(International Print/Online Journal)

SJIF IMPACT FACTOR: 5.565
PUBMED-National Library of Medicine ID-101739732

ISSN (Print): 2209-2870
ISSN (Online): 2209-2862

International Journal of Medical Science and Current Research (IJMSCR)
Available online at: www.ijmscr.com
Volume 6, Issue 6 , Page No: 570-574
November-December 2023

IJMSCR

Gorlin Syndrome - An Intresting Inherited Case Report In A 48 Years Old Female

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Type of Publication: Case Report
Conflicts of Interest: Nil

Abstract

Gorlin Syndrome is a rare autosomal dominant inherited disease, with high penetration and variable expressivity. This disease caused by mutation in the Sonic hedgehog signaling pathway PTCH1 gene. It's characterized by the presence of numerous basal cell carcinoma, along with skeletal, ophthalmic and neurological abnormalities

Keywords: Gorlin syndrome, Multiple basal cell carcinoma, Rare disease

Introduction

Gorlin syndrome first described by Brinkley and Johnson, later Dr. Robert Gorlin and Dr. Robert Goltz reviewed it.[1] Gorlin syndrome affects 1 in 40,000 - 60,000.[2] This is a rare autosomal dominant disorder that exhibits higher penetration and variable expressivity. This syndrome is caused by mutations in PTCH 1 gene.[3] Thus, resulting in multiple basal cell carcinomas, keratotic odentogenic tumor (KCOT), palmar and plantar pits and ectopic calcifications of flax cerebri. Herein, we report an inherited case of a women with multiple skin lesions in more than 10 different sites similar complaints we noted in her mother also.

CASE REPORT: A 48 years old female patient presented with chief complaint of multiple non healing hyper pigmented lesions over scalp, face and body associated with pain and discharge since 20 years. There was a significant family history with similar complaints from patient's mother, and congenital syndactyly was noted.The patient underwent cryotherapy and CO2 laser therapy eight years ago. All the lesions were excised and sent for histopathological examination (Figure 1,2).

Figure 1 : Patient with multiple skin lesions

Figure 2 : Patient's mother with multiple skin lesions

GROSS FINDINGS : Received 13 bottles of grey brown to dark brown soft tissue bits from different sites largest measuring 6x5x0.5 cm from right fronto-temporal region and smallest measuring 1x1 cm from right lower canthus of eye (Figure 3).

Figure 3 : Gross showing grey brown to dark brown soft tissue bits at multiple sites

MICROSCOPIC FINDINGS : Sections studied show skin with epidermis and dermis. Epidermis lined by keratinized stratified squamous epithelium. Tumor arising from the basal layer of epidermis and extending into the dermis. Tumor cells are arranged in nests, cords, tubular, gland like and lace like patterns with peripheral palisading and peritumoral clefting. Individual cells are basaloid, round to oval with high N/C ratio, hyperchromatic nuclei and scanty basophilic cytoplasm. Focal areas show melanin pigment. Few lumina are filled with amorphous material and intervening areas shows inflammatory cell infiltrates consisting of neutrophils, lymphocytes and plasma cells. Adjacent area shows adnexal structures along with fibrocollagenous tissue. Also seen areas of hemorrhage, necrosis, adipose tissue, skeletal muscle bundles, congested and dilated blood vessels. Microscopic picture is reported as Basal Cell Carcinoma- Adenoid cystic variant (Figure 4,5,6,7)

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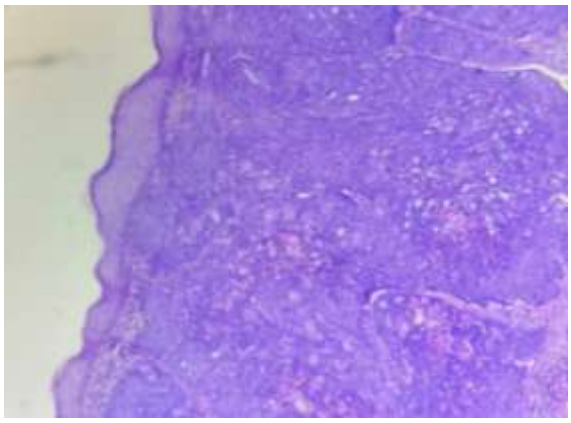

