ROBERTS SYNDROME

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Medical Genetics
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HISTORY

John B Roberts (1919)
- Studied three affected siblings whose parents were first cousins
- All three showed limb malformations, bilateral cleft chin, and protruding intermaxillary region

Hermann et al. (1969)
- Described a syndrome with growth retardation, limb malformation, and facial defects
- Named it SC phocomelia syndrome

HISTORY

There was much controversy over whether the syndromes noted by Roberts and Hermann were the same disorders

Van Den Berg and Francke (1993), Schule et al. (2005)
- Compared Roberts and SC phocomelia patients
- Noted high phenotypic variance
- Concluded that Roberts Syndrome and SC Phocomelia were clinical variants of the same disorder

FACTS

Autosomal recessive inheritance
- Both parents are carriers

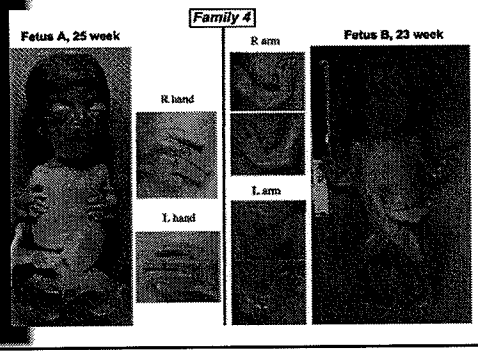
Very rare occurrence
- 150 cases recorded as of 2009

Common to have parents related in some way before marriage

Most die in infancy

CLINICAL DIAGNOSIS

Limb malformations

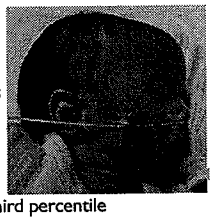


CLINICAL DIAGNOSIS

Types of limb malformations
- Tetraphocomelia
  - Deformation of all four limbs
- Hypomelia
  - Hypoplasia (underdevelopment) of part or all of a limb
- Oligodactyly
  - Less than five fingers/ toes per limb
- Syndactyly
  - Two or more fingers/ toes joined together

Clinical Diagnosis

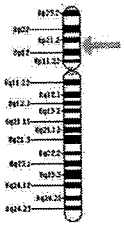
normal facial features
Bilateral cleft lip and palate
Micrognathia – undersized jaw
Exophthalmos – bulging eyes
Downslanting palpebral fissures
Ear malformations
Hypoplastic nasal alae



enatal growth retardation
Height and weight below the third percentile
ssible mental retardation

Genoypic Abnormality

ESCO2
- Locus 8p21.1
- 11 exons
- 3376 bp coding region
- 601 amino acid protein
- N-acetyltransferase
  - C-terminal acetyltransferase
  - N-terminal end
  - Binds to chromatin and plays a role in binding the sister chromatids after S phase

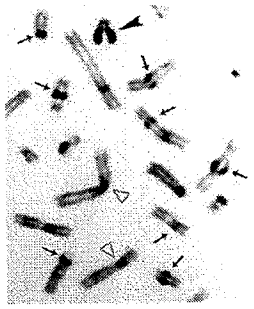


Genotypic Abnormality

Frameshift or nonsense mutation of ESCO2
- Leads to truncation or alteration of the amino acid chain
- Loss of acetyltransferase activity
- Interference in the cohesion of the heterochromatic regions

Cytogenetic Testing

C-banding
▷ Normal cohesion of heterochromatin
→Heterochromatin regions separated
→Separated Y chromosome



Prenatal Testing

Ultrasound testing to assess the limbs, palate, and any heart defects
Amniocentesis at 15 to 18 weeks gestation
Chronic Villi Sampling at 10 to 12 weeks gestation
Molecular testing to identify both the disease causing alleles

Risks

An affected individual can rarely reproduce if survived past infancy
- Only two cases such cases reported
  - One had an unaffected child
  - One had a miscarriage

