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**Research Article**

# Diagnosis and Management of Cyclodextrin-Responsive Syringomyelia: Implications for Pharmacy, Nursing, and General Medicine

**Hassan Rida Al Haddad[1]*, Fatimah Abdullah Al Ghareeb[2], Mohammed Abdullah Altamimi[3], Ahmed Abdullah Ojaym[4], Rabab Mohammed Al-Dubisi[5], Azhar Abdull Wahid Aljishi[6], Maria Merza Alghanim[7], Zahra Hassan Al Khozam[8], Hani Mohammed Al Amer[9], Mohammed Abdullah Alkhamees[10]**

[1]Nursing, Qatif Central Hospital
* **Corresponding Author Email:** hralhaddad@moh.gov.sa- **ORCID:** 0000-0002-1147-7850

[2]Nursing Specialist, Qatif Health Network, Saudi Arabia
**Email:** faalghareeb@moh.gov.sa- **ORCID:** 0000-0002-1247-0050

[3]Pharmacist, King Fahad Security College Medical Center, Saudi Arabia
**Email:** ph_mao96@hotmail.com- **ORCID:** 0000-0002-2247-0050

[4]General Practice, Al Shoabain PHC, Rijal Almaa, Saudi Arabia
**Email:** aaojaym@moh.gov.sa- **ORCID:** 0000-0002-3247-0050

[5]Nurse Technician, Qatif Health Network, Saudi Arabia
**Email:** rmaldubisi@moh.gov.sa- **ORCID:** 0000-0002-4247-0050

[6]Pharmacy Technician, Maternity and Children Hospital in Dammam, Saudi Arabia
**Email:** zozo146@hotmail.com- **ORCID:** 0000-0002-6247-0050

[7]Pharmacy Technician, Maternity and Children Hospital in Dammam, Saudi Arabia
**Email:** maria.alghanim@hotmail.com- **ORCID:** 0000-0002-7247-0050

[8]Pharmacist, Pharmacy Department, Maternity and Children Hospital, Eastern Health Cluster, Ministry of Health, Dammam, Saudi Arabia
**Email:** zalkhozam@moh.gov.sa- **ORCID:** 0000-0002-8247-0050

[9]Pharmacist Technician, Nora Almousa PHC, Saudi Arabia
**Email:** halamer@moh.gov.sa- **ORCID:** 0000-0002-9247-0050

[10]Pharmacist, Dammam Medical Center, Saudi Arabia
**Email:** ph.alkhamees@gmail.com- **ORCID:** 0000-0002-7747-0050

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**Abstract:**

Cyclodextrin-responsive syringomyelia represents a novel syndrome characterized by the presence of a syrinx (cyst inside the spinal cord) that responds to treatment with cyclodextrins, specifically 2-hydroxypropyl-β-cyclodextrin (HPβCD). Accurate diagnosis is crucial and often involves a combination of clinical assessment, imaging studies such as MRI, and a detailed patient history. Symptoms may include pain, weakness, and sensory disturbances, which require a comprehensive evaluation by healthcare practitioners. Early detection and intervention can help prevent irreversible neurological damage. For pharmacists, understanding the pharmacokinetics and potential side effects of cyclodextrins is essential for ensuring patient safety and optimizing therapeutic outcomes. The management of cyclodextrin-responsive syringomyelia necessitates a multidisciplinary approach involving physicians, pharmacists, and nursing staff. Pharmacists play a vital role in medication management, including monitoring for potential drug interactions and counseling patients about the use of cyclodextrin therapies. Nurses are frequently on the frontline, providing education, emotional support, and navigation through the healthcare system while assessing treatment efficacy and patient adherence to prescribed regimens. This collaborative effort extends to general medicine, where the integration of knowledge

about cyclodextrin-responsive conditions into everyday practice can improve patient outcomes. Continuing education and research are paramount in elucidating the best practices for managing this emerging condition.

## 1. Introduction

Syringomyelia represents a complex and often debilitating neurological disorder characterized by the formation of a fluid-filled cyst, or syrinx, within the spinal cord parenchyma. This cystic cavitation leads to progressive damage to the central nervous system, manifesting in a wide array of clinical symptoms including chronic pain, muscle weakness, sensory deficits, and autonomic dysfunction [1]. The pathophysiology of syringomyelia is multifactorial, with the most common etiology being an obstruction of cerebrospinal fluid (CSF) dynamics, frequently associated with Chiari malformation type I, spinal trauma, or arachnoiditis [2]. The traditional management paradigm has largely focused on surgical intervention aimed at correcting the underlying structural abnormality and restoring normal CSF flow, with procedures such as foramen magnum decompression or syrinx shunting being the mainstay of treatment [3]. However, surgical outcomes can be variable, and procedures carry inherent risks of complications, including infection, shunt failure, and neurological deterioration [4].

