
Radionuclide Imaging of Infection and Inflammation

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Radionuclide Imaging of Infection and Inflammation

A Pictorial Case-Based Atlas

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Foreword

There have been significant advances in our understanding of microorganisms and the pathogenesis of infection and inflammation as well as an increased availability of antimicrobial therapy in recent decades. Infection, nevertheless, remains a major cause of patient morbidity and mortality throughout the world. While the presence of infection may be suggested by certain signs and symptoms such as pain, loss of appetite, fever, general malaise and abnormal laboratory results, imaging studies often are used to localize or confirm the presence of infection. The imaging studies can be divided into two principal categories: morphological and functional. Morphological, or anatomic, imaging tests, such as radiographs, ultrasound, computed tomography and magnetic resonance, reveal anatomic or structural alterations in tissues or organs, which, in infection, are caused by a combination of microbial invasion and the immune response of the host to the invasion. Functional imaging studies, which are typified by radionuclide tests, make use of small quantities of radioactive material, or tracers that either are taken up by cells, tissues and organs directly, or are attached to native substances that subsequently migrate to the region of interest. Radiolabeled bisphosphonates, for example, are directly incorporated into the bone. Radiopharmaceuticals labeled with indium-111 or technetium-99m bind intracellularly in leukocytes, and are therefore used to monitor white cell accumulation at foci of infection. Other functional imaging tests used for localizing infection include gallium-67 citrate (and more recently the positron emitter gallium-68), and [^{18}F]fluorodeoxyglucose positron emission tomography ([^{18}F]FDG-PET).

Although radionuclide imaging has been used for diagnosing and localizing infection for nearly fifty years, and despite significant advances in agents, equipment, and imaging techniques, “nuclear infectology” has often been overshadowed by other areas of our specialty. One only has to compare the plethora of texts devoted to radionuclide imaging in oncology with the very few devoted to inflammation and infection in order to appreciate the void in our specialty.

Merely publishing a textbook, however, does not ensure its quality. Textbooks, regardless of whether they are of the traditional print or the more recent e-book style, are the foundation of medical knowledge, providing basic facts and a broad overview of a topic. The best textbooks do not contain exhaustive detail, or subtleties of diagnosis or management, all of which can be found in complementary resources. The success and value of a textbook depends on the organization, accessibility, and substantiality, of the information within.

Radionuclide Imaging of Infection and Inflammation: A Pictorial Case-Based Atlas edited by Lazzeri, Signore, Erba, Prandini, Versari, D’Errico and Mariani, admirably fulfills the criteria of the successful textbook. It begins with a thorough review of the commonly used radiopharmaceuticals, including the normal biodistributions, variants and pitfalls in image interpretation. This information not only sets the stage, and is especially useful, for studying the chapters that follow, but also provides the reader a readily accessible section for reference, when questions in other chapters, and even in daily practice, arise. The role of nuclear medicine in the usual clinical scenarios, such as soft tissue and musculoskeletal infections as

well as in fever of unknown origin (FUO), is thoroughly covered, objectively presented, well illustrated and referenced. Equally important are the chapters devoted to somewhat less well known or at least less frequently reviewed, situations such as infections of the lungs, central nervous system, and cardiovascular implantable devices, as well as chronic inflammatory diseases. The clinical cases provided at the end of the chapters provide valuable teaching points to supplement and enhance the text. The illustrations have been thoughtfully chosen and carefully prepared, incorporating the latest in hybrid imaging techniques.

It is gratifying indeed that this atlas has been organized by clinical entity rather than by technology. Our primary focus, albeit through imaging, is that of patient care, and it is both logical and better for the patient and for us, to focus on diseases rather than on technologies.

I now invite you, my fellow student, to read, to enjoy, and especially, to learn from *Radiionuclide Imaging of Infection and Inflammation: A Pictorial Case-Based Atlas*.

October 2012

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Foreword

The publication of this Atlas is an important achievement for the “Infection and Inflammation” Study Group of the Italian Association of Nuclear Medicine (AIMN), not least because it will allow the group’s expertise to be shared with colleagues worldwide. It is also a tangible reflection of the high level of professionalism and cooperation that exists within the group.

The fact that it is published by Springer will certainly help the AIMN in its pursuit of a key aim: to promote the efficient dissemination of scientific data and advances in the field of nuclear medicine that have relevance to other disciplines. In this regard, this Atlas follows in the footsteps of other publications produced within the context of the Italian nuclear medicine community.

As current president of the AIMN, I am therefore delighted by the completion of this volume, which will undoubtedly strengthen our knowledge of diagnostic nuclear medicine.

October 2012

Giovanni Lucignani
President of the Italian Association
of Nuclear Medicine (AIMN)

Preface

Inflammation is the physiological response of the body to any injury, which may be constituted by infection, a simple trauma, reduced blood supply, or also a tumor. The inflammatory response involves endothelial/vascular changes, local production of several chemotactic factors and cytokines, migration and accumulation of different types of immune cells (the task of which is to repair tissue damage and/or to destroy infectious agents), and postinflammatory events (such as granulomas or fibrosis). The pattern of immune cell population and the resulting histopathologic features differ according to the type of injury and its persistence over time. When inflammation is elicited in response to infection, granulocytes are continuously recruited by chemotactic bacterial factors; in trauma and degenerative diseases, granulocytes may be present transiently, but are followed by a lymphocytic infiltration; in the presence of tumor cells, NK cells and macrophages predominate; in autoimmune diseases and graft rejection, it is T- and B-cells in addition to macrophages that predominate. If the pathological injury persists over time, inflammation may further evolve from an 'acute' type reaction to a 'chronic' type reaction, which is generally characterized by a lesser degree of vascular involvement and more important mononuclear cell infiltration, with eventual formation of granulomas or fibrosis.

