Review Article

Access this article online

Quick Response Code:

Website: http://www.braincirculation.org

DOI: 10.4103/bc.bc_72_22

Postcoiling syndrome including headache and fever after endovascular cerebral aneurysmal coil embolization: A narrative review

Yu Okuma, Toshinari Meguro[1], Kentaro Shimoda, Santiago Miyara[2], Nobuyuki Hirotsune[1]

Abstract:

Endovascular cerebral aneurysmal coil embolization is becoming more popular than direct aneurysmal neck clipping due to its noninferiority in long-term outcomes and being less invasive. Neuroradiologists often find postoperative symptoms such as headache and fever after unruptured aneurysmal coil embolization, however, they have not paid much attention because symptoms almost always resolve spontaneously within a few days. Since the concept of this syndrome has not been standardized, we named it postcoiling syndrome (PCS). In this short review, we reviewed the criteria, risk factors, mechanisms, significance, and treatment of PCS based on a few pieces of literature. Almost all literature has regarded that some kind of bioactive reaction might be involved in PCS. Preliminary data showed the possibility of inhibition of PCS by histamine-2 receptor antagonists. PCS also might have the potential of more predictive maker than previously reported risk factors for recurrence after aneurysm coil embolization. Further investigation is needed in the future, including the accumulation of cases, unification of concepts, and mid-to-long-term follow-up.

Keywords:

Endovascular cerebral aneurysmal coil embolization, fever, gastrointestinal symptoms, headache, inflammatory reaction, postcoiling syndrome, postembolization syndrome

Department of Neurological Surgery, Sonoda Daiichi Hospital, Tokyo, [1]Department of Neurological Surgery, Hiroshima City Hiroshima Citizens Hospital, Hiroshima, Japan, [2]Department of Neurological Surgery, Feinstein Institute for Medical Research, Northwell Health System, Manhasset, NY, USA

Address for correspondence:
Dr. Yu Okuma, Department of Neurological Surgery, Sonoda Daiichi Hospital, 4-1-12, Takenotsuka, Adachi-ku, Tokyo 121-0813, Japan.
E-mail: y8u2bear4@hotmail.com

Submission: 04-10-2022
Revised: 04-02-2023
Accepted: 24-02-2023
Published: 30-06-2023

Introduction

There is a disease concept called postembolization syndrome (PES), which presents with fever, pain, and gastrointestinal symptoms after endovascular treatment in other areas, such as uterine artery embolization, splenic artery embolization, and hepatic artery chemotherapy.[1-7] It has been more than 20 years since the development of endovascular coil embolization for cerebral aneurysms, and it has revolutionized the treatment of cerebral aneurysms. In recent years, endovascular coil embolization has been used more frequently than direct aneurysm neck clipping in Europe due to its superiority in short-term results and noninferiority in long-term results in ruptured aneurysms. Although many neuroradiologists have experienced patients' headaches after unruptured cerebral aneurysm coil embolization, it has not been considered a syndrome because it almost always resolves spontaneously and does not require long-term symptomatic treatment.[8] In this short review, we summarized the criteria, risk factors, disease significance, and minimally invasive treatment methods based on PES, based on the limited literature.

How to cite this article: Okuma Y, Meguro T, Shimoda K, Miyara S, Hirotsune N. Postcoiling syndrome including headache and fever after endovascular cerebral aneurysmal coil embolization: A narrative review. Brain Circ 2023;9:64-7.

The Clinical Findings, and Epidemiology

The concept of PES has been proposed to describe fever, pain, and gastrointestinal symptoms after endovascular treatment such as prostatic artery embolization, renal artery embolization, uterine artery embolization, and transarterial hepatic chemoembolization for hepatocellular carcinoma. The symptoms are fever, pain, and gastrointestinal symptoms. The symptoms usually disappear in about a week. The severity of symptoms correlates with the extent and intensity of embolization and can be alleviated by selective embolization when a large area is embolized. Rather than a complication, it is a reaction to embolization, and the main mechanisms are thought to be ischemia and cell necrosis caused by embolization or the induction of an immune response to a foreign body. The incidence of PES is estimated to be 20%–40% after prostatic artery embolization, renal artery embolization, uterine artery embolization, and transarterial hepatic chemoembolization for hepatocellular carcinoma.[1-7]

Likewise, postoperative symptoms such as headache and fever are often observed 24–48 h after coil embolization of unruptured cerebral aneurysms. Takigawa *et al*. reported headache and fever in 40%,[9] Choi *et al*. reported headache in 25%,[10] Hwang *et al*. reported headache in 50%,[11] and Okuma *et al*. reported headache, fever, and gastrointestinal symptoms in 30%. Okuma *et al*. named this syndrome postcoiling syndrome (PCS) [Table 1].[12]

