Human Pathology (2016) **53**, 178–190

Human
PATHOLOGY

www.elsevier.com/locate/humpath

Original contribution

Polymer-induced central nervous system complications following vascular procedures: spectrum of iatrogenic injuries and review of outcomes☆,☆☆,★

Rashi I. Mehta MD[a,*], **Rupal I. Mehta MD**[b,c]

[a]*Department of Radiology, State University of New York Upstate Medical University, Syracuse, NY 13210*
[b]*Department of Pathology and Laboratory Medicine, University of Rochester Medical Center, Rochester, NY 14642*
[c]*Center for Neural Development and Disease (CNDD), University of Rochester Medical Center, Rochester, NY 14642*

Received 6 October 2015; revised 6 January 2016; accepted 6 January 2016

Keywords:
Embolism;
Endovascular procedure;
HPE;
Hydrophilic polymer;
Iatrogenic complication;
Inflammation;
Vascular device

Summary Polymer substances are commonly applied as surface coatings on endovascular catheters and vascular devices. Adverse effects related to their use have been reported, although the overall clinical significance and appropriate methods of detection of these complications have been unclear. In this analysis, we systematically reviewed clinical and diagnostic features in 32 patients (age, 36-87 years; mean, 59 years) in whom intracranial polymer reactions were documented following vascular interventions. Associated neuroradiologic and neuropathologic findings were variable and included cerebral vasculitis or vasculopathy (63%), abscess or granuloma formation (38%), ischemic infarcts (28%), parenchymal hematomas (28%), white matter change (25%), and/or chemical meningitis (22%). Location(s) of polymer reactions varied and included sites adjacent to and/or downstream from instrument insertion or implantation. Presenting clinical signs included focal neurologic deficits (41%), headache (22%), constitutional symptoms (19%), meningitis (16%), seizure and/or involuntary movements (9%), coma (6%), and syncope (3%). Adverse outcomes included stroke (31%), death (28%), delayed communicating hydrocephalus (9%), steroid dependency (9%), steroid complications (6%), and cerebral volume loss (3%). In some cases, these complications necessitated increased cost and length of medical care. In this review, we highlight the diverse features of polymer-induced reactions involving the central nervous system and summarize distinct diagnostic patterns that may enable earlier premortem detection of these lesions in the postprocedural clinical setting. Further work in this area is necessary to identify additional etiologic, preventative and therapeutic strategies. These data have potentially broad implications pertaining to the safety, efficacy, standards of use, storage, manufacturing, and regulation of new and emerging vascular devices and polymer nanotechnologies.

☆ Competing interests: none.
☆☆ Funding/Support: This work was supported by the New York State/United University Professions Joint Labor-Management Committees to R. I. M. R. I. M. is also supported by a grant from the National Institute of Neurological Disorders and Stroke (K08NS089830).
★ This work was presented, in part, at the 89th annual meeting of the American Association of Neuropathologists (Charleston, SC) on June 22, 2013, and in part at the 52nd annual meeting of the American Society of Neuroadiology (Montreal, Canada) on May 22, 2014.
* Corresponding author. Department of Radiology, State University of New York Upstate Medical University, 750 E Adams St, Syracuse, NY 13210.
E-mail address: mehtar@upstate.edu (R. I. Mehta).

http://dx.doi.org/10.1016/j.humpath.2016.01.018
0046-8177/

1. Introduction

Polymers are commonly used as surface coatings on endovascular catheters and vascular devices. Their use on sheaths, catheters, microcatheters, and guidewires, among other vascular devices, allows for less invasive therapeutic approaches and has facilitated novel endovascular techniques. These coating materials enhance device lubrication, maneuverability, and biocompatibility and facilitate access of small vessels while reducing vascular spasm [1]. Polymer-coated aneurysm coils have additionally been shown to improve volumetric occlusion and facilitate early inflammation and thrombus organization within cerebral aneurysms [2,3]. With evolving nanotechnologies and increased use of insertable and implantable vascular devices, applications of these coating materials are expected to increase.