Both parents are carriers
- 25% chance of affected offspring
- 50% chance of carriers
- 25% of normal offspring

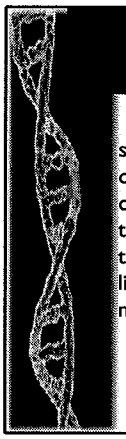
67% chance of an unaffected sibling being a carrier

MANAGEMENT

Diagnosed individuals usually do not survive past infancy

Those who survive

- Treatments depend on the patients' conditions
- Reconstructive surgery to repair malformations
- Speech assessment and therapy for cleft palate
- Treatments for cardiac, kidney, and renal defects
- Full quality of life possible in cases without severe mental retardation



CONCLUSION

Roberts syndrome is a rare disease with severe phenotypes that could limit the scope of life of an affected individual. But with some cooperation from the community to help in the maintenance, the few affected individuals that survive do have a chance to lead a better life than those individuals that are affected by more cruel disorders.

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Multiple Choice Questions

Roberts Syndrome

1. What is the probability that both the phenotypically normal parents of an affected individual are carriers if half of the offspring are affected and half are phenotypically normal?
    a. 50%
    b. 100%
    c. 0%
    d. 25%
    e. Cannot be determined

2. What of the following conditions apply to a Roberts Syndrome patient?
    a. Acetyltransferase mutation
    b. Mutation of the locus 8p21.1
    c. ESCO1 mutation
    d. A and b
    e. All of the above

BREAST CANCER

BY: KATHLEEN CARTER

WHAT WE KNOW

- Advertisements

WHO HAS HAD BREAST CANCER

- Many Celebrities, Mostly Women

INTRODUCTION

- Clinical History of Breast Cancer
  - The first known documents of breast cancer date back to Egypt in 1600 B.C. There was no cure and the treatment was cauterization with a "fire drill".
  - In the 1700's it was discovered that there was a link between breast cancer and a swelling in the lymph nodes in the arm pit.
  - French surgeon Jean Louis Petit and Scottish surgeon Benjamin Bell were the first to remove the cancerous tissue, lymph nodes, and underlying musculature.

INTRODUCTION

- Clinical History of Breast Cancer (cont.)
  - William Halsted performed the first mastectomy in 1882.
  - Radical Mastectomies first performed in 1902.
  - First case-controlled study by Janet Lane-Claypon in 1926
  - In 1955 it was discovered that sex hormones were involved and the first clinical trial for combination cancer chemotherapy was designed.

INTRODUCTION

Clinical History of Breast Cancer (cont.)

- In the 1970's doctors decided that a simple mastectomy was just as effective as a radical mastectomy. Also studies on the lumpectomy were being started.
- In 1988 Dennis Salmon, MD discovered that too much of the cancer gene that produces the her-2/neu receptor was associated with 30% of aggressive breast cancers.

INTRODUCTION

- Clinical History of Breast Cancer (cont.)
  - In 1990 Mary-Claire King, MD found the link between breast cancer and the BRCA-1 gene on chromosome 17.
  - In 1994 David Kingston, MD reported effective results with the drugs Taxol and Taxotere
  - In 1998 the first successful trials of chemoprevention were conducted.

INTRODUCTION

- Clinical History of Breast Cancer (cont.)
  - In 2002 Stephen Friend, MD developed a new DNA technology to predict whether patients will develop mestasis. This led to a decrease in chemotherapy as treatment. Also Bernard Fisher, MD released a 20 year study that concluded that a total mastectomy was no more effective than a lumpectomy and lumpectomy/radiation treatment.

INTRODUCTION

- What is breast cancer?
  - Breast cancer is a malignant tumor that starts in the cells of the breast.
  - Breast cancer is a disease that affects both men and women. However women are 100 times more likely to have breast cancer than men.
  - In their lifetime 1 in 8 women will be diagnosed with breast cancer.

