Honeycomb-like structure in the right coronary artery treated with a drug-eluting stent: a case report and literature review

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Abstract
A honeycomb-like structure (HLS) is a rare entity encountered in catheterization laboratories. The etiology of HLS remains elusive. Moreover, no treatment guideline or consensus for HLS has been proposed. However, with more frequent adoption of intravascular imaging modalities, the number of cases of HLS is rising. We herein present a case of HLS and summarize previous reports in the literature with the aim of providing useful information for interventional cardiologists and promoting further research.

Keywords
Honeycomb-like structure, thrombus recanalization, drug-eluting stent, interventional cardiology, intravascular imaging, coronary artery disease

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Introduction
A multi-channel structure in a coronary artery was first described by Terashima et al.\textsuperscript{1} in 2002 using intravascular ultrasound. Several terms have been proposed for this structural abnormality, including a “honeycomb-like structure” (HLS),\textsuperscript{2–4} “lotus root-like appearance,”\textsuperscript{1,5} or “Swiss cheese pattern.”\textsuperscript{6} However,
many characteristics of HLS remain unknown. We herein present a case of HLS and summarize some important characteristics of HLS by performing a thorough literature review. The overall aim of this study was to provide useful information for interventional cardiologists and promote further research.

Case report

The study protocol was approved by the Ethics Committee of Sun Yat-sen University. The patient described in this report provided written informed consent.

A 54-year-old man with multi-vessel coronary artery disease and a current smoking habit was admitted to our center for a regular check-up. Four years previously, the patient had presented with acute coronary syndrome, and coronary angiography revealed multi-vessel stenosis. Three zotarolimus-eluting stents (Endeavor Resolute; Medtronic Inc., Minneapolis, MN, USA) were deployed in the posterior descending artery (2.25 × 24 mm), left anterior descending artery (3.0 × 15 mm), and left circumflex artery (2.25 × 18 mm).

A borderline stenotic lesion in the midportion of the right coronary artery (RCA) was observed, but the decision was made to treat this lesion medically (Figure 1(a), (b)). During the previous 4 years, the patient was prescribed secondary prevention medicines including dual antiplatelet therapy with aspirin and clopidogrel. The patient had no ischemic syndrome in the preceding 1 year before admission. However, he was advised to recheck his coronary arteries because of his compromised compliance. Electrocardiogram results showed no significant ST-segment change. Echocardiography demonstrated an ejection fraction of 61% and no obvious motion abnormality of the left ventricular wall. Follow-up coronary angiography revealed patent stents and no significant lesion progression in the left anterior descending artery or left circumflex artery. However, a lesion with angiographic haziness, which was once a borderline stenotic lesion 4 years previously, was observed (Figure 1(c)). The blood flow of the RCA was only grade II according to the Thrombolysis In Myocardial Infarction (TIMI) scoring system. We decided to evaluate the lesion by optical coherence tomography (OCT) (St. Jude Medical, Inc., Little Canada, MN, USA). Cross-sectional OCT images acquired from the sites corresponding to the lines in Figure 1(d) showed a honeycomb-like appearance with multiple intraluminal channels of various sizes, separated by tissue with high signal intensity and low signal attenuation (Figure 1(f), (g)), suggestive of fibrous material. Proximal and distal dissections (Figure 1(e), (i)) and residual thrombus (Figure 1(h)) were also visualized within the lumen. A three-dimensional longitudinal reconstruction revealed a complex structure (Figure 1(j)). Another zotarolimus-eluting stent (3.5 × 24 mm; Endeavor Resolute, Medtronic Inc.) was successfully implanted in the midportion of the RCA (Figure 1(k)). Post-procedural OCT revealed full coverage of the dissection and HLS and favorable expansion and apposition of the stent (Figure 1(l)). A 6-month CAG follow-up was scheduled, and adherence to the prescribed medicine regimens was stressed once again.