Diagnosis and Risk Factors

The sum of scores for gastrointestinal symptoms, fever, pain, etc., is often used to diagnose PES, however, there are many different ways to score, and they are not unified, in spite of many reports.[1-7]

In PCS, where the disease concept is not yet established, scoring is reported unevenly. Some reports used their own headache scale and other reports used the International Classification of Headache Disorders criteria.[9-11,13,14] Okuma *et al*. used their original criteria with reference to PES criteria, and defined headache, fever, and gastrointestinal symptoms as scoring during 24–48 h after surgery.[12] For the occurrence of PCS, Takigawa *et al*. reported the use of bioactive coils,[9] Choi *et al*. reported stent-assisted coil embolization,[10] and Hwang *et al*. reported the absence of a history of hypertension as a risk factor.[11] Okuma *et al*. reported patients' age, aneurysm size, total coil length, coil packing density, and postoperative white blood cell count as risk factors.[12]

Mechanism

In all reports of PCS, a biological reaction to the coil is the first possible cause. In the acute phase of the biological reaction, allergic reactions caused by the binding of proteins in the circulation and tissues to antigens and the mechanical force of the coil loop on the aneurysm wall and dura are known. As for the chronic phase, granulation tissue formation and chronic inflammation, as well as a strong foreign body reaction to platinum coils, are known [Table 1].

In addition, Takigawa *et al*. considered bioactive coils as a possible cause of PCS because of the inflammatory effects of polyglycolic acid used to accelerate aneurysm fibrosis and neointima formation as a mechanism.[9] Choi *et al*. considered stent-assisted coil embolization, which had been shown to be associated with fundamental differences in the characteristics of aneurysms, activation of vascular sensory afferent pathways by stents, and the ability of the artery, as a possible cause of PCS.[10] Hwang *et al*. added that the walls of aneurysms in patients without a history of hypertension are more affected by increased pressure in the aneurysmal sac. That dilatation or stretching of intracranial arteries can cause headaches.[11]

Treatment

In PES, the syndrome was treated symptomatically with a combination of analgesics, antiemetics, and antipyretics.[1-7] Moreover, in PCS whose symptoms were usually milder, it is often untreated, as the natural course of the disease leads to recovery.

We have recently obtained preliminary data on the inhibition of PCS by histamine-2 receptor antagonists.

Table 1: Summary of reports of postcoiling syndrome after aneurysmal coil embolization

Author (year)	Total case number/ mean age (years old)	Symptom (frequency percentage)	Risk factors/treatment/raison deter
Takegawa (2011)[9]	88/61.9	Headache (46.6), fever (80.7)	Bioactive coils/none/none
Hwang (2012)[11]	90/57.3	Headache (55.6)	No hypertension history, high packing density/none/none
Choi (2014)[11]	130/62.0	Headache (24.6)	No hypertension history, stent-assisted coiling/none/none
Zhang (2016)[13]	58/50.6	Headache (20.7)	None/none/none
Okuma (2016)[8,12]	36/62.0	Headache, fever, gastrointestinal symptom (30.1)	Elder, aneurysm volume, high packing density/famotidine/ predictive marker of recurrence

According to our review, patients suffered to postcoiling syndrome after endovascular cerebral aneurysmal coil embolization have been reported. None: No information was provided

Gastroprotective agents are now commonly administered during dual antiplatelet therapy (clopidogrel and aspirin) as premedication for endovascular aneurysmal coil embolization. Recently, we compared patients treated with famotidine, a histamine-2 receptor antagonist,[15] with those treated with a proton-pump inhibitor. Consecutive 20 patients (4 men and 16 women) aged 35–78 years (mean age, 57.3 years) were included in this preliminary retrospective investigation. Twenty patients received either oral famotidine (n = 10) or not (n = 10). Statistical analysis with Mann–Whitney U-test was performed. We used JMP 10.1 (SAS Institute, Cary, NC, USA) and GraphPad Prism 8 (GraphPad Software, San Diego, CA, USA) for statistical analyses.[16] One patient in the famotidine group was determined as a PCS; on the other hand, four in the nonfamotidine group [Figure 1]. On the other hand, concerning the patient background, there was no significant difference in patient background between patients in the famotidine and the nonfamotidine groups, including age [Supplementary Table 1]. Concerning the aneurysmal data of the patients, there was no significant difference in the aneurysmal diameter, aneurysmal volume, total coil length, and volume embolization ratio between the famotidine and the nonfamotidine group [Supplementary Table 2]. Concerning the operative factors of the patients, there were no significant differences in general anesthesia time or contrast medium volume between the famotidine and the nonfamotidine group [Supplementary Table 3].[12] Nevertheless, between groups, we recognized significant differences in our PCS scoring of the symptoms. This was only small size preliminary trial, and we need to prepare the next prospective, hypothesis-driven study. Gastroprotective drugs are needed anyway, thus famotidine may be expected to be a noninvasive treatment.[17]

