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Sterile Radial Artery Granuloma After Transradial Procedures: A Unique and Avoidable Complication

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Trans-radial cardiac catheterization has lower rates of arterial access site complications. Hydrophilic-coated sheaths designed specifically for trans-radial procedures have resulted in numerous reports of a foreign body reaction to retained material. Although this is a self-limited condition that should be managed expectantly, it is often confused with an infected pseudoaneurysm, resulting in unnecessary surgery. We searched the FDA MAUDE (Manufacturer and User Facility Device Experience) database to determine which brands of sheath have been associated with this complication. In addition, we performed a literature search for all reported cases of this complication. Only one brand of sheath has been associated with this condition. As trans-radial procedures become more common in the US, knowledge of such complications, which appear to be specific to the Cook radial hydrophilic-coated sheaths, is imperative for all radial interventionalists to prevent unnecessary surgical procedures. © 2010 Wiley-Liss, Inc.

Key words: radial artery; foreign body reaction; complications; granuloma

INTRODUCTION

Driven by advances in device manufacturing, trans-radial diagnostic and interventional procedures through 5 and 6 French sheaths have become routine. While most cardiac catheterization laboratories in Europe, Canada, and Asia routinely perform trans-radial procedures, the US has only recently seen more widespread adoption. Because of the potential benefits in reduced bleeding complications when compared to femoral access [1], many US laboratories have been exploring the radial approach. Trans-radial procedures can be made more difficult by radial artery spasm. Hydrophilic sheaths were specifically designed to address this issue and have been shown to improve the problem of radial spasm [2]. However, there is a growing body of case reports and series that describe the occurrence of an inflammatory granuloma in response to the hydrophilic coating on one type of these sheaths [3–6]. These typically occur at the radial arteriotomy site 2–3 weeks after the procedure. Although the course of the disorder is benign, and the lesions resolve spontaneously, they cause discomfort, are unsightly and may present to physicians who are not familiar with trans-radial techniques. This has resulted in misdiagnosis, biopsy, or even surgical resection, when the appropriate management is observation. As the use of trans-radial procedures increases in the US [7], it is crucial that operators and referring physicians are aware of these unique complications.

After noticing this problem clinically, we sought to investigate the number of reported serious radial sheath access site reactions by using the Food and Drug Administration (FDA) maintained online resource: Manufacturer and User Facility Device Experience (MAUDE). MAUDE data represents reports of adverse events involving medical devices. The data consists of voluntary reports since June 1993, user facility reports since 1991, distributor reports since 1993, and manufacturer reports since August 1996. As stated by the FDA, the MAUDE data is not intended to be used either to evaluate rates of adverse events or to compare adverse event occurrence rates across devices. The disclosure of clinical events, however, allows medical professionals to report and review unexpected device behavior.

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TABLE I. Hydrophilic Sheath Size and Reported Cases of Granuloma

Sheath sizes	Cases *n*(%)
6.0 F × 13 mm	30 (17)
6.0 F × 23 mm	74 (42)
5.0 F × 13 mm	22 (13)
5.0 F × 23 mm	16 (9)
Unknown	32 (19)

METHODS

We investigated the number of reported serious radial sheath access site reactions by using the MAUDE database and searching for the keywords: RADIAL, Check-Flo, RADIAL SHEATH, KCFN, and Manufacturers COOK, TERUMO, CORDIS, and VASCULAR SOLUTIONS. Date of access was August 17, 2009. The radial access site event was typically listed as "other" and was therefore included in the search. All identified reports that did not represent definite radial access sheath reports were excluded. The remaining reports were then reviewed individually and any mechanical failures and associated injuries were excluded. Because the MAUDE database is not curated, some reports may represent duplicate reports listed by the manufacturers, and the initial physician or hospitals reports. All identified radial reports were then reviewed for keywords related to possible or likely granuloma by a board-certified cardiologist with expertise in radial procedures. Typical keywords were "infection, redness, or swelling," antibiotic therapy, drainage, sterile abscess, negative cultures, and granuloma on biopsy.

