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Senior Resident Peer-to-Peer Case Studies

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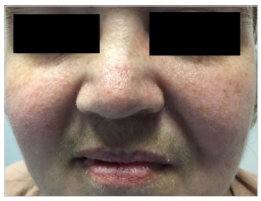
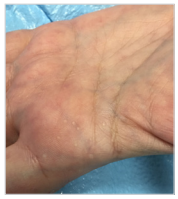
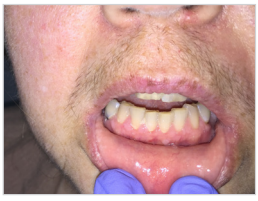
Case Studies authored by our educational partner GW School of Medicine and Health Sciences Dermatology Residency Program

School of Medicine & Health Sciences
THE GEORGE WASHINGTON UNIVERSITY

1)



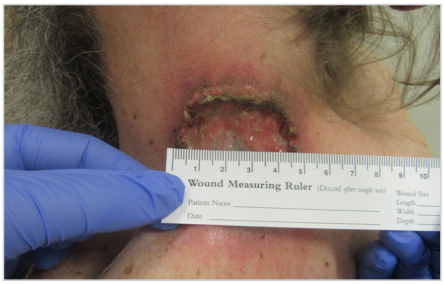




A 40-year-old woman presented to clinic for evaluation of multiple "skin growths" on her face, hands and gums that had increased in number over the past 10 years. Her past medical history was remarkable for invasive ductal carcinoma of the left breast, multiple colon polyps, a benign thyroid nodule and uterine fibroids. Classic phenotypic features of this disease include all of the following features except:

A. Lipomas
B. Macrocephaly
C. Trichoepitheliomas
D. Sclerotic fibromas
E. Hemangiomas

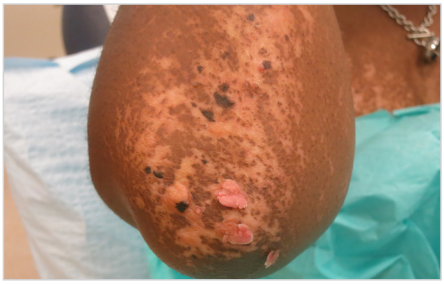
2)

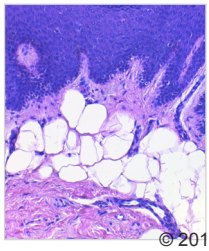


A 65-year-old man presented with an asymptomatic, purulent ulcer on his neck increasing in size for the past four years. Review of systems was notable for a 30-pound weight loss in the past year. Physical exam showed this ulcer and posterior cervical lymphadenopathy. Chest computed tomography found scattered round nodules of varying sizes in both lungs. Oral therapy for this disease targets what factor?

A. p53
B. t(17;22)
C. Patched
D. Smoothened
E. Cytotoxic T-lymphocyte antigen 4

3)





A 38-year-old African American female presents for management of several pink papules growing on her elbows and groin. She also has multiple soft, skin-colored and hypopigmented blaschkolinear nodules with representative pathology shown here. Her daughter and granddaughter have similar skin findings as well as ectrodactyly. Which of the following is true regarding the disorder?

A. The disease is inherited in an X-linked recessive fashion.
B. This is caused by a mutation in the PORCN gene.
C. The disorder progresses through four stages.
D. This condition is associated with an immunodeficiency.
E. Both B and D are correct.

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The content of these case studies, ideal to review during peer study groups, was developed by Elizabeth Robinson, MD and Jennifer Aronica, MD under the guidance of dermatologist Adam Friedman, MD, FAAD, Associate Professor of Dermatology, Residency Program Director, Director of Translational Research, Department of Dermatology GW University.

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Answers

1) The correct answer is C: Classic phenotypic features of this disease include all of the following features except trichoepitheliomas.

Explanation/Literature Review

This patient has Cowden disease. Biopsy of one of her facial papules was consistent with a trichilemmoma. Cowden disease is part of the PTEN hamartoma tumor syndrome that also includes Bannayan-Riley-Ruvalcaba syndrome, SOLAMEN syndrome (segmental overgrowth, lipomatosis, arteriovenous malformation and epidermal nevus) and Lhermitte-Duclos disease. Cowden disease is an uncommon tumor syndrome due to an autosomal dominant mutation with incomplete penetrance in the PTEN gene, a tumor suppressor. The skin is involved in almost all cases of Cowden disease.

