ISSN: 2581 – 3633
PubMed - National Library of Medicine - ID: 101745081

International Journal of Medical Science and Advanced Clinical Research (IJMACR)

Available Online at:www.ijmacr.com

Volume – 6, Issue – 4, July - 2023, Page No. : 173 - 178

Abdominal lump in a young female unveiling the diagnosis of Gorlin-Goltz syndrome

[1]Dr. Bhawna Sethi, Professor, Department of Pathology, SHKM, Government Medical College, Nuh, Haryana, India

[2]Dr. Vibhuti Thukral, Resident, Department of Pathology, PGIMS, Rohtak, India

[3]Dr. Shubham Jain, Resident, Department of Radiodiagnosis, BLK MAX Superspeciality Hospital, New Delhi, India

[4]Dr. Akhil Kumar, Resident, Department of Pathology, PGIMS, Rohtak, India

[5]Dr. Irbinder Kour Bali, Associate Professor, Department of Pathology, MMIMSR Mullana, Ambala, Haryana, India

[6]Dr. Yogesh Kumar, Professor, Department of Opthalmology, SHKM, Government Medical College, Nuh, Haryana, India

Corresponding Author: Dr. Vibhuti Thukral, Resident, Department of Pathology, PGIMS, Rohtak, India

How to citation this article: Dr. Bhawna Sethi, Dr. Vibhuti Thukral, Dr. Shubham Jain, Dr. Akhil Kumar, Dr. Irbinder Kour Bali, Dr. Yogesh Kumar, "Abdominal lump in a young female unveiling the diagnosis of Gorlin-Goltz syndrome", IJMACR- July - 2023, Volume – 6, Issue - 4, P. No. 173 – 178.

Type of Publication: Case Report

Conflicts of Interest: Nil

Abstract

Gorlin-Goltz syndrome (GGS) is an infrequent, inherited, multisystem disorder with autosomal dominant inheritance, complete penetrance and variable expression. A 19-year-old female presented with abdominal lump. Exploratory laparotomy and excision were done. Based on histomorphology, the diagnosis of ovarian fibroma was suggested. Since ovarian fibromas are known to be associated with various syndromes, the patient was advised further workup and investigations, thereby unveiling the diagnosis of Gorlin-Goltz syndrome.

Keywords: Ovarian fibroma, nevoid basal cell carcinoma syndrome, NBCCS, multiple basal cell carcinoma syndrome, jaw cyst basal cell tumour skeletal anomalies syndrome, jaw cyst bifid rib basal cell nevus syndrome, nevoid basalioma, odontogenic keratocysts.

Introduction

Gorlin-Goltz syndrome (GGS) is an uncommon, autosomal dominant, inherited disorder with strong penetrance and extremely variable expressivity.[1] Only few cases are known to occur sporadically. It was first reported by Jarisch and White in 1894.[2] Robert J. Gorlin and W. Goltz described the distinct syndrome, consisting of multiple nevoid basal cell carcinoma (BCC), jaw cysts, and bifid ribs.[3] The incidence varies from 1 in 50,000 to 1,50,000.[4] Other names of this syndrome are nevoid basal cell carcinoma syndrome (NBCCS), multiple basal cell carcinoma (BCC) syndrome, jaw cyst basal cell tumor skeletal anomalies syndrome, jaw cyst bifid rib basal cell nevus syndrome, nevoid basalioma, odontogenic keratocysts skeletal anomalies syndrome

and fifth phacomatosis.[5,6] Males and females are equally affected. Abnormalities in the long arm of chromosome 9(q22.3-q31) and loss or mutations of human patched gene (PTCH1 gene) are main attributes to the pathogenesis.[7] Diagnosis is based upon established major and minor clinical and radiological criteria and ideally confirmed by deoxyribonucleic acid analysis.[3] The main objective of the case is to revisit and draw attention towards the variable expression and huge list of manifestations associated with the GGS, with a special focus on ovarian fibroma, which can even be the initial manifestation. The case also highlights the importance of morphological findings in ovarian fibroma which may prompt further workup so that the syndrome doesn't remain undiagnosed. The present case also emphasizes the importance of a multidisciplinary approach in the patient's early diagnosis as well as prevention and management of few associated abnormalities/malignancies which may lead to better prognosis and survival.