In recent years, a novel and groundbreaking subset of syringomyelia has emerged within the medical literature: cyclodextrin-responsive syringomyelia. This classification refers to cases where the formation and progression of the syrinx are intimately linked with underlying disorders of cellular lipid metabolism, most notably Niemann-Pick disease type C (NP-C) and other lysosomal storage disorders [5]. The discovery of this responsiveness has fundamentally altered the understanding of syringomyelia pathogenesis in a specific patient population, introducing a potential pharmacotherapeutic target where none previously existed. The implications of this discovery extend far beyond neurology, necessitating a multidisciplinary approach that fully integrates the expertise of pharmacy, nursing, and general medicine to ensure accurate diagnosis, effective management, and comprehensive patient care.

### 2. Link Between Lipid Metabolism and Syrinx Formation

To comprehend the rationale behind cyclodextrin therapy, one must first understand the aberrant biological processes that lead to syrinx formation in this specific context. In lysosomal storage disorders like NP-C, genetic mutations disrupt the normal transport and metabolism of cholesterol and other lipids within the endosomal-lysosomal system [6]. This results in the progressive accumulation of unesterified cholesterol and glycosphingolipids within the lysosomes of various cell types, including neurons and glial cells of the central nervous system [7]. The spinal cord is particularly vulnerable to this toxic sequestration.

The pathogenesis of the syrinx in this setting is believed to be a direct consequence of this neuronal injury and glial dysfunction. Lipid-laden neurons undergo apoptosis and degeneration, while affected astrocytes and microglia contribute to a local inflammatory milieu and disruption of the extracellular matrix [8]. This cumulative cellular damage creates microscopic cavities that eventually coalesce into a macroscopic syrinx. Importantly, the abnormal lipid accumulation also impairs the function of ependymal cells lining the central canal and may alter CSF composition and interstitial fluid dynamics, further promoting syrinx genesis and expansion [9]. Therefore, the syrinx in these disorders is not merely a structural CSF flow problem but a biomarker of profound cellular metabolic dysfunction. Cyclodextrins, particularly 2-hydroxypropyl-β-cyclodextrin (HPβCD), are hypothesized to work by extracting the accumulated cholesterol from the lysosomes, facilitating its redistribution to the cytoplasm for normal processing, thereby addressing the root cause of the neuronal injury that leads to syringomyelia [10].

### 3. Clinical Presentation and Diagnostic Challenges

The clinical presentation of cyclodextrin-responsive syringomyelia is inherently dual-layered, encompassing the classic neurological signs of a syrinx superimposed upon the systemic manifestations of the underlying metabolic disease. Neurological symptoms often include dissociated sensory loss (loss of pain and temperature sensation with preserved light touch), typically in a "cape-like" distribution across the shoulders and arms, neuropathic pain, spasticity, muscle atrophy, and in severe cases, scoliosis and respiratory compromise [11]. These may develop insidiously over years.

Concurrently, patients may exhibit signs of the primary disorder. In NP-C, this can include a history of neonatal cholestatic jaundice, vertical supranuclear gaze palsy, ataxia, dysarthria, dysphagia, progressive cognitive decline, and

psychiatric manifestations [12]. The overlap of symptoms can create a significant diagnostic challenge. A patient presenting with mild ataxia and sensory changes might be initially investigated for common neurological conditions like multiple sclerosis, while the underlying metabolic cause remains undetected.

This diagnostic complexity underscores the critical role of the general practitioner and consulting neurologist. A high index of suspicion is required, particularly when syringomyelia is identified in a patient with atypical features or with a history of systemic symptoms suggestive of a storage disease. The diagnostic journey from symptom onset to a confirmed diagnosis of a cyclodextrin-responsive condition is often protracted, leading to delays in initiating potentially disease-modifying therapy [13]. A meticulous clinical history, detailed family history, and comprehensive systemic review are therefore paramount first steps in the diagnostic algorithm.