Prognosis, Significance, and Limitations

Although there are reports that the occurrence of PES is considered a poor prognostic factor in the future, PCS has not been considered a syndrome yet because it almost always resolves spontaneously and does not require long-term symptomatic treatment, thus there are few studies observed mid-to-long-term. Recently, Okuma *et al*. reported mid-to-long-term outcomes and reported that PCS was a more predictive maker than previously reported risk factors for recurrence after aneurysm coil embolization.[8]

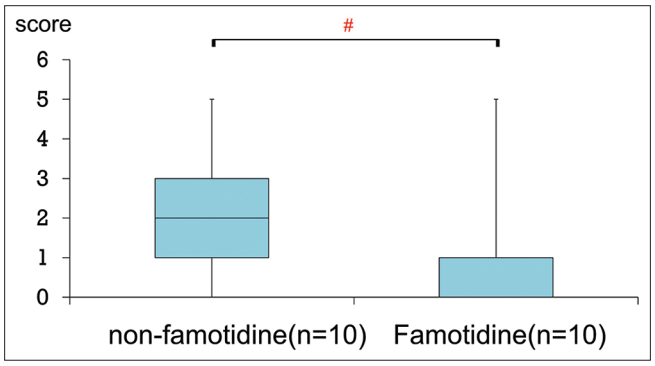

Figure 1: Comparison of PCS criteria scores between the two groups as shown in the boxplots, with significantly lower scores in the famotidine group. #$P < 0.05$ compared with the nonfamotidine group. PCS: Postcoiling syndrome

There are several possible limitations. There is a significant lack of uniformity and consistency among studies, where the disease concept is not well-defined. If we get too strongly caught up in the concept of PES and pathology, we may miss the essence of PCS. If PCS is a predictive marker, we would like to find a way to suppress it in the future.

Conclusion

We have summarized some reports on fever, headache, and gastrointestinal symptoms after cerebral aneurysm coil embolization named PCS. The common recognition of these pieces of literature is that some kind of bioactive reaction is involved in PCS. We are waiting for the definition and standardization of this syndrome, and we believe that medium-to-long-term follow-up is necessary.

Acknowledgments

The authors would like to thank Kenji Sugiu and Isao Date for the mentor of neuroendovascular therapy.

Author contributions

YO: conception, design, data collection, analysis, and interpretation of data, drafting of the manuscript, writing the article; UA, and SM: interpretation of data; NH: critical revision of the article, supervision. All authors contributed to manuscript revision, read and approved the submitted version.

Consent and ethical approval

We obtained written informed consent from the patient for publication as per our standard institutional rules. Our institutional review board approved this study. A copy of the written consent is available from the corresponding author.

Financial support and sponsorship

Nil.

Conflicts of interest

There are no conflicts of interest.