Case Report

A 19-year-old female, married for four months, presented with an abdominal lump and dragging pain abdomen for the past 3 months. The pain got aggravated on work and has increased in grade in last week. On examination, the lump was firm in consistency, irregular and immobile. No history of contraception or menstrual irregularity was obtained. Ultrasonogram revealed a well-outlined intra-abdominal mass measuring 17cm x 7.5cm. Sheets of calcification were seen near the surface. MRI abdomen revealed an abdominal mass extending from the superior aspect of the urinary bladder up to the lower margin of L3 vertebra measuring 12.10cm x 8.07cm x 16.12cm. The exact origin of the tumor mass was not well appreciable on MRI. The possibility of a benign vascular tumour with calcification was given. Exploratory laparotomy revealed two ovarian masses, which were excised and sent for histopathology. Left-sided ovarian mass was larger; already cut and received in four pieces. The piece with attached fallopian tube measured 15cm x 7cm x 5 cm and the attached fallopian tube measured 4.5cm x 0.8cm. The rest of the masses measured 17cm x6.5cm x 5.5cm, 15cm x 6.5cm x 5.0cm and 15cm x 5.5cm x 5.0 cm. Grossly, the masses were multi-nodular, capsulated, grey-white to grey-brown with a smooth external surface (Fig. 1a). The cut surface was firm with vague whorl-like architecture, and foci of hemorrhage and calcification. The right side mass was smaller and measured 1.8cm x 1cm x 1cm, and had a similar gross appearance. Microscopic examination from both the masses revealed a circumscribed spindle cell neoplasm comprising closely packed spindle cells arranged vaguely in intersecting bundles/fascicles (with vague storiform pattern in the smaller tumor), embedded in an eosinophilic collagenous matrix. The cells had bland, ovoid to long and thin spindled nuclei with pointed ends, inconspicuous to conspicuous nucleoli & moderate to abundant eosinophilic cytoplasm (Fig 1b,c). Foci of myxoid change, hemorrhage, ischemic necrosis & calcification were seen (more prominent in sections from large tumor mass). Significant mitosis, atypia and pleomorphism were not evident. Sex cord elements were not evident. Normal ovarian tissue was not evident. The capsule was intact. The attached fallopian tube was unremarkable. Based upon histomorphology, the possibility of ovarian fibroma was kept as the topmost differential. Since ovarian fibromas are known to be associated with various syndromes, and due to bilaterality, multinodularity and foci of calcifications in the present case, the patient was advised further workup

and investigations. Dermatological examination revealed multiple (almost 28) darkly pigmented lesions on the face, arm, neck, chest and trunk, varying in size from 0.1 to 0.5 cm (Fig.2a). Biopsy of the largest lesion (done later) confirmed the diagnosis of basal cell carcinoma. Numerous palmar and plantar pits, polydactyly of both hands and feet (three fingers already being excised in childhood) were also present (Fig. 2b,c).

Radiological examination (X-ray) showed calcification of falx cerebri and bifid ribs (Fig. 2d,e). No tentorium cerebellum calcification, bridged sella turcica, macrocephaly, brachycephaly, frontal bossing, parietal and temporal bossing and coarse face.

On oro-facial examination, an extraoral well-defined swelling was appreciated on left posterior mandible that was hard and non-tender on palpation. Fine needle aspiration from swelling was done and features supported the clinical diagnosis of odontogenic keratocyst. No maxillary hypoplasia, mandibular prognathism, high arched palate or prominent palatine ridges, cleft lip/palate, impacted teeth and/or agenesis, ectopic teeth and malocclusion were observed.

Ophthalmological examination was within normal limits. (Vision - 6/6). No hypertelorism, dystopia canthorum, congenital blindness, internal strabismus, congenital amaurosis, exotropia, glaucoma, ptosis and coloboma were identified. Neurological examination did not reveal any significant finding. No significant family history was obtained.

Discussion

Fibromas are common ovarian tumors that are usually unilateral and most often present after puberty. Ovarian fibromas are neoplasms of ovarian stromal cells and account for approximately 5% of ovarian neoplasms.[8] Grossly, they are usually solid, lobulated, firm, uniformly white, and often without adhesions. The average diameter is 6 cm. Myxoid changes may be seen, sometimes resulting in cystic degeneration. Microscopically, fibromas are composed of closely packed spindle stromal cells arranged in a “feather stitched” or storiform pattern.[9] Hyaline bands and edema may be present. Ovarian fibroma (especially if large) can be accompanied by ascites, sometimes in combination with right-sided pleural effusion (Meigs’ syndrome). Some fibromas occur in young women with basal cell nevus (Gorlin’s) syndrome. These fibromas are mostly bilateral, calcified, and often multinodular. Since the present case had bilateral ovarian fibromas, one being huge, with multinodularity and calcifications on radiological and histopathological examination, the complete workup of the patient was done. Dermatological, radiological, and orofacial examinations revealed findings that unveil the diagnosis of GGS. Gorlin-Goltz syndrome is a multisystem disorder comprising the triad of basal cell nevi, jaw keratocysts, and skeletal anomalies.[2] Since a spectrum of other neurological, ophthalmic, endocrine, and genital manifestations is known to be variably associated with this triad, and the patient may manifest with multiple defects, the proposed investigation protocol includes family history, past medical and dental history, clinical examinations (including examination of oral, skin, central nervous system, head circumference, interpupillary distance, eyes, genitourinary system, cardiovascular system, respiratory system, and skeletal system), genetic testing, radiological examination (chest, anteroposterior and lateral skull, panoramic radiograph, cervical and thoracic spine), hands (for pseudocysts), pelvic (female), ovarian ultrasound (female) for ovarian fibroma and echocardiogram (children) for cardiac

