Commentary
Volume 14:2, 2024

Journal of Blood & Lymph

ISSN: 2165-7831 Open Access

Potential Respiratory Complications in Multiple Myeloma Patients Undergoing Percutaneous Vertebroplasty May Include Non-Thrombotic Pulmonary Embolism

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About the Study

Since the initial description and subsequent development of the Pulmonary Embolism Response Team (PERT) by a multi-disciplinary medical group at Massachusetts General Hospital in 2012 [1] and the more recent enthusiasm over percutaneous thrombectomy for treatment of patients hospitalized with acute intermediate risk Pulmonary Embolism (PE), much attention has been directed to acute care algorithms and subsequent management of acute thrombotic PE [2]. Less commonly occurring, though associated with significant morbidity and mortality are cases of Non-Thrombotic Pulmonary Embolism (NTPE) wherein patients may present with symptoms and signs identical to acute thrombotic PE, including pulmonary vascular obstructive findings on CT Pulmonary Angiogram or perfusion defects on nuclear perfusion imaging, though with a history suggesting a non-thrombotic source such as air, cellular material, infectious organisms, or foreign body upon entry into the venous blood circulation [3].

Early in my career, circa the early 1990s, I was asked to see a patient in pulmonary consultation with hypoxemia despite a clear chest x-ray immediately following a total knee replacement Doppler venous ultrasound of the lower extremities showed no DVT, but the V/Q scan showed multiple mismatched segmental defects consistent with pulmonary embolism. The patient did not have objective findings to support fat embolism syndrome, i.e. petechial rash, thrombocytopenia or fat globules in the urine. And the rest of the history and physical examination did not fit with air or septic embolism. As I recall, this patient was treated with standard anticoagulation and recovered.

Methyl methacrylate (MMA) comprises the bone cement used widely in orthopedics in the U.S. since FDA approval in the 1970s for fixation of joint arthroplasty (surgery to replace all or some of a joint) to the bone and as a temporary spacer during to stage revisions of infected joints [4]. MMA is a clear, colorless liquid with a slight fruity odor, comprised on one end of a polymerizable methacrylate functional group and a reactive ester group on the other. It may dissolve with water and most organic solvents and though the liquid does not easily evaporate at room temperature, its vapor is heavier than air and so, may be more likely to be inhaled by those working with the product. MMA may be combined with another monomer to form Poly Methyl Methacrylate (PMMA), useful due its transparency, high impact strength and UV stability [5].

Although adverse pulmonary effects of bone cement containing MMA had been recognized since the mid-1970s, [6] the causes of which have been poorly understood, and no mention of pulmonary embolism related to the use of bone cement dating back to these early days could I discover in the medical literature. Otherwise unexplained hypoxemia had been attributed to ARDS [7] or acute bronchospasm and bone cement implantation syndrome, a poorly understood syndrome with clinical features that may include hypoxia, hypotension, cardiac arrhythmias, increased pulmonary vascular resistance and cardiac arrest [8]. Since its approval by the FDA in 2001 and again in their 2002 Guidance Document for Industry and FDA, the FDA has identified health risks of MMA bone cement including the aforementioned bone cement implantation syndrome, polymerization setting problems, loosening or migration of the device come infection and fever, adverse tissue reaction, pain and/or loss of function and revision [9]. Interestingly, no mention was made of acute thrombotic or non-thrombotic pulmonary embolism . Although in the case we report elsewhere, [10] we describe what appears to be an agglutination of foreign body material following inadvertent migration of injected methyl methacrylate into the vertebral venous plexus during a percutaneous vertebroplasty, easily seen as radiographically opaque material in the lobar pulmonary arteries, there may also have been an effect of the methyl methacrylate injected on the coagulation system causing a hypercoagulable state suggested recently by Dahl and coauthors, which in turn, may potentiate pulmonary thromboembolic disease [11].

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Rec**eived:** 08-Mar-2024, Manuscript No. JBL-24- 129117; **Editor assigned:** 11-Mar-2024, Pre QC No JBL-24- 129117 (PQ); **Reviewed:** 19-Mar-2024, QC No JBL-24- 129117; **Revised:** 29-Mar-2024, Manuscript No. JBL-24- 129117 (R) **; Published**: 08-Apr-2024, DOI: 10.37421/ 2165-7831.2024.14.321

Kyriakou described in their 2019 consensus for the International Myeloma Working Group the chronic pain suffered by MM, a hematologic malignancy associated with bone marrow infiltration by plasma cells which may be associated with lytic bone disease causing bone pain and spinal cord compression [12]. And as MM patients now live longer since the development of modern therapies including targeted pharmacologic agents with stem cell transplantation, more than half eventually may develop osteolytic or osteopenic disease of the spine. The group writes that while some patients respond to conservative treatments with eventual adequate reduction of pain, many still have refractory and incapacitating pain and may therefore be considered for surgical interventions including percutaneous vertebroplasty to relieve pain and restore function. The consensus overwhelmingly favored such interventions when indicated, only briefly mentioning that “cement embolus to the lungs may occur compromising respiratory function”.

In summary, while the medical literature is replete with warnings of complications of percutaneous vertebroplasty due to MMA, NTPE, though described by us and others in case reports and small case series, it has been given short shrift. Clinicians should consider this diagnosis in cases of otherwise unexplained hypoxemia following percutaneous vertebroplasty. The medical literature does not give standard guidance regarding management for NTPE, though anticoagulation may be prescribed on a case-by-case basis.

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How to cite this article: Scharf , Michael L. "Potential Respiratory Complications in Multiple Myeloma Patients Undergoing Percutaneous Vertebroplasty May Include Non-Thrombotic Pulmonary Embolism". *J Blood Lymph* (14): (2) (2024) :321