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Case Report

SUCCESSFUL RESOLUTION OF NUTCRACKER SYNDROME WITH 3D PRINTED PEEK EXTRAVASCULAR STENT IN AN ADOLESCENT BOY

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SUMMARY – Three-dimensional printed polyetheretherketone (PEEK) extravascular stent was applied to treat a 14-year-old boy with nutcracker syndrome. Digital subtraction angiography revealed a segment of the left renal vein (LRV) with reduced contrast filling immediately before its inflow into the inferior vena cava, and high-pressure gradient. The three-dimensional reconstruction model demonstrated that the LRV and the duodenum were contracted at the aortomesenteric angle, resulting in LRV compression from the abnormal high-level duodenal compartment. When duodenum courses between the abdominal aorta and superior mesenteric artery (duodenal interposition), the LRV entrapment occurs even at <90 aortomesenteric degrees. Three-dimensional printed PEEK extravascular stent was chosen to elevate the superior mesenteric artery and lower the duodenum position, thus relieving LRV compression. This extravascular application has significant advantages over open surgery, endovascular stenting and artificial vessel procedures with expanded polytetrafluoroethylene. It provides better cellular vitality by ensuring soft tissue proliferation. By reducing external acceleration and centrifugal force, a three-dimensional printed PEEK extravascular stent reduces adverse side effects. Such a stent has a distinctive personalized design, good stiffness, and durability that allows blood vessel growth, preventing stent migration and thrombosis. Therefore, it is suitable for both adult and pediatric patients. According to the abdominal ultrasound and multi-slice computed tomography scan, the postoperative follow-up results were satisfactory one year after surgery. The patient felt well, the blood flow in the LRV was not obstructed, and the blood flow velocity was average. The external stent was in place.

Key words: *Nutcracker syndrome; Three-dimensional printing; Polyetheretherketone; Extravascular stent; Laparoscopy*

Introduction

Nutcracker syndrome (NCS) is caused by an impeded outflow from the left renal vein (LRV) into the inferior vena cava due to an aberrant narrow-angle between the abdominal aorta (AA) and the superior mesenteric artery (SMA) or between the AA and the spine[1-3]. NCS is an often missed diagnosis due to its

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variability of symptoms such as hematuria, proteinuria, left flank/abdominal pain, pelvis congestion in females, or left-side varicocele in males. Doppler ultrasonography (DUS), computed tomography (CT), magnetic resonance imaging (MRI) and phlebography are the standard imaging techniques for the diagnosis of NCS. To the best of our knowledge, we report on the first European three-dimensional (3D) printed polyetheretherketone (PEEK) extravascular stent application in a child.

Case Report

A 14-year-old boy with NCS and a history of constant and intense periumbilical pain (pain scale, 8-9) for the last 24 months was overviewed for surgical treatment. All clinical examinations and possible psychogenic upgrades were insufficient to explain the cause of pain, including autoimmune thyroiditis as comorbidity. Only microhematuria and orthostatic proteinuria were found. Compression of LRV was presumed by DUS and MRI, as digital subtraction angiography (DSA) of the LRV showed that a segment of reduced contrast filling was detected immediately before inflow into the inferior vena cava (IVC), and a high LRV-IVC pressure gradient was measured (6.2 mm Hg). After percutaneous transluminal angioplasty of the final segment of the LRV, the renocaval pressure gradient decreased from 6.2 mm Hg to 3.7 mm Hg, resulting in immediate pain relief. The pain recurred after 2 weeks of the procedure.

Minimal probe pressure provided precise visualization of the LRV, SMA, and AA without substantial compression of these vessels. CT angiography showed that the aortomesenteric angle (AMA) was 95 degrees. However, contrast-enhanced CT and DUS results suggested that the LRV was still compressed. In supine position, the anteroposterior diameter ratio and the peak velocity (PV) ratio of LRV (hilar to aortomesenteric) were 4.1 (9.1 mm to 2.2 mm) and 16.4 (180 cm/s to 11 cm/s), respectively. No abnormality was found in the bilateral spermatic vein. 3D reconstruction model disclosed that the LRV and the duodenum were contracted at AMA, resulting in LRV compression from the abnormal high-level duodenal compartment (Fig. 1, left panel). 3D printed PEEK extravascular stent (3DP-EXVS) was chosen to elevate the SMA and lower the duodenum position, thus relieving compression.