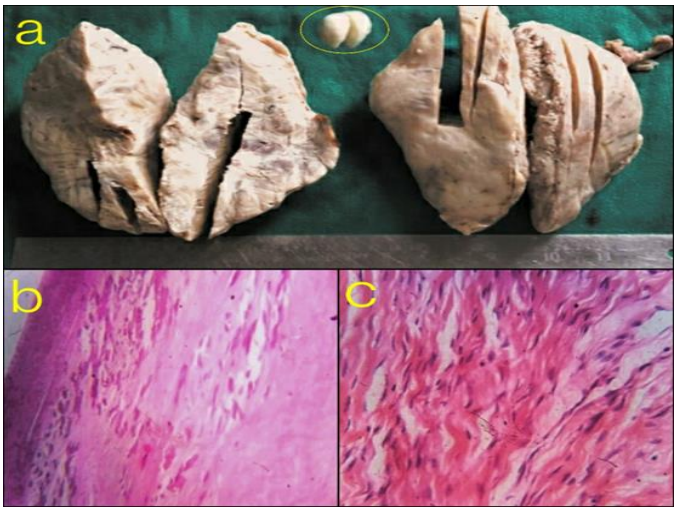
fibroma.[10] The diagnosis is based on established major and minor clinical and radiological criteria, and ideally confirmed by DNA analysis.[11]

The diagnostic criteria for GGS were established by Evans et al in 1991 and modified by Kimmonis et al in 1997.[1] Recent consensus statement from the first international colloquium on GGS proposed less stringent criteria for diagnosis: one major criterion and molecular confirmation or two major criteria or one major and two minor criteria.[12] Major criteria include excessive numbers of basal cell carcinomas out of proportion with prior sun exposure and skin type or basal cell carcinomas prior to 20 years of age, odontogenic keratocysts of the jaws prior to 20 years of age, palmar or plantar pitting, lamellar calcification of the falx cerebri, medulloblastoma, typically desmoplastic, and first degree relative with Gorlin-Goltz syndrome.[12] Minor criteria include rib anomalies, other specific skeletal malformations and radiological changes (vertebral anomalies, kyphoscoliosis, short 4th metacarpals, postaxial polydactyly), Macrocephaly, Cleft lip and/or palate, Ovarian/Cardiac fibroma, Lymphomesenteric cysts, Ocular abnormalities (strabismus, hypertelorism, congenital cataracts, glaucoma, coloboma).[13]

Based upon the clinical, radiological, and histological findings in the concerned case, the presence of four major criteria (falx cerebri calcification, palmar & plantar pitting, and odontogenic keratocyst, basal cell carcinoma) and three minor criteria (bilateral ovarian fibromas with calcification, bifid ribs, and polydactyly), fulfilled the criteria for the diagnosis of Gorlin-Goltz syndrome. The present case had calcification of falx cerebri which has been reported to occur in 37-79% of patients[1] and palmar and plantar pitting, which are seen in 90% of Gorlin syndrome cases.[1] The odontogenic keratocyst of the jaw, found in this case, is a common finding in Gorlin syndrome, affecting approximately 80% of patients, and usually occurs after 7 years of age and on average by 15 to 17 years.[8] This patient had multiple dark lesions on the face, (one confirmed as basal cell carcinoma of skin on histopathology). They are reported to occur in 50-97% of Gorlin syndrome cases, typically developing between puberty and age 35, and commonly affect face, neck, and upper trunk.[1] Bifid ribs were also present, which are seen in 30-60% cases of Gorlin syndrome.[14] The ovarian fibroma in our case showed foci of calcification, a feature typically found in ovarian fibromas of Gorlin syndrome, but rarely in non-syndromic cases. Ovarian fibromas associated with Gorlin syndrome are bilateral in 75% of cases,[8] which was also noted in the concerned case, though one was huge and the other was small. The patients with this syndrome are prone to multiple malignancies, early diagnosis is essential for detection and providing advice concerning management and follow-up. This patient underwent complete possible workup and was encouraged to undergo regular follow-ups at appropriate intervals. In addition, MRI brain & genetic counselling were recommended.