Cowden disease has many cutaneous findings including trichilemmomas, acral keratoses on the dorsal hands and feet, palmoplantar keratoses, oral mucosal papillomatosis, lipomas, hemangiomas, neuromas, lentigines, sclerotic fibromas and macrocephaly. Cowden disease is associated with multiple tumors including breast carcinoma and fibroadenomas, thyroid carcinoma and benign adenomas, endometrial cancer, ovarian cysts, leiomyomas, renal cell cancer, colorectal cancer, hamartomas and melanoma. Once Cowden disease is recognized it is important to initiate cancer surveillance.

Trichoepitheliomas are pink papules usually on the face that appear clinically similar to trichilemmoma. Trichoepitheliomas are associated with several autosomal dominant disorders including Brooke-Spiegler, Rombo and Bazex-Dupré-Christol syndrome.

2) The correct answer is D: Oral therapy for this disease targets smoothened.

Explanation/Literature Review

This image shows a classic rodent ulcer of basal cell carcinoma (BCC). The overall risk of metastasis in all BCCs is quite low, 0.028-0.55%. However, large, ulcerated BCCs have a higher risk of metastasis. The risk of metastasis is 1.9% for BCCs greater than 3.0 cm and up to 45.0% for BCCs greater than 10 cm.

Two hedgehog pathway inhibitors, vismodegib and sonidegib are approved for the treatment of BCCs in patients who are not candidates for surgery or radiation, or whose disease has recurred after surgery. Only vismodegib is approved for the treatment of metastatic BCCs. Both drugs inhibit smoothened. Patched is mutated in BCCs and therefore does not suppress smoothened signaling.

P53 is mutated in squamous cell carcinomas and some melanomas. Imatinib, an inhibitor of protein tyrosine kinase, targets the t(17;22) chromosome translocation resulting in fusion of COL1A1 with the PDGFB gene. This translocation is present in 90% of dermatofibroma sarcoma protuberans. Ipilimumab targets cytotoxic T-lymphocyte antigen 4 (CTLA-4). Ipilimumab is used as a treatment for unresectable or metastatic melanoma.

3) The correct answer is B: This is caused by a mutation in the *PORCN* gene.

Explanation/Literature Review

This patient has Goltz syndrome. Goltz syndrome, also known as focal dermal hypoplasia, is a highly variable X-linked dominant disorder with abnormalities in tissues derived from the primitive ectoderm and mesoderm.[1] Goltz is caused by mutations in the PORCN gene, which is involved in the secretion and signaling of Wnt proteins playing a role in embryonic tissue development. The majority of patients (roughly 90%) are female. Only mosaic males survive as non-mosaic male mutations are antenatally lethal. Almost 95% of all Goltz cases arise de novo, which partly reflects the decreased likelihood of reproduction by severely affected women and the lethality of PORCN mutations.[2] Rare familial cases do show anticipation, with the offspring being much more severely affected than the parent and has a higher burden of mutant cells.[3]

The clinical features of Goltz vary depending on the proportion and distribution of cells expressing a mutant X chromosome. Streaks of vermiculate dermal atrophy and telangiectasias are often present at birth. Later, hypo and hyperpigmentation as well as fat herniations will develop. Histopathologic examination often shows decreased thickness of the dermis with adipocytes extending into the papillary dermis.

Raspberry-like squamous papillomas can appear in any location but tend to favor the lip, distal extremities and anogenital regions. These can be painful, bleed and become enlarged. It is important to recognize that these are features of Goltz syndrome as they can be mistaken as condyloma acuminatum but there is no HPV association and patients are immunocompetent.[4]

Limb abnormalities are present in about half of Goltz cases with the most common findings being syndactyly and ectrodactyly. Imaging of the lower extremities characteristically shows osteopathia striata. Patients may also have unilateral eye abnormalities including coloboma or aniridia. Dystrophic nails, sparse hair, abnormal teeth and dysmorphic facies can also be seen.[4]

Treatment is supportive with appropriate subspecialist referrals based on associated abnormalities. These might include orthopedics, genetics, oral surgeons, physical therapists and ophthalmologists.[1] The telangiectasias may be improved with pulsed dye laser treatment and exophytic squamous papillomas with cryotherapy, curettage or photodynamic therapy.

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