

Pseudoprogession as a novel radiological sign of solid tumors underwent sonodynamic therapy

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Background

Low-intensity focal ultrasound waves sensitize the same photosensitizer used in photodynamic therapy, however; with deeper penetration scale from 4-8 cm below the skin. Photosensitizer excitation by ultrasound waves generates molecular oxygen atom as a free radical, causing oxidative cascade which leads to a targeted cell death without damaging the surrounding healthy tissues and organs.

Patients and Methods

Four patients with solid tumors; one lung cancer, two metastatic ovarian cancer (lung and lymph nodes) and one urothelial carcinoma underwent sonodynamic therapy either as a palliative option after the failure of the standard of care or as a solo treatment after declining the standard of care.

Sonodynamic protocol was applied as follows :

- Oral liposomal formulations* of hypericin and curcumin were administered 10 hours prior session.
- During the session, patient underwent ozone therapy through major autochemotherapy.
- Intravenous albumin-coated microbubbles loaded with riboflavin* were administered 30 minutes prior ultrasound irradiation.
- Sites of tumor were radiated by ultrasonic wave power 3 Watts / frequency 1 - 3 MHz for 10 -15 minutes each.

* Prepared at our research facility.

Results

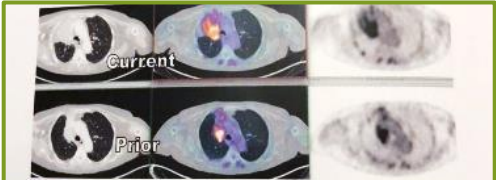
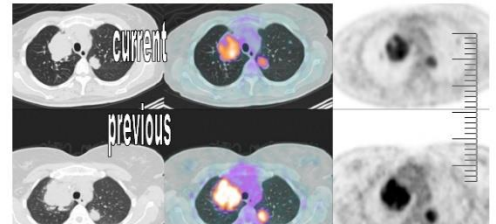
- Three patients performed PET scan after four sessions of Sonodynamic Therapy which revealed metabolic regression, along with reduction in tumor markers and improvement of quality of life despite the morphological progression.
- Urothelial carcinoma patient underwent endoscopic biopsy, after CT morphological progression, histopathological examinations, and immunohistochemistry that unveiled neutrophil infiltration, and increased rate of apoptosis with reduction of the proliferation index KI67 (10%).

Conclusions

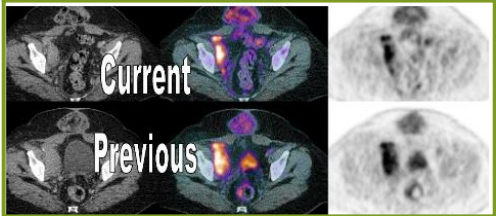
- During cell death process, immune cells infiltration and cavitation properties by ultrasonic radiation result in cell swelling which provides a false impression of morphological progression in regular sonography and CT study (Pseudo-progression).
- PET scan and tissue biopsy (if applicable) are crucial for proper judgment of Sonodynamic Therapy treatment efficacy. PET scan demonstrates both tumor morphology and metabolic activity, whereas tissue biopsy illustrates immune cells infiltration and the degree of cell death.

PET/CT Findings:

- Lungs, metabolic regression with mixed morphologic response the FDG-avid bilateral pulmonary nodules. The right pulmonary supra-hilar mass currently measures 5.4x4.6 cm with SUVmax 8



- Lungs:
- Right lung:
 - Metabolic regression despite morphologic progression of the previously noted right upper lobe trans-pulmonary mass



- Metabolic regression with morphologic progression of the previously described right iliac retro-peritoneal lesion being inseparable from the right psoas muscle, currently measures 7.7 x6.6 cm with SUVmax 7.6 compared to 6.2 X 5.2 cm and SUVmax 15.8.

