Nuclear Medicine imaging of vertebral infections

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Chapter 10

Conclusions and future perspectives

Plasma proteins (like transferrin and lactoferrin), white blood cells and hyperglucidic methabolism of inflammatory cells represent the target of conventional radiopharmaceuticals in nuclear medicine for the diagnosis of vertebral infection.

^{67}Ga-citrate is able to bind infact to transferrin, lactoferrin and white blood cells. The uptake of gallium in infection site is therefore predominantly aspecific. Gallium accumulates in many other conditions, including primary and metastatic neoplasms, aseptic inflammation and traumatic foci. Despite the satisfactory results that have been obtained with gallium, it should be noted that few data are available on its use in postoperative SI. Several investigators have reported increased gallium accumulation in normally healing surgical incisions for up to several months after surgery.

Labelled antibiotics in vitro are able to bind to bacteria wall, bacteria DNA and to white blood cells but their utilization in vivo seem to lose the specificity for bacteria. The data of some studies performed in animal model showed that the uptake of labelled antibiotics was predominantly due to aspecific mechanism.

^{18}F-FDG is extremely sensitive to evaluate the presence of hyperglucidic methabolism but it is not specific for the presence of inflammatory or infective event. Inflammatory cells such as neutrophils and activated macrophages, that are present in case of acute or chronic inflammation, avidly take up the glucose analogue FDG owing to increased glycolytic activity. Moreover, its low physiological bone marrow uptake makes FDG an interesting tracer for imaging the spine. Several investigations suggest in fact that FDG-PET accurately detects SI. Taking into account the published results and our own experience, a negative FDG-PET scan can exclude the presence of SI. The specificity of the test is acceptable, although caution should be taken in interpreting a positive PET study, particularly in the presence of spinal implants.

None of the tracers described is able to bind exclusively to bacteria.

Biotin represents a tracer to allow a different approach in detecting bacterial infection, it represents a growth factor for bacteria and it seems to possess a true specificity for microrganisms detection.

In future, as far as in vitro experiments are concerned, we would like to study the capability of biotin to recognize different kind of microorganisms. We will also evaluate the capability of Biotin to differentiate between bacteria and fungi infection or between pyogens and microrganism with a low-rate of proliferation (like Koch bacillus) infection. To evaluate the relevance of biotin in the growth of microrganism we will test the growth of pyogens, *mycobacterium tubercolosis* and *candida albicans* without biotin, with biotin and with labelled-biotin. Then we plan to evaluate the presence of labelled biotin in bacteria after 2, 4, 6 and 24 hours of incubation, periodic washes, centrifugations and gamma-counter counting. The same evaluation can be made by real-time quantification of radioactivity presence inside bacteria, for example using *ligand tracer* device, where it is possible to evaluate the internalization of labelled-biotin inside bacteria during the incubation with the tracer using a Petri plate.

Some patients, who performed ^{111}In-biotin scintigraphy during antibiotic therapy, showed a disappearance of uptake of labelled biotin, this matches with the resolution of infection (accompanied by normalization of flogosis index, disappearance of back-pain etc) but in some patients a clearly evident reduction of tracer could be found in lesions even if the infection was not present any more. For this reason we would like to determine retrospectively, a semi-quantitative evaluation of all studies of patients performed during follow-up to calculate the cut-off level of pathologic uptake of ^{111}In-biotin.

In our patient population two patients with vertebral metastasis showed no accumulation of ^{111}In-biotin then we will plan a prospective study to compare ^{111}In-biotin SPECT/CT with ^{18}F-FDG-PET/CT in patients with vertebral infection and vertebral tumors to better prove the specificity of labelled biotin.

Last but not least we will consider the possibility to label biotin with a radionuclide available for PET/CT diagnostics. Chemical structure of biotin linked with chelator diethylenetriamino pentaacetic acid (DTPA), should allow the labelling of the vitamin with ^{68}Ga. ^{68}Ga, with a half-life of 68 min, offers cyclotron-independent, convenient and low-cost access to PET radiopharmaceuticals. This radionuclide is readily available by elution from a ^{68}Ge/^{68}Ga generator system possessing about a 2-year life span (^{68}Ge t1/2=270.8 days). Furthermore, the ^{68}Ga decays 90% by the emission of positrons (1.921 MeV), without any gamma contribution, and 10% by electron capture; it is thus an ideal nuclide for PET/CT imaging. The possibility to employ labelled biotin with ^{68}Ga allows furthermore its quantitative evaluation of the uptake in site of infection. This characteristic seems to be necessary and important especially in the follow-up of patients during therapy.