The Effects of Oral Chemotherapy Treatment on Friction Skin

Southern California Association of Fingerprint Officers (SCAFO)
Ontario, California - September 2011

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NOTICE

Introduction

- December 2008 a 62 year old male entering the United States from Singapore was detained by U.S. Customs and Immigration Service because his fingerprints were not detectable
- Individual was released after four hours of detainment once officials were satisfied he was not a threat to national security
- Later learned through a report in the "*Annals of Oncology*" the individual was suffering from metastatic nasopharyngeal carcinoma and was prescribed capecitabine as treatment which caused his fingerprints to degrade and thus not be recorded

Introduction

- Capecitabine is a recently developed orally administered chemotherapy agent for a number of different types of cancers
- Capecitabine has increased in popularity because it benefits patients by less hospitalization time and associated costs compared to other treatment regimens with superior chemotherapeutic results

Introduction

- A side effect to capecitabine is Hand and Foot Syndrome (HFS)
- Overall incidence of HFS observed with capecitabine treatment reported to be around 50% with 17% of patients reporting severe forms of HFS
- Severe cases of HFS may interfere with normal daily activities of patient
  - HFS severity considered dose limiting toxicity
- Treatment interruption followed by dose reduction or withdrawal usually leads to rapid reversal of symptoms with no long term medical consequences

Introduction

- HFS is *symptomatically* characterized as:
  - Numbness
  - Unpleasant/Abnormal tingling, prickling feeling
  - Redness of skin
  - Painless swelling or discomfort
  - blisters
  - ulceration
  - peeling of skin
  - moderate to severe pain on palms of hands and soles of feet

Introduction

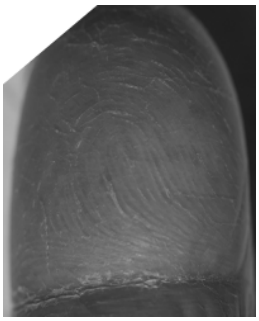
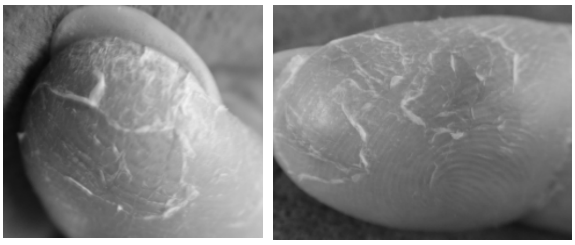


Image represent symptoms of HFS due to capecitabine treatment (77 Days into treatment)

Introduction



Images represent symptoms of HFS due to capecitabine treatment (89 Days into treatment)

Introduction

Image represent symptoms of HFS due to capecitabine treatment (106 Days into treatment)

Introduction

- HFS is *histologically* characterized as:
  - Premature keratinization of basal cells
  - High concentration of white blood cells in Stratum Spinosum (immune system response)
  - Isolated cellular death

Introduction

- Pathogenesis of capecitabine induced HFS is speculated
  - Evidence suggests that capecitabine is attacking basal keratinocytes in the same manner in which malignant cells are attacked
    - Capecitabine ⟶ 5'-deoxy-5-fluorocytidine (5'-DFCR)
    - 5'-DFCR ⟶ 5'-deoxy-5-fluorouridine (5'-DFUR)
    - 5'-DFUR ⟶ 5'-Fluorouracil (5'-FU)

Thymidine Phosphorylase (TP)

Introduction

- TP has been found to be associated with tissues having a high rate of proliferation (i.e. malignant (cancerous) cells and keratinocytes)
- High concentration of TP in malignant tissues acts to localize cytotoxic effects to malignant tissues *(main focus of treatment)*
- Friction skin also has high concentration of TP due to keratinocyte hyperproliferation (high rate of keratinocyte division) which acts to localize cytotoxic effects to keratinocytes *as a side effect of treatment*
- Metabolites of 5'-FU inhibit DNA and RNA synthesis causing cell cycle arrest and cellular death

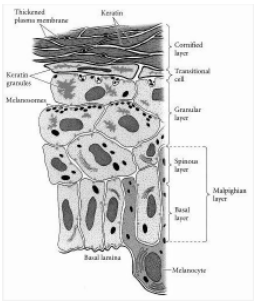
Introduction

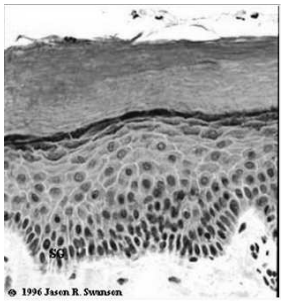
• Capecitabine induced HFS is thought to be caused by inhibiting proper basal keratinocyte proliferation due to toxic effects of 5'-FU metabolites on basal keratinocytes

- Premature keratinization
- Isolated death of keratinocytes
- Causing visual HFS symptoms
  - Redness of skin
  - Blisters
  - Ulceration
  - Peeling of skin

Introduction

• Normal epidermal strata and cellular proliferation of keratinocytes

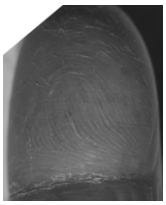




Study Purpose

• Focus of this study is to assist latent print examiners to understand the association between capecitabine induced HFS and the reproducibility of friction ridge skin for forensic and other comparative purposes.

