Fluorescence Diagnosis For Follow-Up Of Mycosis Fungoides Therapy

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Mycosis Fungoides

- It is a chronic slowly evolving cutaneous T cell lymphoma.
- A malignant neoplasm of memory T – helper cell.
The natural course of MF is divided into: early stages (IA, IB, IIA) and advanced stages (IIIB, III, IV).

Early stage CTCL may be controllable, NOT curable.
Treatment and Prognosis

There are three major categories of therapy in CTCL:

- (a) Skin-directed therapy (SDT)
- (b) Biologic response modifiers
- (c) Chemotherapy

Thickness of cutaneous infiltrate has a high prognostic value: it gives information about the quantity of skin tumoral mass: TUMOR BURDEN.
During Mycosis fungoides (MF) treatment, regular clinical examination as well as obtaining multiple biopsy specimens to follow up the response to therapy is needed.

An invasive technique can be a significant burden for patients.

Thus a non-invasive technique for treatment follow-up would be of great value.
FD for Malignant/Premalignant Skin Lesions

FD is well-documented for follow-up of tumors of keratinocytic origin.

- SCC
- BCC
- Actinic Keratosis
- Bowen’s disease
Aim

Could fluorescence diagnosis (FD) be used as a valid non-invasive diagnostic technique for follow up of MF patients during therapy?
Patients & Method

- Twenty-two patients of early stage Mycosis fungoides were subjected clinical evaluation followed by fluorescence diagnosis of their most affected skin lesion before and after 12 weeks of therapy.
Method of FD

- 20% ALA cream was prepared from ALA powder supplied by Sigma Pharmaceuticals ® in cold cream.
- ALA cream was applied under an occlusive dressing to affected and surrounding normal skin in an area of 2x4 cm.
- Occlusion was performed by Alu-foil to prevent photobleaching of the photosensitizer.
Timing

- After 3 hours of incubation, fluorescence intensity on the skin was recorded.
- This time point was found to have optimal tumor/normal skin contrast ratio when performing FDAP.
PpIX may accumulate intracellularly because of limited capacity of ferrochelatase to metabolize it to heme by introducing an iron (Fe) molecule.
DIGITAL PHOTOANALYSIS

This system consists of a

- Handpiece with LED lighting (405 nm).
- & Camera (12-bit charged coupled device CCD) combined in one arm.
- Connected to a computer system equipped with custom image capturing software (Dyaderm, Biocam GmbH, Germany).
Visualization of the PpIX represents the basis of the photodynamic diagnosis (PDD) of the skin tumours.

Or

Fluorescence-diagnosis-with Aminolevulinic Acid induced-Porphyrins

FDAP
METHOD OUTLINE

Emits blue light, simultaneous photography of the color- and fluorescence image

Data processing

Patient monitoring

3h ALA-treatment

ALA-Creme

query lesion

skin

Blue Light

Fluorescence

Image data

Visible Lesion

ALA-treated

skin
Pseudo-Colored Digital Images

- The human eye can distinguish colors better than shades of brightness (grey).
- The fluorescence diagnosis system can display fluorescence emitted from lesions as colored image:

The blue color represents the lowest value of relative fluorescence, while red color represents the highest value.
Calculation of protoporphyrin IX (PpIX) accumulation factor (AF) was performed, this denotes the fluorescence ratio between tumor tissue and normal skin.

The mean of the accumulation factor, was found at time of start of study to be 2.2.

This mean decreased significantly after 12 weeks of therapy.
Fig. 1: Fluorescence Diagnosis image of patient No 17 from Mycosis Fungoides skin lesion, A: before treatment (week 0): note high number of red/orange spots (arrow) denoting high release of PPXI from malignant hyperproliferative cells, compared to the yellow/green color of less active cells. B: Same lesion after treatment (week 12): denoting decreased number and scattered red spots of malignant cells (arrow).
Fluorescence Diagnosis

Tamer Fadel

Date of birth 19.09.1986
Examination date 25/07/2010
Localisation Trunk - 2

Findings
No finding

Histology:

Follow up:

Proceeding:

Finding Remarks

Image remarks
In comparison flow cytometric assessment of skin biopsies for CD4+/CD7- malignant T-cell count

- It was evaluated before and after therapy from skin biopsy of the same lesion.
- Result: The percent of CD4+/CD7- cells also showed a statistically significant decrease after treatment.

Fig. 2: Representative flowcytometry histogram of patient no. 17. A: Before treatment (week 0) shows predominately CD4+ve/CD7-ve malignant T-cells, 60.6%. B: Same lesion after treatment (week 12): shows predominately CD4+ve/CD7+ve normal T-cells, 85.25%. 
Final Remarks

- In cases of patches and plaques of MF, FD can represent a prognostic tool for evaluating the response to therapy.
- Changes in accumulation factor values can be used for follow-up of therapy in the same patient, as it parallels changes in clinical response. It should not be used as an absolute value.
Fluorescence imaging is an attractive diagnostic technique for skin tumor assessment.

It is well established for tumors of keratinocytic cell origin.

It has the potential to come more and more into clinical use, especially for tumors of lymphocytic cell origin.
Thank you for your attention

Does fluorescence diagnosis have a role in follow up of response to therapy in mycosis fungoides?

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