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Bronchial Atresia

Bronchial atresia is a rare congenital condition marked by the interruption of a bronchial segment, most often at the segmental or subsegmental level. This interruption leads to the accumulation of mucus in the obstructed bronchial stump—referred to as a bronchocele or mucocele—and hyperinflation of the distal lung parenchyma. This hyperinflation occurs due to collateral ventilation from nearby alveoli, as air enters the obstructed segment through pores of Kohn, canals of Lambert, or channels of Martin, but cannot exit efficiently. The segment becomes overinflated and may appear more lucent on radiographs, often prompting further evaluation. Although the condition is typically discovered incidentally, particularly in adolescents and young adults, it can also present with recurrent pulmonary infections, dyspnea, cough, hemoptysis, or even pneumothorax.

Computed tomography has become the gold standard for diagnosing bronchial atresia. Radiographically, the condition often appears as a perihilar mass with adjacent hyperlucency. On high-resolution CT, hallmark findings include a branching or tubular mucocele with surrounding emphysematous lung. The characteristic "finger-in-glove" sign is frequently observed due to mucoid impaction within a dilated bronchus. In a study reviewing 23 confirmed cases, every patient exhibited both a mucocele and hyperinflation of the surrounding parenchyma. These findings were consistently unilateral, most commonly affecting the apicoposterior segment of the left upper lobe, followed by the right lower and upper lobes. Additional findings such as subsegmental atelectasis, bronchial wall thickening, and small cysts may occur, though less frequently.

Histologically, bronchial atresia reveals a blind-ending bronchus filled with mucus, surrounded by hyperinflated alveoli. There is typically no acute inflammation unless secondary infection has occurred. Pathological examination of surgical specimens frequently confirms emphysematous change, mucus plugging, and bronchiectasis. Occasionally, the lesion coexists with other congenital lung anomalies such as congenital pulmonary airway malformation (CPAM), bronchopulmonary sequestration, and lobar emphysema. These associations suggest a common developmental pathway or timing in embryogenesis, although precise causative mechanisms remain speculative.

There is considerable debate regarding the management of bronchial atresia, particularly in asymptomatic individuals. While some centers advocate for surgical resection even in asymptomatic patients to prevent long-term complications such as infection or damage to adjacent lung tissue, others favor a conservative approach with careful monitoring. A pediatric cohort followed over a median of 29 months demonstrated that conservative management could be safe and effective in selected patients. Of the 12 children monitored

without surgery, only one became symptomatic during follow-up. This finding supports the position that surgery should be reserved for patients who develop significant symptoms or complications.

In contrast, adult cases are more likely to be managed surgically, especially if there is diagnostic uncertainty or persistent symptoms. Surgical intervention can include lobectomy, segmentectomy, or wedge resection, depending on the extent and location of the lesion. Recent advances in thoracoscopic techniques have made minimally invasive resection a viable and often preferred option. Case reports of thoracoscopic sublobar resections in adults have shown good outcomes, with resolution of symptoms such as cough, recurrent fever, or dyspnea. Importantly, three-dimensional CT reconstruction has emerged as a valuable tool in surgical planning by clearly delineating the absence of bronchial branches and helping define resection margins.

Operative data from adult cases indicate that thoracoscopic resection is safe, with minimal blood loss and short hospital stays. Common postoperative complications include air leaks and minor pneumothorax, typically managed conservatively. Histologic analysis after surgery often confirms the diagnosis and may reveal additional findings such as infection, bronchiectasis, or associated anomalies. In one surgical series, 5 out of 8 patients had postoperative complications, all of which were minor and resolved with conservative measures. This supports the notion that while surgery carries some risk, it is generally well tolerated and often curative in symptomatic patients.

Despite its rarity, bronchial atresia may be underrecognized. Improved imaging technology has led to more frequent incidental discoveries, particularly during evaluation for unrelated conditions. The diagnostic process relies heavily on high-resolution imaging, and in some cases, bronchoscopy may aid in detecting a blind-ending bronchus. However, a normal bronchoscopy does not rule out bronchial atresia, especially if the lesion is peripheral. Clinical awareness and radiologic expertise are essential for accurate diagnosis and appropriate treatment planning.

Given the association of bronchial atresia with other congenital pulmonary abnormalities, a multidisciplinary approach is often beneficial. Radiologists, pulmonologists, thoracic surgeons, and pediatric specialists must collaborate to determine the best course of action for each patient. In children and adolescents, conservative management with structured follow-up can be effective, particularly in asymptomatic cases. In adults or patients with recurrent infections or significant functional impairment, surgical resection remains the standard of care.

Ultimately, bronchial atresia represents a spectrum of clinical presentations, from benign incidental findings to complex symptomatic cases requiring surgical intervention. The decision to operate must balance the risks of surgery with the potential for disease progression or complications. Long-term prognosis is excellent in most cases, whether managed conservatively or surgically. However, close clinical monitoring and patient education are critical, especially for those who forgo surgical treatment. Early recognition

and individualized management strategies offer the best outcomes for patients with this uncommon but important congenital anomaly.