References

1. Leung DA, Goin JE, Sickles C, Raskay BJ, Soulen MC. Determinants

of postembolization syndrome after hepatic chemoembolization. J Vasc Interv Radiol 2001;12:321-6.
2. Mason MC, Massarweh NN, Salami A, Sultenfuss MA, Anaya DA. Post-embolization syndrome as an early predictor of overall survival after transarterial chemoembolization for hepatocellular carcinoma. HPB (Oxford) 2015;17:1137-44.
3. Khalaf MH, Sundaram V, AbdelRazek Mohammed MA, Shah R, Khosla A, Jackson K, *et al*. A predictive model for postembolization syndrome after transarterial hepatic chemoembolization of hepatocellular carcinoma. Radiology 2019;290:254-61.
4. Ubillus WJ, Munoz J, Vekaria M, Wollner IS, Getzen T, Hematology – Oncology Division IRd. Post-embolization syndrome: Outcomes regarding the type of embolization. J Clin Oncol 2011;29:e14582-e.
5. Svarc P, Taudorf M, Nielsen MB, Stroomberg HV, Røder MA, Lönn L. Postembolization syndrome after prostatic artery embolization: A systematic review. Diagnostics (Basel) 2020;10:659.
6. Gong M, Liu Z, Su H, Zhao B, Kong J, He X. Urgent transcatheter arterial embolization for wunderlich syndrome with hypovolemic shock secondary to ruptured renal angiomyolipoma. Front Surg 2021;8:704478.
7. He JJ, Yin XX, Wang T, Chen MY, Li XL, Yang XJ, *et al.* Factors influencing postembolization syndrome in patients with hepatocellular carcinoma undergoing first transcatheter arterial chemoembolization. J Cancer Res Ther 2021;17:777-83.
8. Okuma Y, Sugiu K, Hirotsune N, Hishikawa T, Muraoka K, Hiramatsu M, *et al.* Post coiling syndrome might predict recurrence after coil embolization of unruptured cerebral aneurysms. J Neuroendovascular Ther 2017;11:235-9.
9. Takigawa T, Matsumaru Y, Nakai Y, Nakamura K, Hayakawa M, Tsuruta W, *et al.* Bioactive coils cause headache and fever after endovascular treatment of intracranial aneurysms. Headache 2012;52:312-21.
10. Choi KS, Lee JH, Yi HJ, Chun HJ, Lee YJ, Kim DW. Incidence and risk factors of postoperative headache after endovascular coil embolization of unruptured intracranial aneurysms. Acta Neurochir (Wien) 2014;156:1281-7.
11. Hwang G, Jeong EA, Sohn JH, Park H, Bang JS, Jin SC, *et al.* The characteristics and risk factors of headache development after the coil embolization of an unruptured aneurysm. AJNR Am J Neuroradiol 2012;33:1676-8.
12. Okuma Y, Sugiu K, Tokunaga K, Nishida A, Hishikawa T, Itami H, *et al.* Clinical analysis of fever, headache, and gastrointestinal symptoms after endosaccular coil embolization in patients with unruptured cerebral aneurysms – A study of "post coiling syndrome." J Neuroendovascular Ther 2016;10:177-82.
13. Zhang L, Wu X, Di H, Feng T, Wang Y, Wang J, *et al.* Characteristics of headache after an intracranial endovascular procedure: A prospective observational study. Headache 2017;57:391-9.
14. Schwedt TJ, Gereau RW, Frey K, Kharasch ED. Headache outcomes following treatment of unruptured intracranial aneurysms: A prospective analysis. Cephalalgia 2011;31:1082-9.
15. Samimagham HR, Hassani Azad M, Haddad M, Arabi M, Hooshyar D, KazemiJahromi M. The efficacy of famotidine in improvement of outcomes in hospitalized COVID-19 Patients: A structured summary of a study protocol for a randomised controlled trial. Trials 2020;21:848.
16. Okuma Y, Becker LB, Hayashida K, Aoki T, Saeki K, Nishikimi M, *et al.* Effects of Post-resuscitation normoxic therapy on oxygen-sensitive oxidative stress in a rat model of cardiac arrest. J Am Heart Assoc 2021;10:e018773.
17. Yamao J, Kikuchi E, Matsumoto M, Nakayama M, Ann T, Kojima H, *et al.* Assessing the efficacy of famotidine and rebamipide in the treatment of gastric mucosal lesions in patients receiving long-term NSAID therapy (FORCE – Famotidine or rebamipide in comparison by endoscopy). J Gastroenterol 2006;41:1178-85.

Supplementary Table 1: Background of the patients of nonfamotidine and famotidine groups

	Nonfamotidine (*n*=10), *n* (%)	Famotidine (*n*=10), *n* (%)	*P*
Age (years old)	54.1±13.5	60.5±19.2	0.27
Female	7 (70)	9 (90)	0.58
Weight (kg)	54.3±11.5	57.5±18.9	0.68
Hypertension	4 (40)	5 (50)	1
Diabetes mellitus	0	1 (10)	1
Hyperlipidemia	2 (20)	1 (10)	1
Cardiac failure	0	0	1
Renal failure	0	1 (10)	1
Smoking	0	3 (30)	0.21
Family history	3 (30)	3 (30)	1

Supplementary Table 2: Aneurysmal data of the patients of nonfamotidine and famotidine groups

	Nonfamotidine (*n*=10)	Famotidine (*n*=10)	*P*
Aneurysms diameter (mm)	6.7±2.4	7.4±3.7	0.97
Neck diameter (mm)	4.3±1.7	4.4±1.3	0.94
Aneurysms volume (mm^3)	111±96	177±245	0.62
Total coil length (cm)	60±53	77±107	0.88
Volume embolization ratio (%)	34±11	30±10	0.57

Supplementary Table 3: General anesthesia time and contrast medium volume of the patients of nonfamotidine and famotidine groups

	Nonfamotidine (*n*=10)	Famotidine (*n*=10)	*P*
Contrast medium (mL)	125±26	115±35	0.34
Time (min)	146±40	138±45	0.82