Conquest Of A Man-made, Worldwide Human Disease

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INTRODUCTION

In the long history of human disease, it has been uncommon to encounter a completely unique disease. In the 21st century, when this did occur, the disease was manmade. It is a credit to the hard work of researchers that they have been able to unravel the mysteries of a complex biologic process in slightly over one generation. Furthermore, it is remarkable that they have been able to create the means for prevention of an entire disease. Such is the story of periprosthetic osteolysis. The four decade saga from the iatrogenic creation of the disease, to the identification of its pathology, to the unraveling of its molecular biology, and subsequently to its prevention, is a fascinating report of medical detective work.

Periprosthetic osteolysis is a unique disease. It had never been seen prior to the widespread use of total hip arthroplasty. It is the most important long-term complication of total hip arthroplasty[1,2]. The osteolysis is most often secondary to particulate debris generated through wear of ultra high molecular weight polyethylene (UHMPE) at the articular surface of total hip replacement. During a forty-four year interval, this unique disease has been created, identified, explained, and now prevented.

The history of the unraveling and prevention of this worldwide, unique, never previously encountered, severe disease is a fascinating story of the integration of surgical innovation, molecular biology and material science.

Not only is periprosthetic osteolysis the single dominant long-term complication of total hip arthroplasty, it is also the major cause of acetabular component loosening, necessitating revision of acetabular components, a major contributor to loosening of femoral components, and the single most important process behind pathologic fractures of the femur and pathologic fractures of the acetabulum following total hip arthroplasty.

Recognizing a new disease

Prior to the widespread adoption of total hip arthroplasty, osteolysis arising from the prolonged, continuing liberation of micron and submicron particulate debris within the human body did not exist as a disease mechanism. As a result, this disease is unique, occurring only during the last fifty years.

Because of the obscure and unprecedented nature of this disease, it was 14 years after the first total hip replacement had been done that the true nature of the disease was effectively identified. In 1976 Willert published his concept of the migration of the particulate debris into the periprosthetic effective joint space [3, 4]. That same year we reported 4 cases of periprosthetic osteolysis[5], in which the initial consideration of the leading diagnostic possibility was metastatic malignancy or myeloma. In all four cases, sheets of macrophages, without any evidence of malignancy, characterized the histology.

The nature of the disease

We initially observed in 1983[6, 7] that the so-called fibrous membrane, which was commonly removed at revision surgery and discarded, had the capacity to generate PGE-II, and collagenase. This opened the door for the understanding of the molecular biology of the disease. We also showed that this fibrous tissue had the capacity to resorb bone when placed on rat calvarias, and that this capacity could be partially inhibited by NSAIDs.

Subsequently, far more detailed investigations into the synthetic capacity of the cellular constituents of this membrane have been performed. This multifaceted elaboration of the molecular biology associated with particulate periprosthetic disease has been a triumph of the investigative capacity of orthopaedic surgeons, rheumatologists and molecular biologists, leading to a substantial understanding of the mechanism of this disease[8].

Prevention of periprosthetic osteolysis

Since periprosthetic osteolysis is a disease of a prolonged generation of multiple small particles within the body, the prevention of this condition hinges on improved articulations. That goal was achieved when innovations in improving the articular surface were initiated. This happened over four decades ago with metal on metal articulations[9], over three decades ago with ceramic on ceramic[10,11] articulations, and more recently with the advent of highly crosslinked polyethylenes[12-15]. All three approaches have demonstrated that alternate bearing surface

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Supported by a grant The William H. Harris, MD Foundation

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combinations are distinctly superior to the original ultra high molecular weight polyethylene in terms of the prevalence of osteolysis after total hip arthroplasty.

Current status

Superimposed on the excellent long term results of the three alternate bearing surfaces are the excellent intermediate term clinical results of the more contemporary versions of each alternate bearing surface. Extrapolation of this intermediate term data suggests that the use of these three contemporary alternate bearing surfaces will extensively reduce, and possibly eliminate, periprosthetic osteolysis in the patient population receiving them.

Thus, over a period of four decades, an entirely new disease was created as a unanticipated byproduct of the ingenuity of the pioneers who created total hip arthroplasty. The invention of THA, unwittingly, also created periprosthetic osteolysis. That devastating complication, subsequently, became the number one long-term complication of this operation. Through the insightful investigations of a cadre of clinical and basic researchers, the disease was first identified, and subsequently more clearly defined as a biologic process. The use of alternate bearing surfaces now dominates much of total hip arthroplasty. These events have led to a set of circumstances with a high probability of major reduction or near elimination of a unique worldwide, never seen before human disease. In short, this is a fascinating, compelling and important story of the conquest of a unique worldwide human disease without prior precedent in the entire human experience.

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