Because only COOK devices were noted within the MAUDE database, the specific device numbers for the Cook Medical hydrophilic radial sheath were further recorded as either 6 French (KCFN-6.0) or 5 French (KCFN-5.0) with additional identification of short or long sheaths (13 and 23 mm), to determine the effects of either sheath size or length on reported events. Incomplete listings were identified as "unknown."

Literature review was performed through PubMed, searching for keywords: radial artery granuloma, radial artery abscess, radial artery foreign body reaction. All studies in English describing trans-radial cardiac catheterization resulting in foreign body reaction, granuloma, or clinical presentation with redness, swelling, and tenderness were included.

RESULTS

From August 16, 1999 to April 29, 2009, we identified 174 cases of likely radial granuloma in the FDA MAUDE database. Every case was associated with the Cook brand of sheath. Cases were reported with both the short and long Cook sheaths (see Table I). No cases were reported using other brands of sheaths.

TABLE II. Literature Reports of Radial Foreign Body Granuloma

Study	No. of patients	Sheath manufacturer	Outcome
Kozak et al. [3]	30	Cook	Varied
Tharmaratnam et al. [6]	3	Cook	Surgery on radial artery
Ziakis et al. [8]	1	Cook	Surgery on radial artery
Cogliano et al. [9]	3	Cook	–
Subramanian et al. [10]	1	Cook	Surgery on radial artery
Zellner et al. [11]	1	Cook	Surgery on radial artery
Fealey et al. [4]	2	Cook	Both had surgery on radial artery
Rathore et al. [12]	21	Cook	Surgery in one, conservative in the rest
Sado et al. [5]	4	Cook	Unknown

Literature review documented the occurrence of radial artery foreign body granuloma after trans-radial cardiac catheterization (see Table II). Again, only Cook brand sheaths were reported in connection with this complication. Many patients underwent surgical exploration/resection of the granuloma for presumed infection, but in no case was there any tissue or microbiological evidence of infection. Furthermore, after switching from the Cook sheath to other brands of hydrophilic sheath, two high volume trans-radial centers encountered no further radial artery granulomata [13,14].

DISCUSSION

The hydrophilic-coated Cook Radial Artery Sheath (Cook Flexor Check-Flo Proforma Radial Access Introducer Set) has been associated with an increased incidence of sterile granulomas and adverse local access site reactions such as pain, swelling, and sensory abnormalities in the cardiology literature. Here we report that 174 cases have also been reported to the FDA as well. Previous reports have ranged from case reports to mainly single-center observations including postprocedure questionnaires (see Table II). Because granulomas occur between 2 and 3 weeks after the procedure, most patients present to their primary care provider unless specifically instructed by their Interventional Cardiologist, and the incidence may therefore be underestimated. In addition, the possibility for misdiagnosis is high when patients are seen by physicians inexperienced in trans-radial procedures. This can lead to biopsy or surgical resection for such misdiagnoses as thrombosed or infected radial artery pseudoaneurysm or even abscess.

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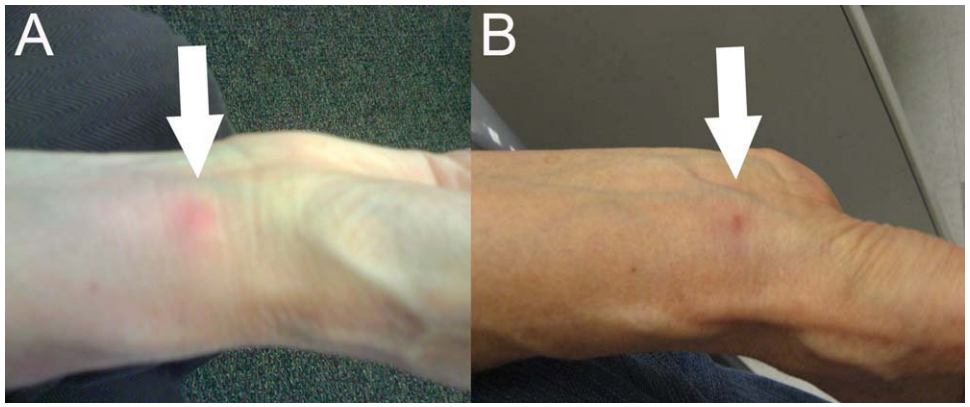

Fig. 1. Sterile radial artery granuloma. Sterile radial artery granulomata present as an erythematous swelling over the site of prior radial arteriotomy (white arrows). Panel A demonstrates a mild case presenting weeks after trans-radial cardiac catheterization. The patient described pain, swelling, redness, and pruritus in the area. Ultrasound ruled out a pseudoaneurysm, the patient was afebrile, and white blood cell count was normal. Conservative management resulted in near complete resolution of symptoms, swelling, and redness over 4 weeks (B). [Color figure can be viewed in the online issue, which is available at wileyonlinelibrary.com.]

