Corneal Transplant Related Galli-Galli Disease

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Galli-Galli Disease (GGD)

- Very rare autosomal dominant *genodermatosis* (~27 reported cases)

- Member broader family of *reticulated pigmented skin disorders*

  - Galli-Galli disease (GGD)
  - Dowling-Degos disease (DDD)
  - Reticulate acropigmentation of Kitamura
  - Reticulate acropigmentation of Dohi
  - Haber Syndrome
Galli - Galli Disease (GGD)

- First described by Bardach in 1982
- Identified in two brothers named Galli
- Presented with a reticulated hyperpigmented skin eruption affecting skin folds
Galli - Galli Disease (GGD)

- Initially thought to represent a distinct clinical entity
  - Clinical presentation indistinguishable from DDD
  - Consistent histopathology finding of *acantholysis* which was unique to GGD
Acantholysis

- Loss of connection between epidermal keratinocytes secondary to breakdown of desmosomal intercellular attachments

Note the rounded and detached, free floating keratinocytes
Acantholysis

- Characteristic of various skin conditions including;
  - Galli-Galli Disease
  - Pemphigus vulgaris
  - Herpes virus vesicular eruptions
Galli - Galli Disease (GGD)

- Subsequent research identified common genetic defect for both GGD and DDD
- Identical frameshift and nonsense mutations located on KRT5 gene
- Consequently GGD now considered an *acantholytic variant* of Dowling-Degos Disease
Clinical Presentation GGD

- Multiple 1-2 mm red - dark brown puritic papules
Clinical Presentation GGD

- Focally confluent in a reticulated (*net-like/chicken wire*) pattern
Clinical Presentation GGD

- Predilection for *flexural* (skin fold) areas including the *neck*
Clinical Presentation GGD

- Predilection for *flexural* (skin fold) areas including the *axilla*
Predilection for *flexural* (skin fold) areas including the *inframammary* and inguinal regions.
Variant Manifestations GGD

- Grover disease-like erythematous, keratotic papules and lentigo-like macules of the trunk and extremities.
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GGD Disease Characteristics

- Age at onset varies widely: teens – 70’s
- Inheritance pattern:
  - Autosomal dominant with incomplete penetrance
  - Sporadic
- Disease is progressive without spontaneous remission
Histopathology

- Digitiform elongation of the rete ridges
- Basal layer hyperpigmentation
- Focal suprabasal acantholysis (hallmark feature)
Association With Immune Suppression
Association with Immune Suppression

- Grover’s Disease
  - *Transient* (weeks-months) acantholytic dermatosis of unknown cause
  - Manifests as a papular skin eruption on trunk and proximal extremities
  - Clinically similar to and high on the differential dx list for GGD
Grover’s Disease has a well documented association with immunosuppressive conditions including:

- HIV
- Hematologic malignancies
- Bone-marrow allotransplantation (1.8% incidence)
- Renal transplantation (solid organ)
Association with Immune Suppression

- GGD has been documented in a liver transplant case (clinically an atypical Grover-like variant)
  - Skin lesions involved the trunk
  - Skin flexural areas unaffected

Implications

- Systemic immune suppression may in some way trigger or effect disease penetrance in a genetically predisposed individual.
An “E – Ticket”
(Case Presentation)
“E – Ticket”

- TL: a 37 yo caucasian female

- POH
  - Hyperopia
  - SCL wear (20/20 OU)

- PMH
  - Negative except for gall bladder surgery
  - Allergies: Sulfa and Keflex
  - FH: negative for dermatologic disorders
Tammy

- September 2002 “jacuzzi splashed” at pool party while wearing SCL’s
- One day later noted pain, redness and photophobia OD
- Treated by local MD with Q-1 hr topical antibiotics/ antivirals/steroids
- Experienced increasingly severe pain, photophobia and vision loss
- Referred to myself ~6 weeks after symptom onset
Based on history and presentation, dx’ed with *acanthamoeba keratitis*

On initial visit:
- Epithelial debridement culture performed (AK+)
- PHMB + broline initiated / AB’s continued / steroid weaning attempted

Responded poorly:
- Developed PED
- Was steroid weaning intolerant
- Developed progressive stromal opacification and VA loss
- Persistent spores identified by serial confocal microscopy (Dr Irvine/Dr Hopp)
- Eventually required addition of systemic tx for spore eradication
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Tammy’s E-Ticket Journey

- PED
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- PED

- Acute strep crystalline keratopathy (overlying ring infiltrate)
Tammy’s E-Ticket Journey

- PED
- Acute strep crystalline keratopathy
- Acute onset white mature cataract
Tammy’s E-Ticket Cascade

- PED
- Acute strep crystalline keratopathy
- Acute onset white mature cataract
- Successful CE + PC IOL
Tammy’s E-Ticket Journey

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- Successful CE + PC IOL
- Acute onset of malignant glaucoma
Tammy’s E-Ticket Journey

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- Acute strep crystalline keratopathy
- Acute onset white mature cataract
- Successful CE + PC IOL
- Acute onset of malignant glaucoma
- Successfully treated with vitrectomy
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- Acute strep crystalline keratopathy
- Acute onset white mature cataract
- Successful CE + PC IOL
- Acute onset of malignant glaucoma
- Successfully treated with vitrectomy
- Progressive secondary glaucoma
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- PED
- Acute strep crystalline keratopathy
- Acute onset white mature cataract
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- Successfully treated with vitrectomy
- Progressive secondary glaucoma
- Placement Ahmed valve (9/08/06)
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- Placement Ahmed valve (9/08/06)

