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Original contribution

Hydrophilic polymer embolism and associated vasculopathy of the lung: prevalence in a retrospective autopsy study☆

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Summary Hydrophilic polymers are commonly applied as surface coatings on vascular devices and have been shown to dissociate during endovascular use, causing hydrophilic polymer embolism (HPE). Adverse effects related to this phenomenon have been recognized and reported. The prevalence of this complication is unknown. We conducted a retrospective study to determine the prevalence of HPE among hospital autopsies over a 29-month period. Postmortem tissue was histologically evaluated for the presence, location(s) and extent of HPE. HPE findings were correlated with documented clinical and laboratory data and patient outcome. Of 136 hospital autopsies examined, 18 (13%) showed evidence of HPE involving the lungs (n = 18), heart (n = 1) or central nervous system (n = 1). Localized pulmonary HPE was seen in 12 patients (9%). Multifocal pulmonary HPE was found in 6 patients (4%) and was associated with clinical vasculitis (33%; $P < .0001$), suspected pulmonary ischemia (50%; $P = .008$), coagulopathy (67%; $P = .002$), and constitutional disease (83%; $P = .01$). Within affected lung, associated histopathologic changes included occlusive intravascular or perivascular inflammation (89%), intravascular fibrous response (56%), microthrombus formation (44%), vasculitis (28%), and/or pulmonary microinfarction (28%). Statistically significant differences in hospital days ($P = .008$) and number of vascular interventions ($P = .01$) were noted between affected and unaffected patients. We conclude that HPE is an underdiagnosed phenomenon with primary involvement of the lungs, where secondary vascular changes are common. Additional studies may be needed to clarify risks and to identify preventative strategies for this iatrogenic complication of catheterizations and "minimally invasive" endovascular techniques.

1. Introduction

Hydrophilic polymers are increasingly used for biomedical applications. Enhanced lubrication and biocompatibility, made possible by hydrophilic coats on cardiovascular and neurointerventional devices, allow for less invasive

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approaches for common endovascular procedures [1-3]. The advent of drug-eluting polymers additionally allows for sustained, targeted release of intravascular drugs, which improve therapeutic efficacy and compliance while reducing systemic drug toxicities. With advanced nanotechnologies and evolution of bioengineered insertable and implantable "smart devices," manufacturers will continue to incorporate this material on new and emerging vascular devices [4-6].

Despite their technological advances, polymer coating materials have been shown to dissociate from device surfaces during endovascular manipulation [7-16] or after implantation of devices in patients [9]. These foreign materials may then deposit in unexpected locations within the body. Recent studies conducted by our group document morbidity and mortality attributable to embolization of polymer particles within the bloodstream [12,13]. Thus, *hydrophilic polymer embolism* (*HPE*), a term we introduced in 2010, has recently been established as a potentially fatal iatrogenic phenomenon [13], although its frequency in populations at risk has not been clear.

Although vascular devices undergo friction, durability, and particulate trials required by the US Food and Drug Administration (USP XXII, sec 788) [17], complications associated with intravascular polymer applications are not fully recognized by the medical community [12,13,18,19]. To date, the clinicopathological effects associated with HPE have not been systematically evaluated. The recent observation of widespread polymer microemboli in a new fatal case prompted us to perform a retrospective analysis at a tertiary care hospital. Herein, we report the detectable frequency of this condition and analyze associated pulmonary vascular changes in affected patients who died in a hospital setting and underwent autopsy.

2. Materials and methods

2.1. Autopsy material and tissue processing

During a 29-month interval, from January 1, 2010 to May 30, 2012, 2766 patients died at the University of Maryland, Baltimore, Medical System. Of the total deaths, 198 in-hospital autopsy requests were made during this period. Of these, 54 fetal, stillborn, or infant pediatric autopsies were excluded from this study; slides were unavailable in our files on 6 cases; 2 cases consisted of gross examination only. Corresponding tissue slides for the remaining 136 cases were included in this study.

During routine autopsies, standard blocking protocols were used, with expanded organ sectioning used in cases with prominent gross pathology (eg, infarction or hemorrhage) or restricted autopsies. Autopsy blocks ranged from 10 to 71 (mean, 36 total blocks), per case. Overall mean per organ (and range in sampled organs) were 10 from the central nervous system (range, 11-38), 6 from the lungs (range, 4-20), 6 from the heart (range, 3-29), 2 from the gastrointestinal tract (range, 1-5), 2 from the genitourinary organs (range, 2-4), 1 from the liver (range, 1-5), 1 from vertebral bone (range, 1-2), 1 from skin (range, 1-3), 1 from muscle and peripheral nerve (range, 1-2); and 1 from aorta (range, 1-4). Tissue blocks were processed per standard protocol, including formalin fixation (5-10 days duration), paraffin embedment, 5-μm-thick sectioning, and hematoxylin and eosin (H&E) staining.

2.2. Quantification of polymer emboli and autopsy diagnoses

Autopsy cases were routinely diagnosed by attending staff pathologists at the University of Maryland Medical Center and were retrospectively rereviewed by an autopsy pathologist who was blinded to demographic and clinical information. Slides was scanned by light microscopy (×200 and ×600) and in some cases were additionally evaluated on serial step cuts and special staining [13,20,21]. *Localized HPE* was defined by polymer deposition within a single organ, whereas *multifocal HPE* was defined by widespread involvement of both lungs and/or spread to multiple organ systems. Representative slides on HPE-positive cases were re-reviewed by a senior autopsy pathologist to confirm presence of foreign polymer materials. Alternate diagnoses were ruled out on histologic evaluation conducted by an autopsy pathologist with expertise on vascular diseases.

2.3. Clinical data and hospital course

Demographic and clinical data were collected from electronic medical records by a coinvestigator who was blinded to autopsy results. Age, sex, previous medical history, and drug habits were noted from admission notes. Inpatient vascular procedures, clinical signs, symptoms, and clinically suspected cause of death were determined by review of inpatient and death notes originating during the final month of life. Number and duration of admissions during the final year of life were also tabulated. Postadmission laboratory values were recorded from inpatient flow sheets.

2.4. Associated factors and statistical analysis

To investigate factors associated with a diagnosis of HPE, several demographic, clinical, laboratory, and pathology variables were examined. The number of percutaneous vascular interventions incorporating hydrophilic polymers during the final month of life was tabulated. Numbers of tissue blocks evaluated at autopsy were additionally analyzed. Two-group comparisons were made among patients with HPE (multifocal, localized, or all) and without HPE. Statistical analysis was performed using JMP software (V8.0.2 SAS Institute, Inc., Cory, NC, USA). Categorical variables were compared using the χ^2 (Pearson) test.