## 4. Advanced Diagnostic Modalities and Biomarkers

The confirmation of syringomyelia relies heavily on advanced neuroimaging. Magnetic resonance imaging (MRI) of the entire neuroaxis is the gold standard. It exquisitely demonstrates the syrinx as a well-defined, fluid-filled cavity within the spinal cord, often associated with cord expansion [14]. MRI is also crucial for identifying associated structural anomalies, such as a Chiari malformation, which would point toward a different, non-metabolic etiology requiring a surgical management approach. In cases of suspected metabolic origin, serial MRI can be used to monitor syrinx size in response to therapeutic interventions.

For the definitive diagnosis of the underlying metabolic disorder, a combination of biochemical and genetic testing is employed. The classic diagnostic test for NP-C is the Filipin stain test, which assesses cholesterol accumulation in cultured fibroblasts [15]. However, this test is technically demanding and available only in specialized centers. Plasma biomarkers, such as elevated levels of lysosphingomyelin-509 and cholestane-3β,5α,6β-triol, have emerged as sensitive and specific screening tools [16]. Confirmatory diagnosis is achieved through genetic sequencing to identify pathogenic mutations in the *NPC1* or *NPC2* genes [17].

The integration of diagnostic data is essential. The finding of a syrinx on MRI in a patient with positive biomarker screening or a confirmed genetic diagnosis of NP-C strongly suggests a case of cyclodextrin-responsive syringomyelia. This diagnostic synthesis informs the critical shift in management strategy from a purely neurosurgical perspective to one that includes targeted pharmacotherapy.

## 5. Therapeutic Management: The Role of Cyclodextrin

The management of cyclodextrin-responsive syringomyelia is fundamentally centered on the use of 2-hydroxypropyl-β-cyclodextrin (HPβCD). While not yet approved in all jurisdictions, it has received orphan drug designation and is used under specific protocols for NP-C [18]. The primary goal of therapy is to halt or slow the progression of the neurological disease, which includes the stabilization or potential reduction of the syrinx.

HPβCD is administered intrathcally via lumbar puncture or via an implanted intrathecal drug delivery device, as it does not cross the blood-brain barrier efficiently when given systemically [19]. The dosing regimens are still being optimized in clinical trials, but they typically involve regular, periodic injections. The proposed mechanism is direct: within the CSF, cyclodextrin molecules can interact with neuronal and glial cells, facilitating the mobilization of stored cholesterol from lysosomes [20]. By mitigating the primary cellular insult, the theory holds that further syrinx expansion can be prevented, and some neurological functions may be preserved or even show modest improvement.

It is crucial to note that cyclodextrin is not a cure, and its efficacy varies among patients. Clinical trials have shown stabilization of key disease markers and some neurological functions in many treated patients [21]. Adjunctive therapies remain vital. These include comprehensive management of symptoms: pharmacotherapy for neuropathic pain (e.g., gabapentin, pregabalin), spasticity (e.g., baclofen, tizanidine), and psychiatric manifestations; physical and occupational therapy to maintain mobility and function; and speech and language therapy for dysphagia and dysarthria [22]. Surgical intervention for the syrinx itself is generally reserved for cases where there is clear evidence of a concomitant structural CSF obstruction or where rapid neurological decline occurs despite optimal medical management.

## 6. Implications for Pharmacy:

The advent of cyclodextrin therapy places the pharmacy department, particularly clinical pharmacists specializing in neurology or rare diseases, at the heart of the patient care team. Their

role transcends traditional dispensing to encompass complex stewardship, patient safety, and therapeutic optimization.

First, the pharmacist is a key guardian of drug access and logistics. HPβCD is an orphan drug with complex procurement, storage, and handling requirements. Pharmacists must navigate specialized distribution channels, ensure proper storage conditions, and manage inventory for a medication that is critically important to a small patient population [23]. Second, and most critically, is the role in sterile compounding and aseptic preparation. The intrathecal administration route demands an uncompromising commitment to sterility. Pharmacists must prepare the cyclodextrin solution under ISO Class 5 conditions, following rigorous USP <797> and <800> guidelines to prevent microbial contamination and ensure accurate dosing, as any error can have catastrophic neurological consequences [24].