To conclude, the present case highlights the significance of morphological findings, which if kept in mind with the knowledge of other diagnostic criteria, may unveil the diagnosis of syndromic manifestation. To the best of our knowledge, most of the cases finally discovered and diagnosed with GGS, and reported in the literature, had an initial presentation of multiple pigmented skin lesions or odontogenic keratocyst. In the present case, an abdominal lump has been the initial manifestation, wherein pathological findings guided the complete

workup, and picked up other abnormalities leading towards the diagnosis. This case also focuses on the importance of a multidisciplinary approach for early and prompt diagnosis with proper treatment and genetic counselling of the patient.



Fig,1 Gross and histopathological findings of the patient: (a) Gross image of ovarian masses; larger mass received in four big pieces (Smaller mass is encircled); (b) Photomicrograph showing benign spindle cell neoplasm with calcification underneath the capsule (40x); (c) Photomicrograph revealing bland spindle cells embedded within wavy collagenous matrix (400x).

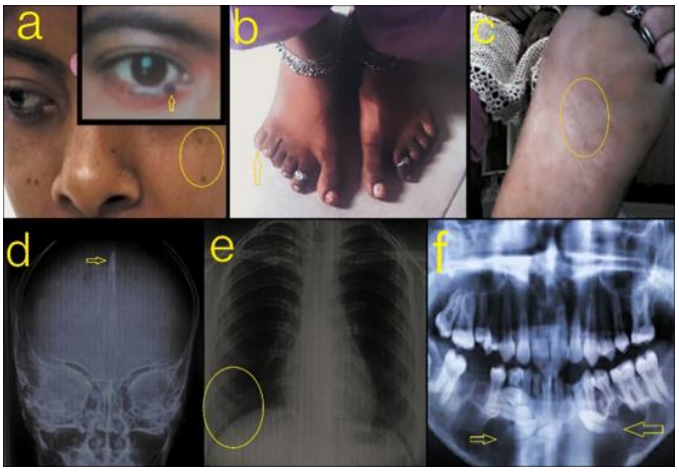


Fig. 2 Clinical and radiological findings of the patient: (a) Multiple darkly pigmented lesions on face (arrow and encircled); (b) Postaxial polydactyly (arrow) in right foot; (c) Plantar pits in left foot (encircled);(d) X-ray skull showing calcification of falx cerebri (arrow);(e) Frontal chest radiograph depicting bifid right 6th rib (encircled); (f) Orthopantomogram showing multiple keratocysts in mandibular region (arrows).

References

1. Ramesh, M. et al., 'Gorlin-Goltz Syndrome: Case report and literature review', J Oral Maxillofac Pathol, vol. 19(2), 2015, pp. 267.
2. Agrawal, A. et al., 'Gorlin-goltz syndrome: Case report of a rare hereditary disorder', Case Rep Dent, vol 2012, 2012, doi: 10.1155/2012/475439.
3. Joshi, PS., Deshmukh, V., and Golgire, S., 'Gorlin-Goltz Syndrome' Dent Res J, vol 9, 2012, pp. 100-106.
4. Patil, K., Mahima, VG., and Gupta, B., 'Gorlin syndrome: A case report' J Indian Soc Pedod Prev Dent, vol.23, 2005, pp. 198-203.
5. Acocella, A. et al., 'Genetic and clinicopathologic aspects of Gorlin-Goltz syndrome (NBCCS): Presentation of two case reports and literature review', Minerva Stomatol, vol.58, 2009, pp. 43-53.
6. Mamatha, GP.et al. 'Gorlin Syndrome. A case report' Indian J Dent Res, vol.12, 2001, pp. 248-252.
7. Kalogeropoulou, C., et al., 'Gorlin-Goltz syndrome: Incidental finding on routine CT scan following car accident' Cases J, vol.2, 2009, pp. 9087.
8. Finch, T. et al., 'Gorlin syndrome presenting with a unilateral ovarian fibroma in a 22-year-old woman: a case report', J Med Case Rep, vol. 6, 2012, pp. 148.
9. Rosai, J., Rosai and Ackerman's Surgical Pathology, 10th ed. Elsevier, Lyon, France, 2011.
10. Muzio, L., 'Nevoid basal cell carcinoma syndrome (Gorlin syndrome)' Orphanet J Rare Dis, vol.3, 2008, pp. 32.

11. Pandeshwar, P., Jayanthi, K., and Mahesh, D., 'Gorlin-goltz syndrome' Case Rep Dent, vol.3, 2012, pp. 2012.
12. Ramanathan, S. et al., 'Delayed diagnosis of Gorlin syndrome: Learning from mistakes!' J Pediatr Neurosci, vol. 10(4), 2015, pp. 359-361.
13. Bree, AF., and Shah, MR., 'BCNS Colloquium Group. Consensus statement from the first international colloquium on basal cell nevus syndrome BCNS' Am J Med Genet A, vol. 155A, 2011, pp. 2091-2097.
14. Thomas, N. et al., 'Gorlin–Goltz syndrome: An often missed diagnosis', Ann Maxillofac Surg, vol.6, 2016, pp. 120-124.