Right ventricular outflow tract histology post-stenting and in-stent stenosis

Sudesh Prabhu[1], Siddhant Mehra[1], Shravan Kanaparthi[1], Shreesha Shankar Maiya[1,2], Sruti Rao[1]

[1]Department of Pediatric Cardiac Services, Narayana Institute of Cardiac Sciences, Bengaluru, Karnataka, India, [2]Department of Pediatric Cardiology, Leicester Royal Infirmary, Leicester, England, UK

ABSTRACT

The right ventricular outflow tract (RVOT) stenting is used for the treatment of Fallot-type lesions when not amenable to complete correction or when surgical palliation carries a substantial risk. Despite the increasing clinical application, there is a lack of data that describe the RVOT morphology after stenting. This article elucidates post-RVOT stenting and in-stent stenosis, which is thought to be a zonal phenomenon, in this case, predominantly occurring proximally, in the portion of the stent apposing the RVOT infundibulum.

Keywords: In-stent stenosis, neointima formation, right ventricular outflow tract stenting, tetralogy of Fallot

INTRODUCTION

Right ventricular outflow tract (RVOT) stenting is being used for the treatment of cyanotic congenital heart diseases with decreased pulmonary blood flow that are not amenable for total correction or when surgical palliation carries very high risk.[1] It has been shown that RVOT stenting promotes superior pulmonary arterial (PA) growth and oxygen saturations compared with Blalock-Taussig shunt in the initial palliation of Fallot-type lesions.[2] The natural history of the RVOT stent includes luminal narrowing due to in-stent stenosis (ISS). In this article, we describe the morphology of the RVOT after stenting and ISS based on histological evidence.

CASE REPORT

A 3-month-old, 3.5 kg tetralogy of Fallot (TOF) patient with a hypoplastic pulmonary annulus (z score = −3), presented with sepsis and cyanotic spells, poorly responding to medical management. Surgery was thought to be of higher risk, and RVOT stenting was performed using a 7 mm × 18 mm bare-metal stent (Herculink Elite®, Abbott Vascular, CA, USA) across the pulmonary valve. After 15 months, the child underwent total correction with stent retrieval. Intraoperative photograph and preoperative computerized tomogram scan demonstrated adequately grown branch PAs (right PA z-score = −1.4 to + 2.09; left PA z-score = −1.04 to +1.84) [Figure 1]. The stent with surrounding tissues was harvested during surgery. Since we do not have the facility to perform tissue sections with stent *in situ*, we had to tease the tissue of the stent for slide preparation.[3] Parental consent and ethics committee approval (NHH/AEC-CL-2020-473) were obtained.

On gross examination, ISS in this case demonstrated a zonal phenomenon in RVOT as described below [Figure 1].

1. Zone-1: Portion of the stent protruding into main pulmonary artery (MPA) beyond the pulmonary valve, which is not adherent to any part of the vessel and without ISS
2. Zone-2: Portion of the stent opposing the pulmonary

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Address for correspondence: Dr. Sudesh Prabhu, Narayana Institute of Cardiac Sciences, Bengaluru - 560 099, Karnataka, India.
E-mail: sudesh006@gmail.com

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valve is adherent to the leaflets. The lumen is open and without ISS

3. Zone-3: Portion of the stent in the infundibulum, between the conal septum and septoparietal bands. Luminal narrowing due to ISS is observed.

The histological examination also demonstrated a zonal phenomenon as described in Figures 2 and 3.

DISCUSSION

Vascular stenting is an established practice for stenosis, and like any other stenting (coronary stents, peripheral artery stents, and carotid artery stents), the natural history of the RVOT stent is luminal narrowing due to ISS.

Multiple studies have demonstrated the cause of restenosis poststenting for atherosclerotic coronary artery disease,[4,5] contrary to which, the pathophysiology of ISS in RVOT stenting is different. Intraluminal protrusion of the endocardium, subendocardial tissue, and cardiac muscle fibers occurs through the interstices of the stent as the metallic portion cuts through the cardiac tissue during deployment and during each cardiac cycle. Breach of the endocardium and exposure of the subendocardial tissue trigger acute inflammation and microthrombus formation and initiate neointimal proliferation. Neointimal formation is the response of the vascular structure to several forms of injury and is one of the mechanisms contributing to the development of restenosis. Apart from this, apposition of the cardiac muscle against the metal of the stent leads to chronic inflammatory process (foreign body reaction), which causes lymphoplasmacytic infiltration and foreign body giant cell formation. These chronic inflammatory changes cause luminal narrowing and ISS. The absence of ISS in the portion of the stent apposing the pulmonary valve leaflet is difficult to explain, but most probably due to the absence of leaflet penetration by stent struts. Finding pertaining to a single patient is a limitation. Future studies with a larger sample size are required to precisely validate our results.