- Explantation of valve secondary to painful irritation and poor IOP control
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- Repeat shunt (Doheny; Dr Brian Francis)
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Penetrating keratoplasty with AMT
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- Penetrating keratoplasty with AMT

**Posterior Ischemic Syndrome**
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- PED
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- Acute onset white mature cataract
- Successful CE + PC IOL
- Acute onset of malignant glaucoma
- Successfully treated with vitrectomy
- Progressive secondary glaucoma
- Placement Ahmed valve (9/08/06)
- Explantation of valve secondary to painful irritation and poor IOP control
- Repeat shunt (Doheny; Dr Brian Francis)
- Penetrating keratoplasty with AMT
- Posterior Ischemic Syndrome

- Retrobulbar alcohol injection (unsuccessful)
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- PED
- Acute strep crystalline keratopathy
- Acute onset white mature cataract
- Successful CE + PC IOL
- Acute onset of malignant glaucoma
- Successfully treated with vitrectomy
- Progressive secondary glaucoma
- Placement Ahmed valve (9/08/06)
- Explantation of valve secondary to painful irritation and poor IOP control
- Repeat shunt (Doheny, Dr Brian Francis)
- Penetrating keratoplasty with AMT
- Posterior Ischemic Syndrome
- Retrobulbar alcohol injection (unsuccessful)

- Progressive anterior dislocation of PC IOL (to corneal touch)
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- Acute strep crystalline keratopathy
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- Successful CE + PC IOL
- Acute onset of malignant glaucoma
- Successfully treated with vitrectomy
- Progressive secondary glaucoma
- Placement Ahmed valve (9/08/06)
- Explantation of valve secondary to painful irritation and poor IOP control
- Repeat shunt (Doheny; Dr Brian Francis)
- Penetrating keratoplasty with AMT
- *Posterior Ischemic Syndrome*
- Retrobulbar alcohol injection (unsuccessful)
- Progressive anterior dislocation of PC IOL to corneal touch

- 2009 developed chronic pruritic rash (Grover disease distribution)
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- Acute onset white mature cataract
- Successful CE + PC IOL
- Acute onset of malignant glaucoma
- Successfully treated with vitrectomy
- Progressive secondary glaucoma
- Placement Ahmed valve (9/08/06)
- Explantation of valve secondary to painful irritation and poor IOP control
- Repeat shunt (Doheny; Dr Brian Francis)
- Penetrating keratoplasty with AMT
- Posterior Ischemic Syndrome
- Retrobulbar alcohol injection (unsuccessful)
- Progressive anterior dislocation of PC IOL to corneal touch
- Developed chronic pruritic Grover distribution rash (2009)

- Second tube shunt explantation with concomitant CPC (10/09)
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- Acute strep crystalline keratopathy
- Acute onset white mature cataract
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- Acute onset of malignant glaucoma
- Successfully treated with vitrectomy
- Progressive secondary glaucoma
- Placement Ahmed valve (9/08/06)
- Explantation of valve secondary to painful irritation and poor IOP control
- Repeat shunt (Doheny; Dr Brian Francis)
- Penetrating keratoplasty with AMT
- Posterior Ischemic Syndrome
  - Retrobulbar alcohol injection (unsuccessful)
  - Progressive anterior dislocation of PC IOL to corneal touch
  - Developed chronic pruritic Grover distribution rash (2009)
  - Second tube shunt explantation with concomitant CPC (10/09)
- Repeat penetrating keratoplasty with IOL explantation

- Total retinal detachment (3/29/13)
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- Acute strep crystalline keratopathy
- Acute onset white mature cataract
- Successful CE + PC IOL
- Acute onset of malignant glaucoma
- Successfully treated with vitrectomy
- Progressive secondary glaucoma
- Placement Ahmed valve (9/08/06)
- Explantation of valve secondary to painful irritation and poor IOP control
- Repeat shunt (Doheny; Dr Brian Francis)
- Penetrating keratoplasty with AMT
- Posterior Ischemic Syndrome
- Retrobulbar alcohol injection (unsuccessful)
- Progressive anterior dislocation of PC IOL to corneal touch
- Developed chronic pruritic Grover distribution rash (2009)
- Second tube shunt explantation with concomitant CPC (10/09)
- Repeat penetrating keratoplasty with IOL explantation
- Total retinal detachment

- Galli-Galli disease diagnosed (10/12/14)
Tammy’s Galli-Galli Disease

- Initially diagnosed as “gluten” allergy
- Ultimately required 5 years/5 dermatologist for correct diagnosis
- Definitive dx made by Dermatopathology Service at UCSF
- Underwent ~successful UV-B phototherapy
Tammy’s E-Ticket Journey

- Eviseration 9/15/15
Tammy’s E-Ticket Journey

- Eviseration 9/15/15
- Galli-Galli disease continues
Tammy’s E-Ticket Journey

- Eviseration 9/15/15
- Galli-Galli disease continues
- Received 13 years worth of continuous and at times high dose topical steroids
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- Grovers Disease has strong/well documented association with immune suppression including organ transplantation
Summary

- TL represents only the ~28\textsuperscript{th} case of GGD ever reported
- Clinically manifested as Grover-like variant of GGD
- Grover's Disease has strong/well documented association with immune suppression including organ transplantation
- Documented case of Grover-like variant GGD associated with organ transplant immune suppression
Summary

- TL represents only the second organ transplant (PK) associated case of GGD ever reported
Summary

- TL may represent the first ever report of a corneal transplant associated noninfectious systemic disease (GGD)
Summary

- TL may also represent the first ever report of a topical steroid immune suppression associated noninfectious systemic disease (GGD)
Thank You