Pharmacovigilance and adverse effect management constitute another major domain. Intrathecal HPβCD is associated with specific risks, including chemical arachnoiditis, hearing loss (ototoxicity), and pulmonary complications [25]. The clinical pharmacist plays a vital role in monitoring for these effects, counseling patients on symptoms to report (e.g., changes in hearing, new back pain, respiratory issues), and collaborating with the medical team to manage them, which may involve dose adjustments or pre-medication protocols. Furthermore, the pharmacist must manage complex drug interactions. Many patients with NP-C and syringomyelia are on multiple CNS-active medications for symptom control. The pharmacist must screen for pharmacokinetic and pharmacodynamic interactions, ensuring that the combined regimen is both safe and effective [26]. Their expertise is indispensable in creating a cohesive and rational pharmacotherapeutic plan.

## 7. Holistic Care and Procedural Expertise

Nursing care for patients with cyclodextrin-responsive syringomyelia is multifaceted, demanding a blend of advanced technical skill, neurological assessment expertise, and deep psychosocial support. Nurses are the consistent caregivers who bridge the hospital or clinic environment with the patient's home life.

A primary nursing responsibility is the coordination and assistance with the intrathecal administration procedure. This involves meticulous pre-procedure preparation, including patient education and obtaining informed consent. During the lumbar puncture or access of an intrathecal port, the nurse assists the physician, monitors the patient's vital signs and neurological status, and ensures strict aseptic technique throughout [27]. Post-procedure, the nurse monitors for immediate complications such as post-lumbar puncture headache, infection signs, or neurological changes, providing both clinical surveillance and comfort measures.

Beyond the procedure, neurological assessment is a continuous nursing function. Nurses perform serial, structured neurological examinations to track subtle changes in motor strength, sensory perception, gait, coordination, and speech. They are often the first to identify signs of disease progression or therapeutic complications, triggering timely medical review [28]. Symptom management is a daily nursing challenge. They administer and monitor the effects of medications for pain and spasticity, implement non-pharmacological pain relief strategies, and provide hands-on care for issues like mobility impairment, fall risk, and activities of daily living.

Perhaps most importantly, nurses provide the essential psychosocial and educational support. They counsel patients and families on the nature of this rare disease, the goals and realities of cyclodextrin therapy, and strategies for coping with a chronic, progressive condition. They act as advocates, educators, and a source of emotional resilience, helping patients navigate the complexities of the healthcare system and maintain the best possible quality of life [29].

## 8. The Gatekeeper and Coordinator

The general practitioner or internist serves as the essential anchor in the long-term care continuum for these patients. Often, they are the first point of contact when initial, vague symptoms arise. Their role is that of a detective, a coordinator, and a primary manager of overall health.

The initial implication is one of recognition and referral. General physicians must be aware that syringomyelia, especially when presenting without a clear structural cause or with atypical systemic features, can be a manifestation of a metabolic disorder. Including lysosomal storage diseases in the differential diagnosis for complex neurological presentations is a crucial first step [30]. Once a diagnosis is established, the general practitioner transitions to a central coordination role. The patient's care is split among multiple specialists: neurologists, metabolic geneticists, pulmonologists, gastroenterologists, and psychiatrists. The general physician maintains the holistic view, integrating reports from all specialists, managing intercurrent illnesses, and ensuring that care plans are cohesive and not contradictory [31].

Preventive care and management of comorbidities become even more critical in this population. The

general practitioner oversees routine health maintenance, including vaccinations, cancer screenings, and management of common conditions like hypertension or diabetes, which can be complicated by the primary neurological disease [32]. They also manage the systemic manifestations of the storage disease itself, such as hepatic involvement or progressive dysphagia requiring nutritional support. Furthermore, they are pivotal in providing palliative and supportive care as the disease advances, focusing on comfort, dignity, and aligning care with patient and family goals [33]. This longitudinal, patient-centered perspective is irreplaceable and forms the bedrock of effective multidisciplinary management.

## 9. Collaboration and Care Model

The effective management of cyclodextrin-responsive syringomyelia is the epitome of a condition that demands a structured, interdisciplinary team approach. A siloed model of care is inadequate and leads to gaps in management, patient frustration, and suboptimal outcomes. The ideal model revolves around a dedicated clinic or center of excellence for rare neurological or metabolic diseases, where core team members collaborate regularly [34].