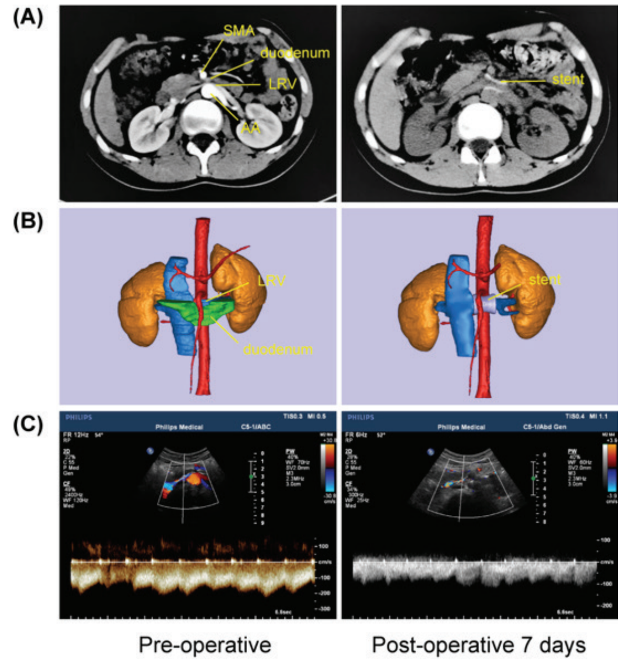

Fig. 1. Imaging comparisons before and 7 days after three-dimensional printed extravascular stenting: (A) computed tomography; (B) three-dimensional model reconstruction; (C) Doppler ultrasound.

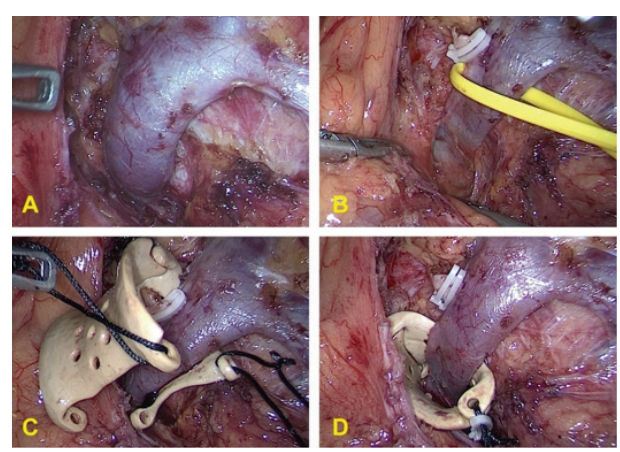

Fig. 2. Intraoperative photographs demonstrate surgical procedure for extravascular stenting: (A) exposure of the dilated left renal vein and gonadal vein; (B) release of the preaortic fibrous ring between the aorta and superior mesenteric artery; (C) placement of the stent around the left renal vein; (D) fixation of the stent to the surrounding fibrous tissue where the left renal vein was compressed, and immediate relief of the venous engorgement.