The mechanism by which this complication occurs appears to be by stripping of the coating from the sheath and retention under the skin. This has been suggested by several papers that include histological evaluation of the inflamed tissues showing likely foreign material trapped below the skin [3,4,10]. It is possible that the combination of the Cook sheath and powdered latex gloves makes this more common, although that does not appear to be the only factor involved [3].

The true incidence of this complication of the Cook sheath is difficult to ascertain. In a recent study, Rathore et al. [12] randomized 790 patients undergoing trans-radial cardiac catheterization to Cook hydrophilic-coated or noncoated sheaths. The incidence of local complications reported as abscess or infection was higher with the hydrophilic-coated sheaths than the noncoated sheaths (5.1% vs. 0.3%; $P < 0.001$). It is not known if these were actual infections or sterile granulomata due to foreign body reaction to the hydrophilic coating. Furthermore, their follow-up was only completed in 79% of patients, and therefore the incidence was likely underestimated. Only one of their 21 patients underwent surgical drainage, the rest were treated conservatively with antibiotics. Sado and Witherow [5] performed a survey of all hospitals in the UK and found that 46% of radial centers used the Cook sheath, and 60% of them had experienced radial artery granuloma. This suggests that the actual incidence is higher than the literature might suggest. We present here the number of complications, but were unable to ascertain the number of Cook sheaths used in the US. The company did not furnish us with this data upon request and we were unable to find this data online. Thus the true incidence remains unknown.

There are no reports in the literature or in the MAUDE database describing this complication with other brands of sheath. Furthermore, there are reports that switching from Cook to other brands of hydrophilic sheaths do not result in sterile granuloma formation [13,14]. Anecdotally, since we switched from Cook to Terumo Glidesheath we have also had no recurrence of this complication in hundreds of cases.

The MAUDE database contains the following comment by the manufacturer Cook Bloomington, IN regarding the most current listing "...This product is provided with a hydrophilic coating and supplied with information for use booklet (ifu) t_kcfn_rev. 0), which states: 'possible allergic reactions or access site infection should always be considered, a sterile inflammatory response possibly associated with the use of the product in conjunction with latex and powered nonlatex-based gloves have been reported with the use of this product.' To reduce the likelihood of this failure mode recurring, corrective action was issued in 2006, and was implemented in 2008. A review of our records indicates this lot was manufactured after implementation. This is the third complaint from this hospital group involving this lot number. Nevertheless, quality engineering has reviewed the associated risk and determined that the risk will remain at an acceptable level with the addition of this complaint. At this time, we are unable to determine the root cause of the skin irritation from the information received. However, we have notified the appropriate individuals and we will continue to monitor for similar events..." [15].

If faced with this clinical situation, we recommend the following based on the scant literature on the topic. First, one should perform an ultrasound to exclude a

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true pseudoaneurysm (which are very rare), as these require a very different treatment. If there is a mass seen on ultrasound adjacent to the radial artery, and no blood flow is seen in the mass, then it is likely that this represents a sterile foreign body reaction. In the absence of fever or leukocytosis, we recommend expectant management (see Fig. 1). If there is clinical suspicion of infection, then a course of antibiotics is reasonable. If the lesion fails to resolve, surgical biopsy or drainage may be required. Resection or ligation of the radial artery should be a last resort.

In conclusion, Cook brand hydrophilic-coated sheaths have been associated with numerous reports of sterile radial artery granuloma formation, both in the literature and reported to the FDA, over the past 10 years. Postmarketing surveillance is paramount in identifying such trends. As alternative sheaths are available, users should be aware of this complication before considering the use of Cook sheaths. The prognosis of radial artery foreign body granulomatous reactions is benign and can be treated expectantly.

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