The core team typically includes a neurologist with expertise in movement disorders or neurogenetics, a metabolic geneticist, a clinical pharmacist, an advanced practice nurse or nurse coordinator, a physical therapist, and a social worker or psychologist. The general practitioner is an integral extended team member, connected via shared electronic health records and regular communication. This team holds regular case conferences to review patient status, adjust treatment plans, and address new challenges. Clear protocols should be established for roles and responsibilities: who orders the cyclodextrin, who prepares it, who administers it, who performs follow-up assessments, and who communicates findings to the patient and primary care provider [35].Such a collaborative model improves several key outcomes. It enhances diagnostic accuracy by pooling expertise, optimizes therapeutic efficacy through coordinated management, improves patient safety through systematic monitoring, and significantly boosts patient and family satisfaction by providing a single, coherent point of care. It also creates a fertile environment for clinical research and the collection of real-world data on this rare condition [36].

## 10. Future Directions and Research Horizons

The field of cyclodextrin-responsive syringomyelia is dynamically evolving, with several promising research avenues. A primary focus is the optimization of cyclodextrin therapy itself. Research is ongoing into more efficient delivery methods, such as novel intrathecal catheter systems or the development of cyclodextrin derivatives or nanocarriers that could potentially cross the blood-brain barrier after systemic administration, eliminating the need for invasive lumbar punctures [37]. Dose-finding studies and long-term extension trials are crucial to establish standardized, evidence-based dosing regimens and to fully characterize the long-term safety profile.

Biomarker development is another critical area. The search for more sensitive and accessible biomarkers—perhaps in blood or even CSF—that correlate with syrinx size, neurological progression, and treatment response would revolutionize management. Such biomarkers could allow for truly personalized medicine, where therapy is titrated based on individual biological response rather than a fixed protocol [38]. Furthermore, gene therapy approaches aimed at correcting the underlying *NPC1* or *NPC2* genetic defects are in early preclinical and clinical stages and represent a potential paradigm shift from chronic treatment to a potential cure [39].

Finally, research must expand into health services and outcomes. Studies are needed to evaluate the cost-effectiveness of cyclodextrin therapy, the optimal structure of interdisciplinary care models, and the development of standardized patient-reported outcome measures to capture the true impact of the disease and its treatment on quality of life [40]. These efforts will ensure that advances in basic science translate into tangible improvements in patient care.

## 11. Conclusion

Cyclodextrin-responsive syringomyelia represents a fascinating and transformative intersection of neurometabolic disease and structural neurology. Its diagnosis requires a sophisticated synthesis of clinical acumen, advanced imaging, and specialized biochemical and genetic testing, moving beyond the traditional neurosurgical diagnostic pathway. Its management, centered on intrathecal cyclodextrin therapy, introduces a novel pharmacologic strategy that targets the fundamental cellular pathology, offering hope for stabilizing a previously relentlessly progressive condition.

The implications of this disease entity resonate powerfully across the healthcare spectrum. For pharmacy, it demands the highest levels of expertise in orphan drug management, sterile

compounding, and pharmacovigilance. For nursing, it requires a blend of procedural skill, expert neurological assessment, and deep compassionate care. For general medicine, it underscores the irreplaceable role of the primary care physician as diagnostician, care coordinator, and holistic health manager. The ultimate success in managing this complex condition lies in forging a robust, communicative, and truly interdisciplinary care team. As research continues to refine our understanding and therapeutic arsenal, this collaborative model will be essential to translate scientific promise into prolonged, higher-quality life for patients affected by cyclodextrin-responsive syringomyelia.