Figure 4: Skin with underlying tumor H&E 100X

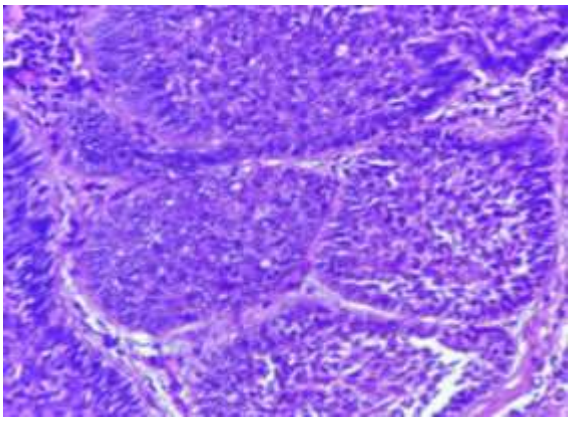

Figure 5: Islands of tumor cells show peripheral palisading H&E 400X

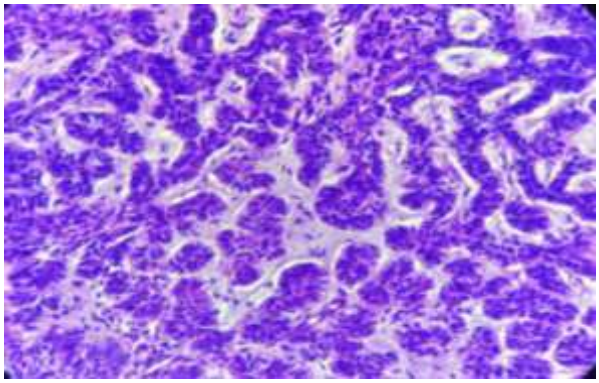

Figure 6 : Tumor cells arranged in lace like pattern H&E 400X

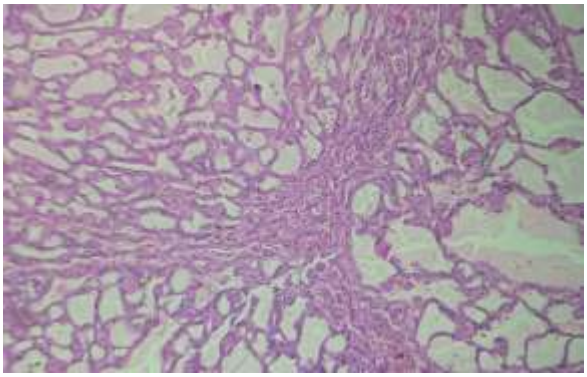

Figure 7 : Adenoid cystic change H&E 400X

DISCUSSION : Gorlin syndrome is also known as Gorlin- Goltz syndrome(GGS), or Basal cell Nevis syndrome(BCNS) or Nevis basal cell carcinoma (NBCCS). Gorlin Syndrome is a rare autosomal dominant inherited disease, with high penetration and variable expressivity.[4] It is caused by loss of heterozygosity of the tumor suppressor gene PTCH1, maps to chromosome 9q22.3.[5] PTCH1 forms part of the Sonic hedgehog (SHH) signaling pathway. Hence mutations in this gene leads to over expression of SHH pathway[6]. This pathway was described in Dorsophilia.[7] It is essential for development, as it intervenes in tissue polarity and stem cell population. Clinical presentation of the syndrome involves a wide spectrum of cutaneous and extracutaneous signs and symptoms. Diagnosis of the syndrome is made by using Kimonis diagnostic criteria.[8] (TABLE 1). There has to be presence of 2 major criteria or 1 major and 2 minor criteria 1 major plus molecular confirmation. In our patient diagnosis of Gorlin syndrome was made by the presence of 2 major criteria, i.e first degree relative with Gorlin syndrome(her mother) and more than 2 basal cell carcinoma under 20 years of age and syndactyly is also there.

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Table 1 . KIMONIS Diagnostic Criteria

Major criteria	Minor criteria
More than two basal cell carcinomas or one in patients under 20 years of age	Macrocephaly after adjustment for height
Histologically proven odontogenic keratocysts of the mandible	Congenital malformations: cleft lip or palate, frontal bossing, coarse facies, moderate or severe hypertelorism
Three or more palmar or plantar pits	Other skeletal abnormalities: Sprengel's deformity, marked chest wall deformity and marked finger syndactyly
Bilamellar calcifications of falx cerebri	Radiological abnormalities:Sella turcica bridge, hemivertebra, fusion or lengthening of vertebra body, malformations of the hands and feet, and flame-shaped lucencies in hands or feet.
Fused or markedly extended bifida ribs	Ovarian fibroma
First-degree relative with Gorlin-Goltz syndrome	Medulloblastoma

Other symptoms include epidermal cyst, calcified flax cerebri, hamartomas, pertussis excavatum or carinatum, short 4th metacarpal , kypshoscoliosis, lumbarizaion of the sacrum, enlarged occipitofrontal circumference, which present as macrocephaly and prominent forehead, spina bifida occulta, syndactly, strabismus, medulloblastoma, meningioma, cardiac fibroma's and ocular hypertelorism. Basal cell carcinoma(BCC) are one of the most frequently encountered features of this syndrome, BCC in Gorlin syndrome involve both photoexposed and non photoexposed areas.[9] The most frequent sites in men are the upper third of the back, arms and the H zone of the face, where as in females involves mostly

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scalp, back and legs. Planar/ plantar pits are frequent manifestation and are reported in between 70 % and 87 % of patients. The treatment of this syndrome is multidisciplinary depending upon the system involved. For BCC surgical excision, MOHs surgery, electrocoagulation, cryotherapy, laser ablation, photodynamic therapy and topic chemotherapy.

CONCLUSION

Gorlin syndrome can be aggressive so it's mandatory that these patients has to be monitored by an multidisciplinary medical team. There will be high risk of recurrence. Aggressive BCC can cause death due to tumor invasion to brain or other vital structures.

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