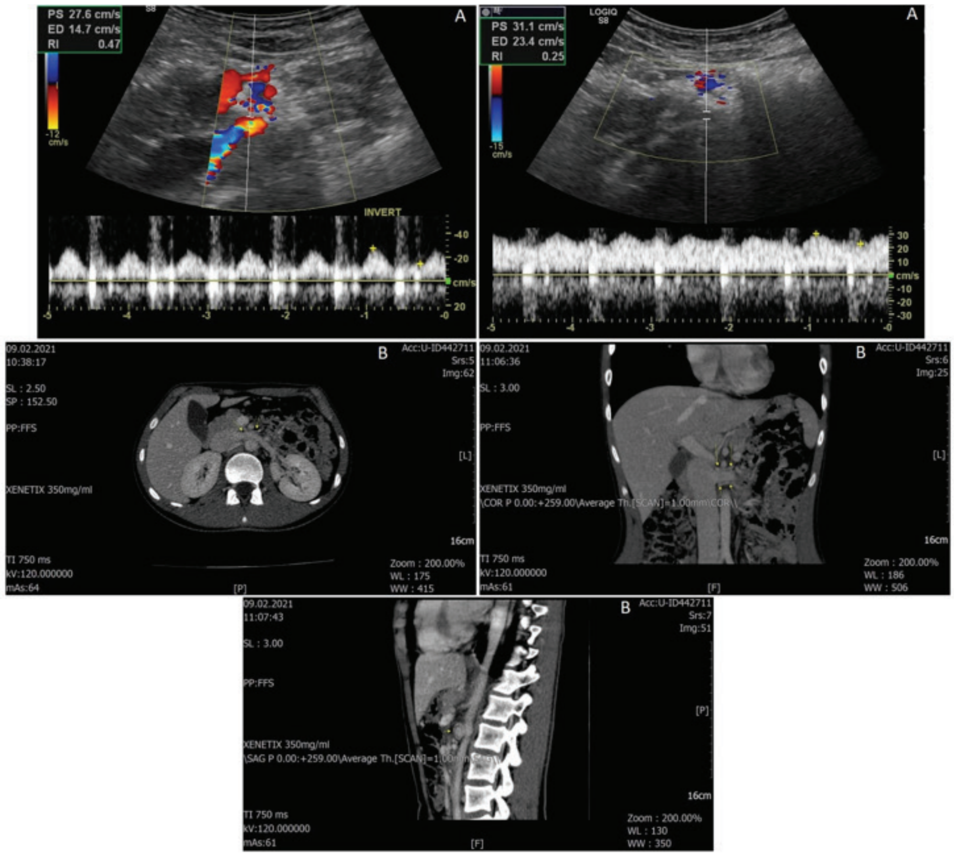

Fig. 3. One-year follow-up: Doppler ultrasound (A); and magnetic resonance imaging (B).

The patient was placed in the lateral decubitus position under general anesthesia. The operation was performed by laparoscopic technique through transabdominal approach. During the procedure, the LRV, duodenum, IVC, and AA were exposed successively. Although the AMA was not narrow, an anatomic variation of the duodenum and fibrous bundles between the AA and SMA was causing pressure. Besides, moderate stenosis of LRV caused by a narrow fibrous ring at the IVC entrance was found. Therefore, dissection of fibrous bundles was performed to free the duodenum, and the LRV was dissected out medially from the renal hilum to the IVC until it was completely mobilized. Complete resection of the narrow fibrous ring between AA and SMA was necessary. The LRV became flat after the fibrous ring had been resected, and a 3DP-EXVS was placed and bound to the narrowed portion of LRV to prevent blood vessel compression (Fig. 2). The left and adrenal veins remained intact. When the stent correct position was verified, the stent was fixed firmly into the surrounding fibrous tissue at the distal edge with a non-absorbable 4.0 Prolene suture to prevent its slipping.

The operation time, bleeding volume, and postoperative recovery time were 80 min, 10 mL, and 7 days, respectively. LRV anteroposterior diameter on postoperative CT decreased from 8.0 mm to 6.3 mm (hilar to aortomesenteric, 1.7 mm in total). DUS showed unobstructed blood flow within the stent and decreased PV of LRV at IVC entrance (120 cm/s). Even though high velocity remained in both veins, it showed significant improvement. The 3DP-EXVS was visualized on CT and DUS for possible stent migration (Fig. 1, right panel). The postoperative course was uncomplicated, and the patient noted that his abdominal pain completely faded away on day 6.

The 1-year postoperative follow-up showed satisfactory results according to the abdominal US and multislice computed tomography scan (Fig. 3). The patient felt well and performed all normal physical activities. Blood flow in the LRV was not obstructed and blood flow velocity was normal. The external stent was in place.