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Nutcracker Syndrome

Nutcracker Syndrome (NCS) in children presents a diagnostic and therapeutic challenge due to its nonspecific symptoms, varied clinical presentation, and lack of standardized criteria. Despite its rarity, recent studies offer increasing insight into its pathophysiology, diagnostic approaches, and treatment strategies.

NCS refers to the compression of the left renal vein (LRV), most commonly between the aorta and the superior mesenteric artery (SMA)—a configuration termed anterior NCS. Less commonly, the LRV may be compressed posteriorly between the aorta and vertebral column, or even have dual compression in cases of vascular anomalies like circumaortic veins. In pediatric populations, anterior NCS is overwhelmingly dominant. Compression results in renal venous hypertension, leading to the development of collateral venous pathways and subsequent clinical symptoms.

The most frequent presenting symptom in children is hematuria, observed in approximately 55% of cases, followed closely by proteinuria in nearly half of patients. Both microscopic and macroscopic hematuria have been documented, with the former often discovered incidentally. Flank pain is less common, found in roughly one in five cases, despite being traditionally associated with the syndrome. These symptoms are believed to arise from venous hypertension causing rupture of small varices in the renal collecting system, or from immune-mediated mechanisms triggered by abnormal venous flow. Additionally, fatigue, orthostatic intolerance, and dizziness have been linked to autonomic nervous system involvement.

Orthostatic proteinuria in children is often attributed to positional changes affecting renal hemodynamics. A compelling finding is the role of a low body mass index (BMI), which reduces mesenteric fat that otherwise supports the SMA, increasing the likelihood of renal

vein compression. Some studies even suggest resolution of symptoms with weight gain, supporting a conservative approach in many pediatric patients.

Diagnostically, Doppler ultrasonography (DUS) is the frontline noninvasive tool, favored for its accessibility and safety. In pediatric NCS, peak velocity ratios of the LRV between the aortomesenteric and hilar portions greater than 4.7 to 5.0 are considered indicative. However, the technique is operator-dependent and may yield variable results in children due to patient cooperation and anatomical factors.

Cross-sectional imaging like computed tomography angiography (CTA) and magnetic resonance angiography (MRA) adds anatomical detail. MRA, in particular, offers a radiation-free alternative with high accuracy in assessing the SMA angle and LRV compression. In one study, pediatric NCS patients had a significantly lower SMA angle (mean ~26.5°) and a smaller aortomesenteric distance (~3.3 mm) compared to controls, reinforcing MRA's diagnostic utility.

Invasive studies, such as venography with pressure gradient measurement, are considered the gold standard but are reserved for ambiguous or refractory cases due to their invasiveness. They are more often used in surgical candidates, especially when conservative management fails after extended monitoring.

Treatment in children is typically conservative. The literature consistently supports this approach, with more than 86% of pediatric cases managed non-surgically and nearly 95% of these showing symptom resolution or improvement. Conservative management includes observation, weight gain, and, in some cases, pharmacologic therapy like angiotensin-converting enzyme inhibitors to manage associated orthostatic symptoms.

Surgical interventions, including LRV transposition, renal autotransplantation, and endovascular stenting, are reserved for persistent or severe cases, particularly when complications such as varicocele, pelvic congestion, or progressive pain are evident. However, their application in children is limited due to long-term risks, including stent migration and the potential need for reintervention.

Autonomic dysfunction in NCS has recently gained attention. A case-control study demonstrated that over half of the pediatric patients experienced orthostatic symptoms, primarily dizziness and fatigue. Holter monitoring revealed altered heart rate variability, suggestive of autonomic imbalance. These findings reinforce the systemic implications of LRV compression beyond renal manifestations.

Despite growing research, the overall quality of pediatric NCS studies remains limited, with most evidence derived from case reports or small case series. This hampers the establishment of standardized diagnostic algorithms and outcome benchmarks. Nevertheless, the literature increasingly emphasizes a diagnostic pathway beginning with DUS, followed by MRA when needed, and cautious use of invasive diagnostics. A trial of conservative treatment with close follow-up is generally endorsed before considering surgical options.

In conclusion, Nutcracker Syndrome in children is a multifaceted condition marked by variable symptoms, often subtle or nonspecific, and requiring a tailored approach. High clinical suspicion, especially in cases of unexplained hematuria or proteinuria, is key. Noninvasive imaging remains central to diagnosis, and most cases can be managed without surgery. However, ongoing research is essential to clarify its natural history, refine diagnostic criteria, and optimize management strategies, especially in symptomatic or refractory cases.