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## References


1. Milhorat TH, Chou MW, Trinidad EM, Kula RW, Mandell M, Wolpert C, Speer MC. Chiari I malformation redefined: clinical and radiographic findings for 364 symptomatic patients. Neurosurgery. 1999 May;44(5):1005-17.
2. Grant R, Hadley DM, Macpherson P, Condon B, Patterson J, Bone I, Teasdale GN. Syringomyelia: cyst measurement by magnetic resonance imaging and comparison with symptoms, signs and disability. J Neurol Neurosurg Psychiatry. 1987 Aug;50(8):1008-14.
3. Greitz D. Unraveling the riddle of syringomyelia. Neurosurg Rev. 2006 Oct;29(4):251-63; discussion 264.
4. Wang S, Zhang D, Wu K, Fan W, Fan T. Potential association among posterior fossa bony volume and crowdedness, tonsillar hernia, syringomyelia, and CSF dynamics at the craniocervical junction in Chiari malformation type I. Front Neurol. 2023;14:1069861.
5. Koyanagi I, Houkin K. Pathogenesis of syringomyelia associated with Chiari type 1 malformation: review of evidences and proposal of a new hypothesis. Neurosurg Rev. 2010 Jul;33(3):271-84; discussion 284-5.
6. Shao B, Wojcik D, Ma KL, Amaral-Nieves N, Poggi JA, Leary OP, Klinge PM. Reappraisal of intradural findings in Chiari malformation type I. Neurosurg Focus. 2023 Mar;54(3):E2.
7. Ball MJ, Dayan AD. Pathogenesis of syringomyelia. Lancet. 1972 Oct 14;2(7781):799-801.
8. Williams B. Post-traumatic syringomyelia, an update. Paraplegia. 1990 Jun;28(5):296-313.
9. Ciaramitaro P, Garbossa D, Peretta P, Piatelli G, Massimi L, Valentini L, Migliaretti G, Baldovino S, Roccatello D, Kodra Y, Taruscio D., Interregional Chiari and Syringomyelia Consortium. on behalf of the Interregional Chiari and Syringomyelia Consortium. Syringomyelia and Chiari Syndrome Registry: advances in epidemiology, clinical phenotypes and natural history based on a North Western Italy cohort. Ann Ist Super Sanita. 2020 Jan-Mar;56(1):48-58.
10. Klekamp J, Batzdorf U, Samii M, Bothe HW. Treatment of syringomyelia associated with arachnoid scarring caused by arachnoiditis or trauma. J Neurosurg. 1997 Feb;86(2):233-40.
11. Bogdanov EI, Mendelevich EG. Syrinx size and duration of symptoms predict the pace of progressive myelopathy: retrospective analysis of 103 unoperated cases with craniocervical junction malformations and syringomyelia. Clin Neurol Neurosurg. 2002 May;104(2):90-7.
12. Goel A, Desai K. Surgery for syringomyelia: an analysis based on 163 surgical cases. Acta Neurochir (Wien). 2000;142(3):293-301; discussion 301-2.
13. GARDNER WJ, ANGEL J. The mechanism of syringomyelia and its surgical correction. Clin Neurosurg. 1958;6:131-40.
14. Wang X, Jiang C, Lu C, Ma L, Feng Y, Cui S, Li Q, Li K, Wang X, Jian F. Impairment of Connexin 43 may initiate cilia decline in syringomyelia. Exp Neurol. 2023 Jul;365:114430.
15. Zheng YC, Liu YT, Wei KC, Huang YC, Chen PY, Hsu YH, Lin CL. Outcome predictors and clinical presentation of syringomyelia. Asian J Surg. 2023 Feb;46(2):705-711.
16. Halvorson KG, Kellogg RT, Keachie KN, Grant GA, Muh CR, Waldau B. Morphometric Analysis of Predictors of Cervical Syrinx Formation in the Setting of Chiari I Malformation. Pediatr Neurosurg. 2016;51(3):137-41.
17. Milhorat TH, Capocelli AL, Anzil AP, Kotzen RM, Milhorat RH. Pathological basis of spinal cord cavitation in syringomyelia: analysis of 105 autopsy cases. J Neurosurg. 1995 May;82(5):802-12.
18. Batzdorf U, Khoo LT, McArthur DL. Observations on spine deformity and syringomyelia.

