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Detection of cancer of unknown origin by means of SPECT and PET tracers

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Carcinoma of unknown primary origin (CUP) includes a heterogenous group of cancers, accounting for a small proportion of all human tumours (0.5-0.6 %) characterized by an overall poor prognosis, with a median survival of only 7 months and a five years survival rate of 5 % (1). CUP is a syndrome presenting with localized or diffuse biopsy-proven malignancy with an unidentified primary lesion, after careful medical history, physical examination and relevant clinical tests. CUP may present with different histological features, the most common of which is adenocarcinoma of well to moderate differentiation (50 %), followed by undifferentiated to poorly differentiated carcinomas (30 %), squamous cells carcinoma (15 %) and undifferentiated neoplasms (5 %). Although extensive effort and expense is expended to identify the primary lesion site, only 20-27 % of tumours are identified by conventional tests ante-mortem and autopsy studies have reported that 70 % of cases remained undiagnosed. The primary tumour may remain undetected when the primary lesion is too small or when there is involution of the primary tumour after seeding metastasis, which is likely related to an angiogenic incompetence leading to marked apoptosis. Identification of the primary tumour site is crucial to change the prognosis in patients with CUP. Recent studies reported longer surival rates for patients with CUP and an identified primary lesion subsequently treated with specific therapy.

During the years a number of diagnostic procedures have been proposed for identifying CUP, including nuclear medicine techniques (2). The use of nuclear medicine investigations is based on the capability of radiotracers of detecting tumors. For this purpose several SPECT and PET tracers have been suggested, namely most oncological tracers were employed. Gallium67citrate scintigraphy was suggested for identifying melanoma, lung cancer and lymphoma, but with limited results. Somatostatin receptor scintigraphy (SRS) may play a role for localizing tumors of neuroendocrine origin: at present 111In-Pentetreotide is likely to be the only really useful SPECT tracer in CUP. Other SPECT tracers may be used in selected cases with a comlpementary role, for example bone scanning could help identifying skeletal metastases and thyroid scanning could help localizing thyroid cancer.

Indeed the most useful radiotracer was found to be 18F-fluorodeoxyglucose (FDG) (3,4). In fact FDG positron emission tomography (PET) scan is known to be useful in the detection and staging of a variety of tumours, including squamous cells carcinoma of the head and neck, lung cancer, breast cancer, melanoma, lymphoma, and colorectal cancer. FDG PET can detect the primary lesion in 24–40 % of patients with CUP and negative conventional diagnostic procedures. In last 10 years several papers have demonstrated the usefulness of FDG PET in patients with cervical adenopathy (suspect head and neck tumor) but also visceral metastases and other unknown primary, including isolated axyllary adenopathy. At present FDG PET is considered an indicate diagnostic procedure in patients with CUP. As many new PET tracers are currently under develpoment, it is possible that in the near future further radiotracers may help in the diagnostic challenge of CUP. 18F-DOPA and 68Gallium-DOTA-NOC may be suggested as an alternative to somatostatin receptor scintigraphy for localizing CUP of neuroendocrine nature.

The introduction of integrated PET/CT systems further enhanced the detection power of this imaging technique. PET metabolic information can be coupled with CT anatomical data, increasing the identification of primary tumours particularly in anatomically difficult districts, such as head and neck, abdomen and pelvis, where the physiological tracer uptake (for example, by the tonsils, lymphatic tissue, stomach, bowel and urether) could lead to misinterpretation of small areas of increased radiotracer uptake. Preliminary data indicates that FDG PET/CT has a very good accuracy in the detection of the primary tumour (5) and is therefore highly recommended in the diagnostic work up of patients with CUP.

References

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