Discussion

Nutcracker syndrome is challenging to diagnose due to the lack of leading symptoms, and is often a diagnosis of exclusion. Clinical manifestations in patients with NCS vary from asymptomatic to pelvic congestion syndrome[1-5]. Left abdominal/flank pain, hematuria, and proteinuria are the most common symptoms in NCS. The left flank/abdominal pain or pelvic pain as the only manifestation of NCS is comparatively rare and can often be alleviated[6-10] (Table 1). The pain is related to LRV hypertension or pelvic congestion caused by NCS. Its exact incidence and prevalence are still unknown as the majority of patients are probably underdiagnosed. NCS is challenging to diagnose due to the lack of criteria and is often a diagnosis of exclusion of other causes compatible with the patient clinical features. The diagnosis of NCS relies on imaging results, including CT, DUS, MRI, and DSA of LRV. DUS is a practical, economical, and noninvasive technique that should be the first evaluation after NCS is suspected or when a large LRV diameter ratio is noted between its narrowed and distended portions on CT or MRI[1,11]. DUS can also accurately measure the speed and direction of blood flow, thus allowing us to observe its hemodynamic effects. Organic causes of LRV entrapment mainly include renal ptosis, a pancreatic mass, lack of retroperitoneal adipose tissue, and a narrow AMA. Earlier studies have reported that the mean AMA is 38-56 degrees; recent studies report <90 degrees in healthy subjects, with angles smaller than half in patients with NCS[12-15]. Despite this reported variability, smaller AMAs have shown high specificity and sensitivity in the diagnosis of NCS. However, when duodenum courses between the AA and SMA (duodenal interposition), the LRV entrapment occurs even at >90 degrees[16]. One should carefully check variations of normal anatomy on imaging before making the diagnosis or predicting the prognosis of NCS. Thus, in cases where noninvasive imaging diagnosis is difficult, phlebography and measurement of the venous pressure gradient between the LRV and IVC is recommended as a gold standard in the diagnosis of NCS[3].

The treatment of NCS is considered controversial. Conservative management is initially recommended for patients younger than 18 years. With physical development, juveniles may increase in fat tissue at the AMA that may relieve the LRV entrapment. One should consider invasive treatment for patients diagnosed with NCS in whom conservative therapy has remained ineffective for more than 24 months and in those patients in whom severe symptoms or worsening of laboratory/imaging results persist[4,17]. Surgical interventions, whether traditional open or minimally invasive surgery, mainly include transposition of the LRV or SMA, gonado-caval bypass, nephropexy, reno-caval reimplantation or kidney auto-transplantation, all of which are designed to relieve LRV hypertension[18,19]. Some surgical procedures have an increased risk of complications, such as venous thrombosis, cardiovascular incidents, anastomotic bleeding, and restenosis[4,20,21]. Endovascular stenting (EVS) is a minimally invasive option with fair results. However, some risks

Table 1. Clinical features and treatment modalities for nutcracker syndrome

Reference	Number of patients	Gender	Age (yrs)	Manifestations	Treatment	Outcome
Maloni *et al.*[6]	1	Female	50	Left flank pain	LOV to IVC transposition	Resolved
Agle *et al.*[7]	1	Female	59	Left iliac fossa and flank pain	EVS	Resolved
Altshuler *et al.*[8]	1	Female	25	Left vaginal wall and lower back pain	LRV transposition + embolization of LOV	Resolved
Taneja *et al.*[9]	1	Female	34	Left flank pain	EVS	Resolved
Boyer *et al.*[10]	1	Female	13	Perineal pain	Balloon venoplasty of LRV + embolization of LOV	Alleviated

LOV = left ovarian vein; IVC = inferior vena cava; EVS = endovascular stenting; LRV = left renal vein of serious complications, such as venous thrombosis, in-stent restenosis, and stent migration, still exist, especially in children and adolescents whose LRV diameters are continually changing during physical development[22-24]. A stent migration rate of 6.7% was reported after its placement[25]. However, although EVS treatment outcomes are encouraging, it is not a permanent solution for NCS.

In recent years, the expanded polytetrafluoroethylene (ePTFE) artificial vessel has been used as extravascular stenting for NCS because it involves minimal trauma, fewer complications, and a more straightforward procedure. Such laparoscopic procedure was therefore recommended as a better option for NCS surgical treatment in comparison to EVS[26].

An extravascular stent can act as a remedial measure for the migration of LRV endovascular stents in NCS[27]. Nevertheless, artificial blood vessels are not designed to serve as external vascular stents, and its single design hardly matches the diversity of anatomic features in the compressed portion of the LRV among individuals. The possibility of graft deformation, migration, and restenosis of the LRV still needs to be investigated. To solve these problems, our team proposed the technique of 3DP-EXVS to treat NCS[28,29].