All such features are not highly specific for any particular type of injury, and may in fact have various overlaps, both in terms of type of cell population involved and in terms of time-related patterns. Therefore, the inflammatory response should be considered as a 'dynamic' process self-adapting to an evolving pathophysiologic condition, rather than a 'stereotyped' response elicited indifferently by all injuries.

Diagnostic imaging with modern molecular nuclear medicine is based on the availability of sensitive and relatively specific radiopharmaceuticals tailored for the different targets that can be expressed in this complex scenario.

Three important consequences emerge from the above considerations: i) choice of the 'best' radiopharmaceutical for imaging infection/inflammation should be based on clinical ground, as well as on the timing and etiology of the process; ii) dynamic pathophysiology of the inflammatory process (with its associated histopathologic features) is the basis for distinguishing a 'sterile acute inflammation' from a 'septic acute inflammation', or a 'sterile chronic inflammation' from a 'septic chronic inflammation'; iii) correct diagnosis of infection/inflammation is dictated by optimal use of the available radiopharmaceuticals (in terms of indication for employing a particular imaging agent and in terms of preparation and quality control), as well as by optimal use of image acquisition protocols, image elaboration, and image interpretation.

Throughout this atlas the term 'inflammation' is frequently used as synonymous with 'sterile acute inflammation' or 'sterile chronic inflammation', while the term 'infection' is used as a synonym of 'septic acute inflammation' or 'septic chronic inflammation'.

While several radiopharmaceuticals are now commercially available for imaging infection, many others are currently under investigation, including radiolabeled cytokines, peptides, some monoclonal antibodies, antibiotics, vitamins, etc. This atlas only deals with the routine clinical use of commercially available radiopharmaceuticals or cell preparations, such as radiolabelled leukocytes (^{99m}Tc -HMPAO and ^{111}In -oxine), nanocolloids, monoclonal antibodies, ^{67}Ga -citrate and ^{18}F FDG.

We refer the reader to other textbooks and guidelines for thorough, in-depth understanding of the use of available radiopharmaceuticals, indications, acquisition protocols, and interpretation criteria. Whereas, the goal of this atlas is to guide the practitioners and students through a wide selection of diagnostic images as obtained in the clinical routine of different centers for different clinical conditions involving infection/inflammation. We placed special emphasis on information enabling the recognition of the normal biodistribution patterns of radiopharmaceuticals (including possible pitfalls and artifacts, as discussed in Chapter 1), as well as the main imaging findings in more than 30 different inflammatory/infective disorders.

Some chapters describe the most frequent infection/inflammation conditions that are referred to nuclear medicine departments for diagnosis and characterization, such as bone and joint infection (Chapters 3 and 11), joint prosthesis infections (Chapter 4), vascular prosthesis infection (Chapter 5), fever of unknown origin (Chapter 9), and inflammatory bowel diseases (Chapter 10). All such chapters include some teaching cases, where it is quite easy (also for the untrained eye) to recognize, even on planar imaging, the abnormal accumulation of radiopharmaceutical over time at the site of infection, while in some other cases the comparison between planar and tomographic images emphasizes the added value of hybrid imaging (mostly SPECT/CT) to exactly localize the site of infection and its extension to surrounding structures.

Other chapters describe less common diseases, that are therefore illustrated with fewer diagnostic cases, such as soft tissue infections (Chapter 2), infection of non-orthopedic prosthesis implants and resident electronic medical devices (Chapter 6), infections of the central nervous system and head and neck structures (Chapter 7), infective endocarditis (Chapter 8), lung infections (Chapter 12), and inflammatory, noninfectious diseases such as vasculitis, sarcoidosis, rheumatoid arthritis, etc. (Chapter 13). The scans included in these chapters have been selected so as to indicate how, in the evaluation of some cases such as infective endocarditis or chest vascular prosthesis, SPECT/CT imaging is an essential requirement for correct diagnostic interpretation.

With this atlas we intended to fill an important gap in the nuclear medicine books published so far, by providing the essential background both for understanding the pathophysiologic basis of radionuclide imaging of infection/inflammation and for correctly interpreting the diagnostic images obtained in these conditions. Nevertheless, the role of nuclear medicine imaging in each condition is presented in the general perspective commonly encountered in the clinical practice, which also includes the use of other imaging modalities. The 'clinical cases' have the purpose of demonstrating the clinical impact of nuclear medicine imaging procedures in the workout of patients with suspected infection/inflammation.

This atlas is the result of years of common work with colleagues of the Study Group of Inflammation/Infection of the Italian Association of Nuclear Medicine (AIMN). All authors have contributed both by writing specific chapters and by providing images and clinical cases for all chapters. Not only the authors, but also many other colleagues from Italy and from abroad have contributed interesting pictures and clinical cases. We are therefore deeply indebted to all such contributors, who are acknowledged at the end of each chapter. In particular, our close collaborators, Dr Roberto Boni, Dr Marta Pacilio, Dr Virginia Rossetti, and Dr Martina Sollini deserve special acknowledgements.

Last but not least, we wish to thank the team of publishers at Springer for allowing us to prepare and publish this atlas book in a very short time.

October 2012

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