TYPES OF BREAST CANCER

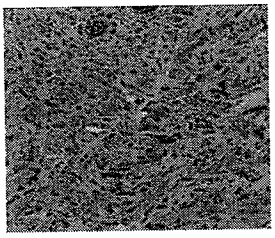
- There Are Three Main Types of Breast Cancer:
  - Ductal Carcinoma In Situ
  - Invasive Ductal Carcinoma
  - Invasive Lobular Carcinoma

TYPES OF BREAST CANCER

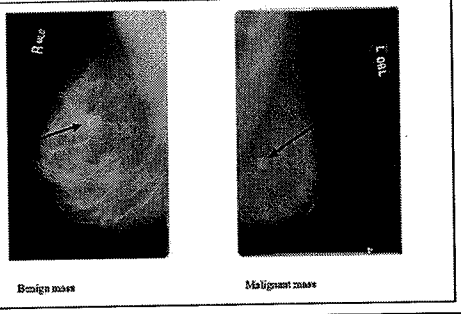
- Less Common Types of Breast Cancer:
  - Inflammatory Breast Cancer
  - Triple-Negative Breast Cancer
  - Paget Disease of the Nipple
  - Phyllodes Tumor
  - Angiosarcoma

WHAT DOES IT LOOK LIKE?

- Human Lobular Carcinoma



WHAT DOES IT LOOK LIKE?



CLINICAL FEATURES

- Can Breast Cancer Be Inherited?
  - In most diagnoses, there is no family history of breast cancer.
  - Only about 5-10% of breast cancer cases are thought to be inherited.
  - The inherited mutation is in the BRCA-1 and BRCA-2 genes.

CLINICAL FEATURES

- Is Breast Cancer Inherited? (cont.)
  - Any family history of breast cancer increases your risk. But if your mother, sister, or daughter was diagnosed, your risk is doubled. Your risk is higher especially if that person was diagnosed with cancer in both breasts or before menopause.

RISK FACTORS

- Some Risk Factors That May Increase Your Chances of Getting Breast Cancer Are:
  - Being Female
  - Increased Age
  - Personal History
  - Family History
  - Radiation Exposure
  - Obesity

RISK FACTORS

- Cont.
  - Beginning your period at an early age
  - Having your first child after the age of 30
  - Postmenopausal hormone therapy
  - Drinking alcohol

DIAGNOSIS

- 5 Ways to Diagnose
  - Breast Exam
  - Mammogram
  - Breast Ultrasound
  - Biopsy
  - Breast MRI

STAGING

- Ways to Determine the Stage of Breast Cancer
  - Blood Tests
  - Mammogram
  - Chest X-Ray
  - Breast MRI
  - Bone Scan
  - CT Scan
  - PET Scan

STAGES OF BREAST CANCER

- Breast Cancer is Identified as Stages 0-IV
  - Stage 0 – Carcinoma In Situ
  - Stage I – Cancer has formed
  - Stage II – Cancer is in breast or lymph node
  - Stage III – Three types A, B, and C
  - Stage IV – Cancer has spread to other organs

TREATMENTS

- Currently 6 Types of Standard Treatment
  - Surgery
  - Sentinel Lymph Node Biopsy Followed by Surgery
  - Radiation Therapy
  - Chemotherapy
  - Hormone Therapy
  - Targeted Therapy

NEW TREATMENTS

- New Treatment Being Used in Clinical Trials
  - High-Dose Chemotherapy with Stem-Cell Transplant

SUPPORT

- Many Types of Support Groups at Hospitals, Community, and on Internet
  - Breastcancer.org
  - Local Hospital and Cancer Clinics
  - Local Chapters of American Cancer Society or Susan G. Komen For the Cure

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Multiple choice questions

Name__Kathleen Carter_____ Presentation on___Breast Cancer___

1. Women are how many times more likely than men to be diagnosed with breast cancer?
    a. 2 times
    b. 10 times
    c. 50 times
    d. 100 times
2. If there is you have no family history of breast cancer, you are not at risk.
    a. True
    b. False