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Hypertrophied Nerves in Hirschsprung's Disease

Hypertrophied nerves play a pivotal role in the diagnosis and understanding of Hirschsprung’s disease (HD), serving as both a diagnostic hallmark and a reflection of the underlying neuroanatomical disruption. HD is defined by the congenital absence of ganglion cells in the distal bowel, with submucosal nerve hypertrophy often emerging as a secondary hallmark due to the proliferation of extrinsic cholinergic nerves in the aganglionic segment.

The histological triad—absence of ganglion cells, presence of hypertrophic nerves, and abnormal acetylcholinesterase (AChE) activity—remains the gold standard for diagnosis. However, the role and reliability of hypertrophied nerves have been subject to scrutiny and evolution across studies.

A key point established in one 2016 study is that hypertrophied nerve fibers (defined as >40 μm in diameter) are not uniformly present in all cases of HD. Particularly in long-segment HD and total colonic aganglionosis, as well as in neonates and premature infants, hypertrophy may be absent. The study found that the absence of hypertrophied nerve fibers in an aganglionic biopsy predicted a transition zone proximal to the rectosigmoid colon, with a specificity of 77.3%. This highlights that while nerve hypertrophy supports the diagnosis, its absence—especially when combined with aganglionosis—may suggest a more extensive disease and requires further attention in surgical planning.

Another study from 2023 emphasizes the relationship between hypertrophic nerves and the transition zone (TZ), a histopathologically abnormal yet ganglionated segment located between aganglionic and normal bowel. Histological markers of TZ include submucosal nerve hypertrophy, myenteric hypoganglionosis, and partial aganglionosis. The identification of hypertrophied nerves within the TZ suggests that this region is not only histologically abnormal but may also be functionally compromised. Surgical precision in identifying the proximal extent of the TZ is crucial, as residual TZ tissue post-surgery may lead to obstructive symptoms.

Calretinin immunohistochemistry (IHC) has become an increasingly favored adjunct in identifying ganglion cells and evaluating the TZ. Recent studies demonstrate calretinin's reliability in clearly distinguishing aganglionic from ganglionic bowel. Notably, the 2024 Heidelberg study reports that switching from AChE histochemistry to calretinin IHC improved diagnostic confidence, reduced the need for repeat biopsies, and enabled earlier definitive surgical intervention. The strength of calretinin IHC lies in its consistent staining patterns and independence from patient age—a critical advantage over AChE staining, which is unreliable in neonates due to immature cholinergic innervation.

The role of calretinin is further emphasized in a 2021 institutional review, which demonstrated that calretinin staining was always positive in the presence of ganglion cells and always negative in aganglionic samples, regardless of nerve hypertrophy or biopsy depth. This underscores its utility not only in diagnosis but also in evaluating whether hypertrophied nerves correspond to functional abnormalities, as hypertrophy alone does not equate to pathology if ganglion cells are present and calretinin is positive.

More recent developments in digital pathology and artificial intelligence are enhancing diagnostic accuracy. A 2023 study introduced deep learning models capable of detecting ganglion cells and hypertrophic nerves in histological slides with over 90% accuracy. This AI-based approach aids in standardizing diagnosis, reducing interobserver variability, and identifying TZ features such as coexisting ganglion cells and hypertrophied nerves—regions requiring extra scrutiny due to potential functional compromise.

However, challenges remain. A 2023 study reviewing inconclusive full-thickness biopsies found that re-evaluation using both hematoxylin and eosin (HE) and IHC resolved only a fraction of the inconclusive cases, with most remaining non-diagnostic. This points to persistent ambiguity in the histopathological criteria and the need for more robust, perhaps integrative, diagnostic protocols combining histology, IHC, AI, and clinical context.

Additionally, the concept of the "shore break" (SB)—an endoscopic marker for the transition from peristaltic to non-peristaltic bowel—was recently correlated with the histopathological TZ. A 2023 surgical pathology study demonstrated that in all examined cases, the SB coincided with histologic features of the TZ, including nerve hypertrophy. This finding offers a functional correlate to histologic abnormalities and suggests a potentially valuable intraoperative tool for guiding resection margins.

In practice, hypertrophied nerves alone are insufficient for diagnosis without correlating evidence of aganglionosis. Their diagnostic value increases when viewed alongside absent ganglion cells and other markers like calretinin negativity or AChE activity. Moreover, while hypertrophy is a common feature in classic HD, its absence—particularly in certain subtypes or younger infants—should prompt consideration of disease extent and histologic variants rather than immediately excluding HD.

In conclusion, hypertrophied nerves in HD represent both a diagnostic clue and a histologic signature of the abnormal neurodevelopment that defines the disease. Their presence, distribution, and relationship to ganglion cells must be interpreted in the broader context of age, disease subtype, biopsy technique, and staining method. Advances in IHC and AI tools continue to refine this interpretive framework, but the complexity of HD pathology demands continued vigilance, multidisciplinary communication, and tailored surgical decision-making to ensure optimal outcomes.

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