Despite their advantages, polymer coatings have the potential to induce significant adverse reactions. Chemical injuries and unanticipated dissociation of polymer particles from vascular device surfaces have been increasingly recognized following routine use in patients [4–8]. These phenomena have been associated with diverse outcomes that depend on organ and site of involvement. In 2009, we reported to the US Food and Drug Administration the first fatal case of polymer embolism, which involved the brain [6]. In spite of limited recognition and reporting of this complication, multiple cases over recent years provide additional evidence that morbidity and mortality associated with these iatrogenic phenomena are underrecognized [5–14]. Further characterization of polymer reactions, including organ-specific effects, and identification of etiologic factors are therefore warranted and have potential to improve the safety of new and emerging vascular technologies.

Sensitive methods of earlier detection are needed to elucidate the true clinical incidence and significance of polymer phenomena. In this study, we review the spectrum of clinical, neuroradiologic, and neuropathologic findings and summarize premortem diagnostic features and outcomes of polymer complications involving the central nervous system. This review is performed with the intent to clarify the nature of clinical risks posed to patients; facilitate earlier diagnosis of polymer reactions by radiologists and pathologists; summarize available preventative and therapeutic strategies for treating physicians; and highlight areas of needed improvement to manufacturers, biomedical engineers, polymer chemists, and regulatory agencies.

2. Materials and methods

This study was performed under exemption from the institutional review board and in accordance with the ethical standards of institutional and national research committees. Published reports, dating from 1997 to 2015, of intracranial polymer reactions due to routine catheterization and/or endovascular procedures were identified using PubMed. Cases previously reported by our group were systematically reanalyzed. Our archives were also searched for additional unreported consult cases. Patients in whom specific histopathologic or cerebrospinal fluid (CSF) laboratory data were unavailable were excluded. Demographics, procedure(s), imaging findings, laboratory and neuropathologic data, and outcomes on the remaining patients were reviewed.

3. Results

Thirty-two patients with documented intracranial polymer reactions and available pathology or CSF laboratory data were identified (age range, 36-87 years). Patients had undergone various procedures, including cerebral angiogram (94%), endovascular aneurysm coil embolization (50%), aneurysm flow diversion (25%), intraarterial thrombolysis (9%), mechanical thrombectomy (6%), peripherally inserted central catheter placement (3%), cardiac catheterization (3%), central venous catheterization (3%), and hemodialysis catheter placement (3%). Polymer phenomena were associated with diverse intracranial reactions that involved variable regions of the brain and spinal cord. Demographic, clinical, neuroradiologic, and neuropathologic findings and outcome on each patient are summarized in Tables 1 and 2. Representative neuroradiologic and neuropathologic patterns of tissue injury are summarized by location below.

3.1. Polymer injuries and deposition local to device implantation

Imaging studies revealed evidence of perianeurysmal inflammation, manifested as aneurysm wall thickening and enhancement, in 2 of 16 patients (13%) who underwent endovascular aneurysm treatment using polymer-coated coils [9]. Perianeurysmal parenchymal edema was present and involved the midbrain in 1 of these patients (6%) (Fig. 1). Additional arterial abnormalities identified on imaging studies included clot within the parent artery adjacent to an occluded aneurysm that was treated with polymer-coated coils (6%) [10]. Postmortem examination revealed abundant polymer materials within the cavernous internal carotid arteries, at the site of stent placement, in 2 of 8 patients (25%) who underwent flow diversion for aneurysm therapy [13].

3.2. Polymer embolization with parenchymal inflammation

Imaging studies revealed inflammatory changes in brain parenchyma downstream from sites of intervention in 10 patients (31%); granulomas were found in 9 patients (28%), whereas sterile abscesses were found in 1 patient (3%) [11,12,15–17] (Fig. 2). Three additional patients (9%) showed