The advantage of a 3D printed PEEK extravascular stent is a custom-made implant that matches better with the body's target structure. To avoid compression of the surrounding major vessels, the dumbbell-shaped stent should match the AA and SMA vascular walls and ought to be trimmed to leave space for the left and right renal arteries. Additionally, the growth/enlargement of the blood vessel in children should be taken into account in the stent design, and it is necessary to leave proper space for blood vessel growth. At present, PEEK implants are widely used in clinical practice, and the research on their biocompatibility continues to advance. We selected PEEK material because it has enough mechanical strength and density similar to the human body. Therefore, it has better cell viability and proliferation with soft tissue, as external acceleration and centrifugal force are less likely to cause adverse effects[30]. Compared to vascular displacement, EVS, or other extravascular stenting techniques, such as the placement of ePTFE grafts, 3D-printed stents exhibit more advantages in terms of distinctive design, good rigidity, and better rationality.

According to our experience, preoperative examination of NCS should be as complete as possible to make a proper diagnosis. Second, the LRV and the duodenum should be dissected and dissociated carefully. The fibrous bundles should be dissected out medially from the renal hilum to the IVC, and further complete resection of the narrow fibrous ring between AA and SMA is necessary. Third, the left gonadal vein and adrenal vein were usually left in place; however, in some cases, they were cut off because of difficulties with stent placement or severe varicocele. Last, the PEEK extravascular stent was inserted into the body through the camera port and placed around the compressed portion of the LRV.

Conclusion

Surgical treatment of NCS should be considered for children whose conservative therapy has remained inefficient for more than 24 months or in children with severe pain, debilitating their everyday life. We believe that treating patients with NCS by the laparoscopic placement of a 3D printed PEEK extravascular stent around the compressed LRV is safe and has advantages over EVS. 3DP-EXVS is an effective method of treating NCS in children as it allows them to grow/expand their blood vessels.

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Sažetak

USPJEŠNO LIJEČENJE SINDROMA ORAŠARA 3D TISKANOM PEEK EKSTRAVASKULARNOM PREMOSNICOM U ADOLESCENTNOG DJEČAKA

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Trodimenzionalno tiskana polietereterketonska (PEEK) ekstravaskularna premosnica primijenjena je u liječenju 14-godišnjeg dječaka sa sindromom orašara. Digitalna subtrakcijska angiografija otkrila je segment lijeve bubrežne vene (LRV) sa smanjenim kontrastnim punjenjem neposredno prije njezina utoka u donju šuplju venu s gradijentom visokog tlaka. Model trodimenzionalne rekonstrukcije pokazao je da su LRV i duodenum kontrahirani pod aortomezenteričnim kutom, što je rezultiralo kompresijom LRV iz abnormalnog visokog duodenalnog odjeljka. Kada duodenum prolazi između trbušne aorte i gornje mezenterične arterije (duodenalna interpozicija), dolazi do uklještenja LRV čak i ispod 90 stupnjeva spoja aorta i mezenterične arterije. Trodimenzionalno tiskani PEEK ekstravaskularni stent odabran je za podizanje gornje mezenterične arterije i spuštanje položaja duodenuma, čime je oslobođena kompresija LVR. Ova ekstravaskularna primjena ima značajne prednosti u odnosu na otvorenu kirurgiju, endovaskularne premosnice i uporabu umjetnih krvnih žila s ekspandiranim politetrafluoroetilenom. Ova PEEK ekstravaskularna premosnica osigurava bolju staničnu vitalnost omogućavajući rast mekog tkiva. Smanjenjem vanjskog ubrzanja i centrifugalne sile, trodimenzionalno tiskana PEEK ekstravaskularna premosnica smanjuje štetne nuspojave. Ovakva premosnica ima prepoznatljiv personalizirani dizajn, dobru krutost i izdržljivost koja omogućava rast krvnih žila, sprječava migraciju premosnice i trombozu. Stoga je prikladna i za odrasle i za pedijatrijske bolesnike. Prema ultrazvuku abdomena i višeslojnoj kompjutoriziranoj tomografiji rezultati poslijeoperacijskog praćenja bili su zadovoljavajući godinu dana nakon operacije. Bolesnik se osjeća dobro, protok krvi u LRV nije bio sputan, a brzina protoka krvi je bila prosječna. Vanjska premosnica je ostala na mjestu.

Ključne riječi: *Sindrom orašara; Trodimenzionalno tiskanje; Polietereterketon; Ekstravaskularna premosnica; Laparoskopija*