G 3 million every 4 hours for 10 days and radiotherapy was scheduled.

The audiological assessment: Impedance impedance studies were carried out, bilateral Jerjes As curves, ipsilateral stapedial acoustic reflex present at all frequencies assessed bilaterally. Otacoustic emissions due to distortion products, finding adequate intermodulation response and signal to noise (S/N) greater than 6 dB at all frequencies evaluated bilaterally, corroborated by normal hearing bilaterally.

Ophthalmological assessment showed visual acuity in both eyes, light rejection and fixation of objects. Fundus: Both eyes have round papilla, regular borders, physiological excavation, central vessels, neuroretinal ring preserved, macula without alterations, peripheral retina without alterations. SA Euchromic conjunctiva, transparent cornea, anterior chamber formed, regular and reactive iris, transparent crystalline lens.

The patient underwent occipital craniotomy, catheter removal and tumour removal 12 days after diagnosis, following resolution of obstructive hydrocephalus. Three months after surgery, bone marrow biopsy and CSF were negative for neoplastic cells.

Based on previous studies, the case was diagnosed with intermediate risk MB and confirmed congenital syphilis (CS). The patient was started on antibiotic treatment for syphilis, occipital craniotomy of the tumour and radiotherapy to the neuraxis was initiated in two phases including weekly vincristine treatment for 4 weeks and oral temozolamide as radiosensitisers.

The registration of CS cases in the last two years (2022 and 2023) in Mexico is shown in Table 2, which summarises the registration of congenital and acquired syphilis in Mexico [16] indicating an increase in this infection and probably an increase in CS cases due to the observed number of males and females with acquired syphilis (Table 2 and Annex 1).

Week	Congenital Syphilis (CIE-10[a] Rev. A50)			Acquired Syphilis (CIE-10[a] Rev. A51-A53)		
	2023 Accumulated		2022 Accumulated	2023 Accumulated		2022 Accumulated
	M	F		M	F	
5	41	26	83	614	555	729
35	333	292	559	7,054	5,617	10,251
48	427	382	802	9,787	7,583	14,518

Modified from Epidemiological Surveillance Week 5,35 and 48, 2023.Register of the 33 entities of the Mexican Republic. M=Male, F=Female

Table 2: Cases of congenital and acquired syphilis up to epidemiological week 5,35 and 48, 2023 compared to 2022

Discussion

Congenital syphilis should be detected early at birth based on maternal prenatal information and care, which would reduce the risk in the couple, as well as timely medical care for the parents. In the case described, although neonatal screening was performed, there was omission of the infectious condition of syphilis, as well as omission of information on the part of the mother, or complete ignorance of the infection. The result was the detection of congenital syphilis as a diagnostic finding of medulloblastoma in the paediatric patient.

Cases of sexually transmitted infections are registered by the health system in maternal and child clinics and hospitals worldwide. The described case of congenital syphilis with evidence of neurosyphilis coincides with the development and diagnosis of medulloblastoma. MB has been linked to JC virus (human neurotropic polyomavirus), however, it is unknown how neuroinfection with syphilis could coexist with MB [17,18]. It has been demonstrated in tumour lines developed in animal models suggesting that neurosyphilis could be an environment conducive to MB, and few clinical manifestations of congenital syphilis.

Late complications reported in the literature such as sensorineural deafness, interstitial keratitis, periostitis, prominent frontal bones, depression of the nasal bridge, deformity with anterior curvature of the tibiae (sabre tibiae), late arthritis of the knees (Clutton joints), dental anomalies (Hutchinson teeth). Bologna, in the case were not identified, this could reflect a latency stage of syphilis even though the mother and infant were brought to treatment with penicillin G [19]. The mother is expected to be effective in preventing vertical transmission of syphilis considering that the mother has a new pregnancy, a situation that could lead to a new case of CS [20-26].

The case is of interest as it has a diagnosis of intermediate risk medulloblastoma together with congenital syphilis. This case should be followed up, as it has undergone surgical treatment, radiotherapy and chemotherapy for MB, as well as antibiotic treatment for congenital syphilis.

