Skin cancers and inherited epidermolysis bullosa: a complication to know 2014 updates

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Inherited epidermolysis bullosa (IEB)

• Skin disorder characterized by increased skin and/or mucosal fragility and blister formation

• Mutations of proteins involved in cohesion of superficial skin layers

* 4 major types according to the level of skin cleavage :

-> Simplex IEB
-> Junctional IEB
-> Dystrophic IEB
-> Kindler Syndrome
Inherited epidermolysis bullosa (IEB)

- More than 30 phenotypic subtypes and hundreds of different mutations

**Minor forms**
- Localized fragility
- Minor handicap

**Severe forms**
- Serious handicap
- Complications (infectious, nutritional, scarring, carcinoma ...)

Images of skin lesions and complications.
Skin cancers

**Squamous cell carcinoma (SCC)**
- From keratinocytes
- ± precancerous lesions
- 25% of skin cancers
- Occurrence > 70 age
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**Basal cell carcinoma (BCC)**
- From keratinocytes
- No precancerous lesions
- 70% of skin cancers
- Occurrence > 70 age

**Treatment:**
- SCC and BCC: Most of the time -> surgery
- Melanoma: Surgery (sometimes systemic treatment)

**Melanoma**
- From melanocytes
- 5% of skin cancers
- Potentially aggressive
- Occurrence ≈ 50 age
- Sun...
To review all documented patients with IEB in whom an SCC developed, to characterize these SCCs and their methods of management:

- Which patients are at risk of developing a SCC?

→ A systematic literature search was carried out:
  * From medical databases available on internet
  * Medical data from scientific literature were collected
IEB and skin cancers

• Basal cell carcinoma
  - Risk may be increased?
  - Mostly for EBS-DM?
  - But remains a very common cancer even in the general population

• Melanoma
  - Risk may be increased?
  - Mostly for RDEB-HS?
  - But it seems to be very uncommon

But remain cautious because very little data are available in the literature

Fine JD et al. JAAD 2009
Medline/Embase/Cochrane Library/Clinical trials.gov
N=168 articles identified
N=150=Medline
N=18=Cochrane Central Register of Controlled Trials

Articles excluded (reading of title or abstract)
N=77
Guidelines and basic research articles, n=33
Not Inherited epidermolysis bullosa, n=5
Other cancers (melanoma, basal cell carcinoma, sarcoma), n=4
Other reasons, n=35

N= 91 articles

Articles excluded (reading of article )
N=21
Basic research articles, n=4
Not confirmation of diagnosis, n=4
Duplicates, n=4
Others reasons, n=9

N=70 articles

RDEB N=45
DDEB N=5
EBS N=3
KINDLER N=6
JEB N=6

Different types in the same article N=5

Fig 1. Study design flowchart.

RDEB; recessive dystrophic epidermolysis bullosa, DDEB; dominant dystrophic epidermolysis bullosa, EBS; epidermolysis bullosa simplex, JEB: junctional epidermolysis bullosa
IEB and skin cancers

- The most significant complication = occurrence of squamous cell carcinoma
  - The most common cancer during IEB
    But still far from being systematical !!

  - 2.6% of IEB population (regardless of the subtype)
    Higher percentage for RDEB-HS

  - Potentially severe especially if diagnosis is delayed

  - Interest of early detection: think about it! Be ready to recognize!

  - Patient involvement/his surrounding

Fine JD et al. JAAD 2009
The risk of developing SCC is depending on the type of IEB

Be careful especially for recessive dystrophic forms (75% of cases)

Risk of early onset compared to non affected population

Be careful throughout life, especially after age of 30
Average age= 37,7 years

Both men and women can be affected
Sex Ratio M/W= 1,15
- All ethnic groups may be involved
  - Be careful, especially for fair phototype
  - 50% caucasian (publication bias)

- A lesion can hide another
  - Be careful, a patient may develop several SCC

- Role of sun exposure? Data are missing
  - But of course, sun protection is essential
  - Interest of REBECCA project
    -> prospective study conducted by the 3 French references centers of IEB
    (Nice, Toulouse-Bordeaux and Necker)
Most of the time the extremities are affected, but any area can be concerned

Be careful, especially of the limbs (legs, hands, arms)

Mucosal SCC is rare but possible (8.5% of cases)

No data are available about the symptomatic nature of SCC
(pain, itching...)

Be careful because an asymptomatic lesion is possible
Squamous cell carcinoma occurs always on injured skin (scar-erosion ...)

With any wound that will not heal after "several months" (> 9 months)
With any unusual lesion
Erosions that could lead to squamous cell carcinoma

If there is any doubt .... biopsy
Non-healing erosions/ulcerations-atrophic scarring
If there is any doubt.....biopsy
• Importance of early detection
  = Smaller tumor accessible to surgery (reference treatment)

Subject of interest for clinical, epidemiological and basic research

Prevention is better than cure!

Several research projects are currently developed in France:

➢ Interest of Photodynamic therapy (PDT) to treat precancerous lesions

➢ REBECCA project