Nokhrin *et al*. very elegantly described the occurrence of ISS due to intimal hyperplasia thought to be from low biocompatibility and hemocompatibility of bare-metal stents.[6] The presence of metals triggers apoptosis or necrosis, resulting in the recruitment of immune cells that promote inflammation locally. They also have described the variability of extracellular matrix thickness between different segments similar to our study. Despite the ISS, relief of right ventricular outflow tract obstruction (RVOTO) offered by stenting facilitates distal perfusion and development of the pulmonary vasculature, making it an attractive palliative option in neonates with TOF.[6]

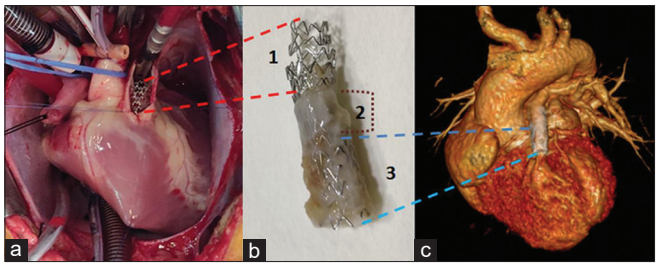

Figure 1: (a) Intraoperative findings after opening the main pulmonary artery longitudinally demonstrating the RVOT stent. (b) Explanted stent in toto with surrounding cardiac tissue. (c) CT scan with 3D reconstruction demonstrating the RVOT stent with adequately grown branch PAs. RVOT - Right ventricular outflow tract, CT - computerized tomogram, 3D - Three-dimensional

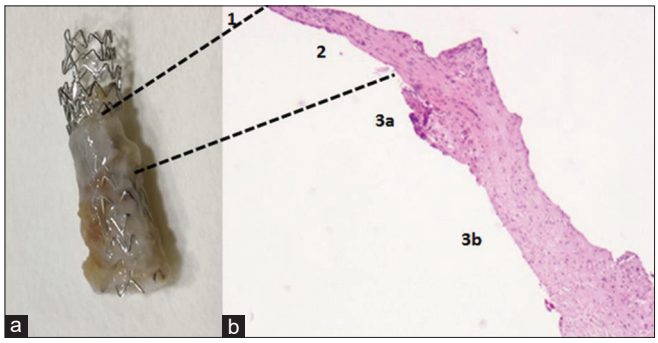

Figure 2: (a) Explanted stent in toto with surrounding cardiac tissue (b) Histopathology of the tissue surrounding the explanted stent (detailed description of histopathology is in Figure 3) (H and E staining, ×100). Zone-1: No adherent tissue. Zone-2: No inflammation seen in the native pulmonary valve. Zone-3: Divided into upper/distal (zone 3a) and lower/proximal (zone 3b). Higher grades of inflammation and neovascularization seen as we move proximally from zone 3a to zone 3b

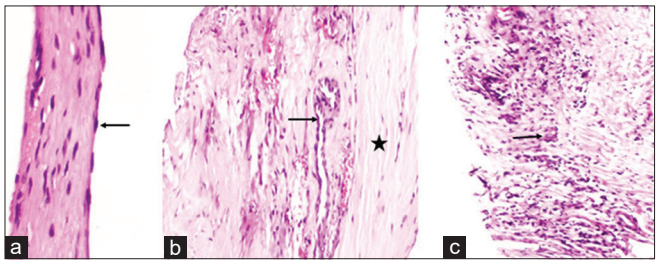

Figure 3: Zonal histopathology (H and E staining, × 400). (a) Zone-2 (native pulmonary valve) demonstrating maintained valvar architecture with endothelial lining (arrow), no evidence of inflammation or foreign body reaction. (b) Zone-3a, tissue protruding into the lumen through the stent interstices demonstrates neointimal formation with neovascularization (arrow) and atrophic myocardial fibers (*). (c) Zone-3b, dense lymphoplasmacytic infiltrate adjacent to the stent with foreign body giant cells (arrow) seen with neovascularization and atrophic myocardium

To conclude, ISS is a zonal phenomenon following RVOT stenting. Only that portion of the RVOT infundibulum with the embedded stent showed chronic inflammation, neointimal formation, and ISS. Studying histopathological changes in the RVOT when using drug-eluting stents might add to our knowledge on the pathogenesis of ISS and aid in stent selection.

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Nil.

Conflicts of interest

There are no conflicts of interest.

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