The registration of congenital syphilis and acquired syphilis in Mexico as documented, different regions and globally there is an increase in the number of cases of syphilis, therefore, it is essential to resume registration strategies and medical care of these patients, treating them could limit their spread insocial mobility that leads to the increase of sexually transmitted infectious diseases [27].

Acknowledgments

The authors would like to thank the Hospital Regional de Alta Especialidad del Bajío for clinical support, immunohistopathology testing and the surgical service for access to tissue and imaging.

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27. Dirección General de Epidemiologia Número 48 | Volumen 40 | Semana 48 | Del 26 de noviembre al 2 de diciembre del 2023

Annex I: Cases by federal entity of sexually transmitted diseases up to epidemiological week 35 of 2023 for congenital syphilis.

ENTIDAD FEDERATIVA	Sífilis Congénita§ CIE-10ª Rev. A50				Sífilis Adquirida CIE-10ª Rev. A51-A53				Infección Gonocócica del Tracto Genitourinario CIE-10ª Rev. A54.0-A54.2			
	2023			2022	2023			2022	2023			2022
	Sem.	Acum. M	Acum. F	Acum.	Sem.	Acum. M	Acum. F	Acum.	Sem.	Acum. M	Acum. F	Acum.
Aguascalientes	-	5	4	20	3	83	106	425	-	6	8	16
Baja California	-	31	46	63	25	458	520	1 058	1	52	35	130
Baja California Sur	-	1	1	7	3	160	93	220	2	26	3	20
Campeche	-	1	1	2	-	51	25	82	2	9	12	32
Coahuila	-	23	16	32	23	139	244	250	4	43	85	136
Colima	-	13	15	15	13	184	110	193	3	34	24	25
Chiapas	-	-	-	1	6	175	73	230	6	109	372	329
Chihuahua	3	26	20	36	11	111	189	379	5	97	25	198
Ciudad de México	-	6	5	9	46	1 142	153	526	6	106	29	71
Durango	-	2	2	3	4	56	74	71	-	3	26	11
Guanajuato	1	9	4	27	24	326	460	829	-	32	144	129
Guerrero	-	2	3	-	2	93	54	165	1	40	230	366
Hidalgo	-	-	1	-	2	44	29	61	2	9	5	42
Jalisco	3	39	34	76	31	476	957	858	1	114	303	805
México	-	3	6	13	14	208	116	331	5	145	545	988
Michoacán	1	6	14	17	6	81	185	283	4	19	13	48
Morelos	-	-	-	-	6	49	52	68	1	15	16	76
Navarit	-	11	3	24	12	156	243	181	2	117	59	175
Nuevo León	-	34	18	45	22	716	147	493	4	150	25	243
Oaxaca	-	-	-	-	10	101	31	84	2	39	180	260
Puebla	-	1	3	15	3	258	61	287	3	35	199	457
Querétaro	-	-	1	3	1	54	45	65	-	5	9	7
Quintana Roo	-	-	-	-	6	475	130	613	-	48	114	98
San Luis Potosí	-	36	16	35	6	157	140	303	1	25	24	57
Sinaloa	-	16	15	8	17	227	343	334	5	18	16	34
Sonora	-	36	40	44	10	206	447	613	4	21	61	131
Tabasco	-	-	-	-	4	48	11	125	6	88	548	941
Tamaulipas	-	16	15	38	12	316	285	609	4	108	175	417
Tlaxcala	-	-	-	1	2	35	7	40	-	17	49	56
Veracruz	-	7	4	9	9	197	173	194	7	173	813	1 309
Yucatán	-	7	3	9	18	223	73	200	2	19	2	9
Zacatecas	-	2	2	7	-	49	41	81	3	23	28	88
TOTAL	8	333	292	559	351	7 054	5 617	10 251	86	1 745	4 177	7 704

§FUENTE: SINAVE/DGE/Salud 2023. Sistema Especial de Vigilancia Epidemiológica, Información preliminar de casos confirmados.
FUENTE: SINAVE/DGE/Salud 2022. Información preliminar, incluye casos probables.

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