Discussion

A detailed literature review was performed and is summarized in Table 1. In total, 20 studies were evaluated.1–20 The diagnosis of HLS was based on coronary intravascular imaging modalities such as intravascular ultrasound and OCT. OCT is the preferred tool with which to demonstrate detailed structures because of its high spatial resolution (10–15 μm). HLS could be found in all three epicardial arteries without significant
Figure 1. Findings of coronary angiography and optical coherence tomography (OCT). Coronary angiogram of the right coronary artery (RCA) in the (a) left anterior oblique view and (b) cranial view obtained 4 years previously showed a borderline stenotic lesion in the midportion of the RCA; this lesion was left untreated. (c) Coronary angiography showed angiographic haziness in the midportion of the RCA (arrow). (d) Magnification of the RCA. Representative cross-sectional OCT images of the RCA showed (f, g) a honeycomb-like appearance, (e, i) distal and proximal dissection, and (h) residual thrombus within the lumen. The intra-luminal thrombus was dominated by a red thrombus (asterisk) but also contained a scattered white component (arrow). (j) Three-dimensional reconstruction revealed a complex structure. (k) The lesion was successfully treated with a zotarolimus-eluting stent. (l) Post-procedural OCT demonstrated favorable expansion and apposition of the stent.
| Authors                      | Sex/Age (y) | Imaging modality | Lesion distribution | Description                        | Possible etiology       | Treatment      |
|------------------------------|-------------|------------------|---------------------|-------------------------------------|-------------------------|---------------|
| Terashima et al. (2002)¹     | M/26        | IVUS             | LAD                 | lotus root-like appearance          | Kawasaki disease        | –             |
| Cho et al. (2010)⁷           | M/50        | OCT              | LAD                 | –                                   | –                       | –             |
| Nakanishi et al. (2010)⁸     | M/66        | IVUS             | LAD                 | lotus root-like appearance          | –                       | DES           |
| Miyamoto et al. (2010)⁹      | M/32        | IVUS             | RCA                 | –                                   | in situ thrombosis      | –             |
| Kato et al. (2011)¹⁰         | M/60        | OCT              | RCA                 | lotus root-like appearance          | –                       | –             |
| Kang et al. (2012)⁶          | 6 patients (3 male, 3 female; age range, 54–72 y) | OCT | 4 RCA, 2 LAD | Swiss cheese pattern | – | DES/follow-up |
| Toutouzas et al. (2012)²     | M/41        | OCT              | LAD                 | HLS                                 | embolic thrombus        | DES           |
| Khoueiry et al. (2014)³      | F/80        | OCT              | RCA                 | HLS                                 | in situ thrombosis      | DES           |
| Koyama et al. (2014)¹¹       | F/61        | OCT              | RCA                 | HLS                                 | in situ thrombosis      | DES           |
| Musashi et al. (2014)¹²      | M/66        | OCT              | RCA/LAD             | HLS                                 | embolic thrombus        | DES           |
| Sakurai et al. (2014)⁵       | M/74        | IVUS/OCT         | RCA                 | lotus root-like appearance          | in situ thrombosis      | –             |
| Gómez-Monterrosas et al. (2014)¹³ | M/29 | OCT | LAD | HLS | – | BVS |
| Fujino et al. (2015)¹⁴       | M/68        | OCT              | LCX                 | HLS                                 | in situ thrombosis      | DES           |
| Kimura et al. (2015)¹⁵       | M/66        | IVUS/OCT         | RCA                 | HLS                                 | in situ thrombosis      | DES           |
| Kadowaki et al. (2016)¹⁶     | M/60        | IVUS/OCT         | RCA/LAD             | lotus root-like appearance          | –                       | DES           |
| Seike et al. (2016)¹⁷        | M/64        | OCT              | LAD                 | HLS                                 | –                       | DES           |
| Suzuki et al. (2016)¹⁸       | F/51, F/62  | OCT              | LAD/LAD             | lotus root-like appearance          | –                       | DES           |
| Harakat et al. (2016)¹⁹      | M/59        | IVUS             | LAD                 | HLS                                 | embolic thrombus        | DES           |
| Nomura et al. (2016)²⁰       | M/70        | OCT              | RCA                 | lotus root-like appearance          | –                       | DES           |
| Watanabe et al. (2016)⁴      | M/56        | OCT              | LAD                 | HLS                                 | –                       | DCB           |

F, female; M, male; BVS, bio-resorbable vascular scaffold; DES, drug-eluting stent; DCB, drug-coated balloon; HLS, honeycomb-like structure; IVUS, intravascular ultrasound; LAD, left anterior descending artery; LCX, left circumflex artery; OCT, optical coherence tomography; RCA, right coronary artery; –, not mentioned.
territory dominance. In very rare cases, several HLSs could be detected simultaneously in multiple coronary arteries. The etiology of HLS is not completely understood. Recanalization of an in situ thrombus has been considered by many researchers to be the pathogenesis of HLS. Moreover, recanalization of an embolic thrombus and coronary vasculitis such as that seen in Kawasaki disease have also been proposed as potential mechanisms for HLS. In the present case, multiple intimal dissections were clearly observed. In addition, no atrial fibrillation or left ventricular thrombi were documented. Therefore, a reasonable etiology was in situ thrombosis secondary to coronary dissection, plaque rupture, or proximal coronary ectasia. HLS should be differentiated from woven coronary artery (WCA), another very rare condition that is recognized as a congenital anomaly without prognostic significance. In most cases, the involved WCA has normal coronary blood flow and the patient is asymptomatic. As a result, WCA is usually an incidental finding and regarded as a benign variation. In contrast, most patients with HLS have symptoms to varying extents. Under intracoronary imaging, the integrity of the vascular wall of the woven portion is generally intact. In HLS, however, pathological manifestations such as thrombi, dissection, and coronary atherosclerosis are commonly encountered. To date, no large cohort study or clinical trial of HLS has been reported. As a result, the management of HLS is mainly determined by the treating physicians and depends on the presence of ischemia. Stress tests, nuclear myocardial imaging, and fractional flow reserve are helpful to assess ischemia in patients with HLS. According to the literature, most cases of HLS are functionally significant and require intervention. Favorable outcomes of treatment with a drug-eluting stent, drug-eluting balloon, or bioresorbable vascular scaffold have been reported. In this particular case, despite the lack of ischemic symptoms and obvious electrocardiogram changes, we decided to perform angioplasty because the blood flow of the RCA was compromised. After intervention, TIMI grade III blood flow was obtained.

Conclusion
HLS was once considered to be rare. However, with the increasing application of intracoronary imaging modalities and the rising awareness among interventional cardiologists, this entity has been increasingly more frequently reported in the literature. Further investigations are warranted for the optimal management of HLS.

Declaration of conflicting interests
The authors declare that there is no conflict of interest.

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