Microbial infection imaging: A novel diagnostic approach

Sir,

The diagnosis of infection is essentially dependent on direct demonstration of the pathogen and its antigenic or genetic signatures. Whereas, host reactions, such as, antibody production, pathological changes in tissue and cellular or biochemical alterations of blood also provide indirect evidence of infection that are often nonspecific in nature. The role of conventional anatomical imaging (sonography, radiography, etc.) in the detection of infection is limited by its inability to delineate the early pathological changes without significant anatomical aberrations.[1] Infection imaging is a unique scintigraphic technique which facilitates rapid detection of infective foci by locating areas with higher leucocytes density. A variety of approaches, including Ga-67 citrate, radiolabelled autologous leukocyte and radiolabelled leukocyte targeting molecules that is, monoclonal antibodies against leukocyte antigens, have been used in these scans.[2] However, these scans cannot differentiate infections from sterile inflammation and also has a limited role in granulocytopenia.[1] Microbial imaging is a novel technique, developed over the last decade, to precisely locate microbes in tissue using a wide array of radiolabelled molecules targeting microbial cells, that is, antimicrobial agents (Tc-99m labelled fluoroquinolones, ceftizoxime, ethambutol, isoniazid, fluconazole), antimicrobial peptides (Tc-99m labeled ubiquitin, human neutrophil peptide, human lactoferrin), bacteriophages and bacterial growth factors (In-111 labelled biotin).[1-4]

The ideal radioconjugate for this purpose should be a stable compound which is radiochemically pure, nonantigenic, nontoxic to microbial and human cells, with rapid clearance and least nonspecific binding and accumulation in human tissue, while having substantially high specific interaction with microbial target sites in planktonic growth as well as in biofilms.[3] Until date, no radiopharmaceutical has achieved all these essential properties. Ubiquicidin 29–41 peptide fragment tagged with Tc-99m is the commonest probe used to study bacterial and fungal infections in human as well as in animals.[1] There is growing concern on limiting the use of antibiotics as probes since it may result in drug resistance in pathogenic bacteria.[3] Despite small mass, large surface-to-volume ratio of bacterial cell ensures extensive radioconjugate binding on its surface in comparison to granulocytes.[1] However, the bacterial load in the host remains as a critical factor. There is insufficient evidence to support the use of radiopharmaceuticals in increasing dose to improve the sensitivity of detection in case of low infective load of bacteria.[1]

Table 1: Various radiopharmaceuticals used for microbial infection imaging

Category	Radiopharmaceutical	Target
Antibiotics	Tc-99m ceftizoxime	Bacterial cell wall
	Tc-99m alafosfalin	
	Tc-99m ciprofloxacin	Bacterial DNA gyrase and topoisomerase
	Tc-99m sparfloxacin	
	Tc-99m enrofloxacin	
	Tc-99m norfloxacin	
	Tc-99m clindamycin	Bacterial cell
	Tc-99m doxycycline hyclate	
	Tc-99m ethambutol	Mycobacteria
	Tc-99m isoniazid	
	Tc-99m fluconazole	Fungal cell
	Tc-99m chitin-binding protein	
Antimicrobial peptides	Tc-99m UBI 29–41	Bacterial and fungal cell
	Tc-99m-HNP 1–3	Bacterial cell
	Radiolabelled bacteriophages	Bacterial cell
	Radiolabelled human lactoferrin	Bacterial cell
Growth factor	Tc-99m biotin	Bacterial cell

HNP: Human neutrophil peptide, UBI: Ubiquicidin

Currently, microbial infection imaging is restricted to acute bacterial infections, mycobacterial infections and candidiasis [Table 1].[3-5] Imaging of filamentous fungi, parasitic

and viral agents are yet to become a reality. Pertaining to the extremely low volume and mass, this approach is reasonably challenging in viruses. Whereas, ease of microscopic demonstration due to larger size and availability of special stains along with rapid progress in molecular methods has reduced the need for microbial imaging of fungi and parasites. This is especially relevant in detecting occult infective foci and discriminating these conditions from inflammation.[1] Hence, it might have potential use in the diagnosis of pyrexia of unknown origin, endocarditis, septicemia, meningitis, visceral and intraabdominal abscesses, extra pulmonary tuberculosis and systemic mycoses. In conclusion, microbial imaging provides a novel diagnostic approach to infection and its scope in medicine and patient care needs further research.

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