#7 Finger (1 Day into Study)



#7 Finger (77 Days into Study)

Participant Background

• Participant initially diagnosed with invasive ductile carcinoma of the breast with a triple negative phenotype which later metastasized into bones

• Participant treatment regimen consisted of multiple 3-week long cycles (1250mg twice a day, two weeks "on", one week "off")

- Treatment lasted for 188 days
- Study lasted for 253 days

Materials and Methods

• Multiple methods of recording the friction skin were utilized

- Traditional Ink Technique (50 impressions per recording)
- Traditional Ink after application of "ID Enhancer Spray" (20 impressions per recording)
- Digital imaging (White light with and without black powder using Nikon D2XS digital camera)
- Post Mortem Technique utilizing black powder and adhesive labels (10 impressions per recording)
- Livescan – Images saved according to EFTS (Cross Match Technologies ID500) (20 impressions per recording)

Materials and Methods

• Record fingerprints obtained on weekly basis (avg)
  - Began on first day of treatment
• Digital imaging method used on a monthly basis
• Powder method used on a monthly basis
• Livescan method three times throughout the course of study
• Quality of record fingerprints objectively evaluated with no digital enhancements using the automated quantitative scoring system of the AFIX Tracker AFIS System

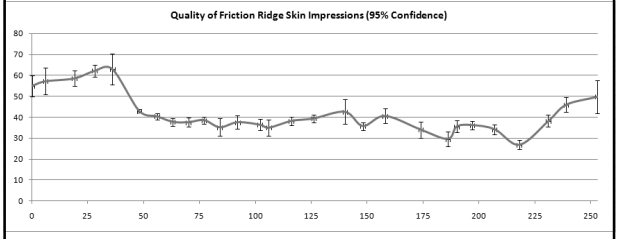
Results

- Quality scores calculated at 95% Confidence
- Avg. AFIX Quality Score for the 50 impressions on Day 1 using the Ink Method: 55.0 +/- 5.1
- Avg. AFIX Quality Score on Day 253 (last day) using the Ink Method: 49.8+/- 7.8
- Avg. Ink Method score (No ID Enhancer) = 41.6 +/- 1.6
- Avg. Ink Method score (With ID Enhancer) = 43.1 +/- 3.4
- Avg. Powder score = 42.4 +/- 10.7
- Avg. Livescan score = 37.3 +/- 7.6

Results

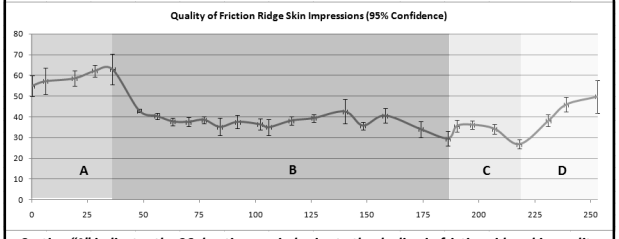
- Quality differences in the methods of recording the impressions were not to a statistically significant degree (p=0.44, Student's t-test)
- Between 36 and 48 days into the study the quality dropped 32%
  - Quality remained at the decreased level until 218 days
- Last dose of capecitabine 188 days into study
  - Quality began improving at 218 days into study (30 days following last dose)
  - Quality reached baseline at 253 days into study (35 days following the onset of quality improvement)

Results



Graph representing the quality of the friction ridge skin impressions using the AFIX Tracker Automated Quality Score during the course of the 253 day evaluation. The graph represents the quality of the impressions recorded using the ink method

Results



Section "A" indicates the 36 day time period prior to the decline in friction ridge skin quality due to the onset of HFS. Section "B" indicates the sustained time period in which the participant continued normal treatment with capecitabine. Section "C" indicates the 30 days time period in which the participant had ceased treatment, but the quality of the friction remained at the decreased quality state. Section "D" indicates the time period in which the quality of the friction ridge skin rapidly improved (30 days post cessation of treatment)

Discussion

- Intervals of dramatic quality decrease/increase are consistent with previous literature suggesting full keratinocyte maturation lasts approximately 30 days from Stratum Basale to Stratum Corneum
- Persistency in ridge formation was evident in the former and latter portions of the study despite the temporary toxicity to the basal keratinocytes

Discussion

Each image represents the appearance of the friction skin of the left index of the study participant recorded using the ink method on (left image) the first day of the study, (middle image) the 84th day of the study, and (right image) the 253rd (last) day of the study. Note that the arrangement of the friction ridges and ridge characteristics were not altered between the first and last days of the study despite the temporary toxicity to the keratinocytes. Middle image demonstrates the poor quality of the friction skin impression obtained using the ink method while undergoing treatment of capecitabine and experiencing HFS.

Conclusion

- Capecitabine treatment may result in HFS
- Friction skin quality may degrade due to toxicity of capecitabine
  - Degradation due to improper keratinocyte proliferation
- Despite temporary toxic exposure, ridge characteristics are persistent upon cessation of treatment
- No statistical differences in the method of recording the impressions
- Further research is needed with more participants and other chemotherapeutic agents

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