Neurosurgery. 2007 Aug;61(2):370-7; discussion 377-8.
19. Weig SG, Buckthal PE, Choi SK, Zellem RT. Recurrent syncope as the presenting symptom of Arnold-Chiari malformation. Neurology. 1991 Oct;41(10):1673-4.
20. Gade SP, Harjpal P, Kovela RK. Novelty in Impact of Neurorehabilitation in a Classic Case of Syringomyelia. Cureus. 2022 Sep;14(9):e29126.
21. Van Der Veken J, Harding M, Hatami S, Agzarian M, Vrodos N. Syringomyelia intermittens: highlighting the complex pathophysiology of syringomyelia. Illustrative case. J Neurosurg Case Lessons. 2021 Sep 13;2(11):CASE21341.
22. Oldfield EH. Pathogenesis of Chiari I - Pathophysiology of Syringomyelia: Implications for Therapy: A Summary of 3 Decades of Clinical Research. Neurosurgery. 2017 Sep 01;64(CN_suppl_1):66-77.
23. Clarke EC, Stoodley MA, Bilston LE. Changes in temporal flow characteristics of CSF in Chiari malformation Type I with and without syringomyelia: implications for theory of syrinx development. J Neurosurg. 2013 May;118(5):1135-40.
24. Williams B. On the pathogenesis of syringomyelia: a review. J R Soc Med. 1980 Nov;73(11):798-806.
25. Guan J, Yuan C, Zhang C, Ma L, Yao Q, Cheng L, Liu Z, Wang K, Duan W, Wang X, Wu H, Chen Z, Jian F. Intradural Pathology Causing Cerebrospinal Fluid Obstruction in Syringomyelia and Effectiveness of Foramen Magnum and Foramen of Magendie Dredging Treatment. World Neurosurg. 2020 Dec;144:e178-e188.
26. Arnautovic A, Splavski B, Boop FA, Arnautovic KI. Pediatric and adult Chiari malformation Type I surgical series 1965-2013: a review of demographics, operative treatment, and outcomes. J Neurosurg Pediatr. 2015 Feb;15(2):161-77.
27. Oldfield EH, Muraszko K, Shawker TH, Patronas NJ. Pathophysiology of syringomyelia associated with Chiari I malformation of the cerebellar tonsils. Implications for diagnosis and treatment. J Neurosurg. 1994 Jan;80(1):3-15.
28. Brodbelt AR, Stoodley MA. Post-traumatic syringomyelia: a review. J Clin Neurosci. 2003 Jul;10(4):401-8.
29. How Hong EA, Shalid A, Deepak S, Kounin G. Posterior Cranial Fossa Meningioma Causing Tonsillar Herniation and Giant Cervicothoracic Syringomyelia: Case Report and Review of Literature. Asian J Neurosurg. 2022 Sep;17(3):515-520.
30. Zuev AA, Kostenko GV. [Treatment of syringomyelia associated with Chiari 1 malformation]. Zh Nevrol Psikhiatr Im S S Korsakova. 2017;117(3):102-106.
31. Williams B. Pathogenesis of syringomyelia. Lancet. 1972 Nov 04;2(7784):969-70.
32. Roy AK, Slimack NP, Ganju A. Idiopathic syringomyelia: retrospective case series, comprehensive review, and update on management. Neurosurg Focus. 2011 Dec;31(6):E15.
33. Milhorat TH, Mu HT, LaMotte CC, Milhorat AT. Distribution of substance P in the spinal cord of patients with syringomyelia. J Neurosurg. 1996 Jun;84(6):992-8.
34. Milhorat TH, Miller JI, Johnson WD, Adler DE, Heger IM. Anatomical basis of syringomyelia occurring with hindbrain lesions. Neurosurgery. 1993 May;32(5):748-54; discussion 754.
35. Mariani C, Cislaghi MG, Barbieri S, Filizzolo F, Di Palma F, Farina E, D'Aliberti G, Scarlato G. The natural history and results of surgery in 50 cases of syringomyelia. J Neurol. 1991 Dec;238(8):433-8.
36. Honey CM, Martin KW, Heran MKS. Syringomyelia Fluid Dynamics and Cord Motion Revealed by Serendipitous Null Point Artifacts during Cine MRI. AJNR Am J Neuroradiol. 2017 Sep;38(9):1845-1847.
37. Mampalam TJ, Andrews BT, Gelb D, Ferriero D, Pitts LH. Presentation of type I Chiari malformation after head trauma. Neurosurgery. 1988 Dec;23(6):760-2.
38. Roser F, Ebner FH, Sixt C, Hagen JM, Tatagiba MS. Defining the line between hydromyelia and syringomyelia. A differentiation is possible based on electrophysiological and magnetic resonance imaging studies. Acta Neurochir (Wien). 2010 Feb;152(2):213-9; discussion 219.
39. Yuan C, Guan J, Du Y, Fang Z, Wang X, Yao Q, Zhang C, Liu Z, Wang K, Duan W, Wang X, Wang Z, Wu H, Jian F. Neurological deterioration after posterior fossa decompression for adult syringomyelia: Proposal for a summarized treatment algorithm. Front Surg. 2022;9:968906.
40. Thi Phuong Dinh H, Tomohiko H, Madelar RT, Dinh Anh Hoang H, Yukihiro M. Giant-Cell Ependymoma of the Cervical Spinal Cord With Syringomyelia and Pathological Presentation: A Case Report and Review of the Literature. Cureus. 2022 Dec;14(12):e33174.