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Calcified ovarian fibroma presentation in nevoid basal cell carcinoma syndrome

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Gorlin-Goltz syndrome, also known as nevoid basal cell carcinoma syndrome, is a rare autosomal dominant syndrome with a predisposition to developmental and neoplastic disorders [1]. Basal cell carcinoma, odontogenic keratocysts, and skeletal abnormalities are the most common symptoms. Its pathogenesis is linked to anomalies on chromosome 9's long arm (q22.3-q31), and the loss of mutations in the PTCH1, PTCH2, and SUFU genes [1, 2]. To screen for a familial susceptibility to this disease, Genetic screening, and counseling of patients and their family members are critical for early detection, in a male-to-female ratio of 1:1. The estimated prevalence ranges between 1/57,000 and 1/256,000, most reports refer to Caucasians, but it can affect any ethnic group [3]. Female patients with Gorlin syndrome are at risk for developing ovarian fibromas 75% of the time [4]. Here, we present an atypical presentation of a case with a calcified ovarian fibroma.

An otherwise healthy nulliparous 36-year-old female presented with a chief complaint of worsening severe dysmenorrhea for 14 months. Additionally, she had experienced 3 years of oligomenorrhoea. Symptoms of oligomenorrhoea and dysmenorrhea worsened over time. The patient had a history of multiple basal cell carcinomas which were removed by the Mohs procedure. After her first basal cell carcinoma diagnosis at age of 14, she tended to use sunscreen and avoid direct sun exposure after 10 AM. She also had epidermoid groin cysts. Past surgical history was unremarkable except for fibroid surgery. Family history revealed non-melanoma skin cancers. Her blood work was unremarkable.

In the physical examination, several pigmented lesions were noted on her trunk, the abdomen was soft and lax without palpable masses. Moderate cervical excitation, as well as bilateral adnexal tenderness, was found on a pelvic examination.

Pelvic ultrasound (Fig. 1A) was performed which showed a calcified ovarian hypoechoic solid lesion measuring 1.4 × 1. 3 × 1.2 cm and bilateral ovarian cysts. Magnetic resonance imaging (MRI) was conducted for further evaluation of this lesion (Fig. 1B) and demonstrated well-circumscribed T1–T2 hypointense nodular lesions (arrowhead) with heterogeneous enhancement on post-contrast sequences (arrow). Bilateral ovarian cysts were also noted.

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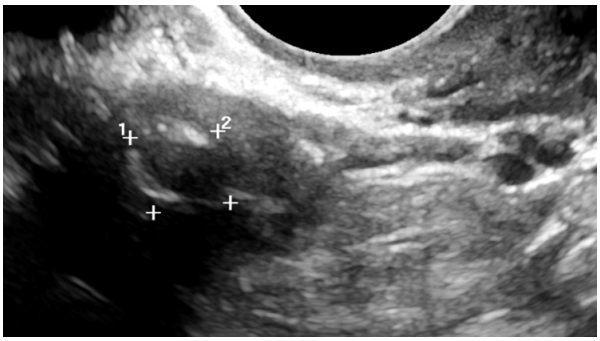

Figure 1A. Pelvic ultrasound shows a calcified ovarian hypoechoic solid lesion measuring 1.4 x 1.3 x 1.2 cm and bilateral small ovarian cysts

The patient underwent robotically assisted laparoscopic ovarian surgery, followed by frozen section pathological examination, which showed variably cellular spindle cell tumor with storiform growth containing hyaline plaques and calcifications, which confirmed ovarian fibroma. Furthermore, the patient's blood specimen revealed a SUFU gene mutation. Genetic study was offered to the patient . The genealogical analysis is important for the determination of the genetic risk and the prognosis for the patients' relatives [8].

Gorlin-Goltz Syndrome, also known as nevoid basal cell carcinoma syndrome (NBCCS), is a rare phacomatosis characterized by multiple odontogenic keratocytes (OKC), multiple basal cell carcinomas (BCC), and other abnormalities including craniofacial anomalies, musculoskeletal anomalies, and neoplasms/hamartomas [3, 4]. In the PTCH1 gene, nonsense-mediated mRNA decay occurs in response to a frameshift mutation that causes premature termination of the PTCH protein. This may cause the synthesis of a truncated protein or nonsense-mediated mRNA decay, which impacts multiple organs [5]. Because affected people are susceptible to various neoplasms at a young age, early detection of Gorlin-Goltz syndrome is critical and it is important to note that especially calcified ovarian fibroma is associated with this syndrome.

When two major or one major and two minor criteria are present, the diagnosis of GGS is made [6, 7]. Clinically, two major and one minor criterion were present in our patient.

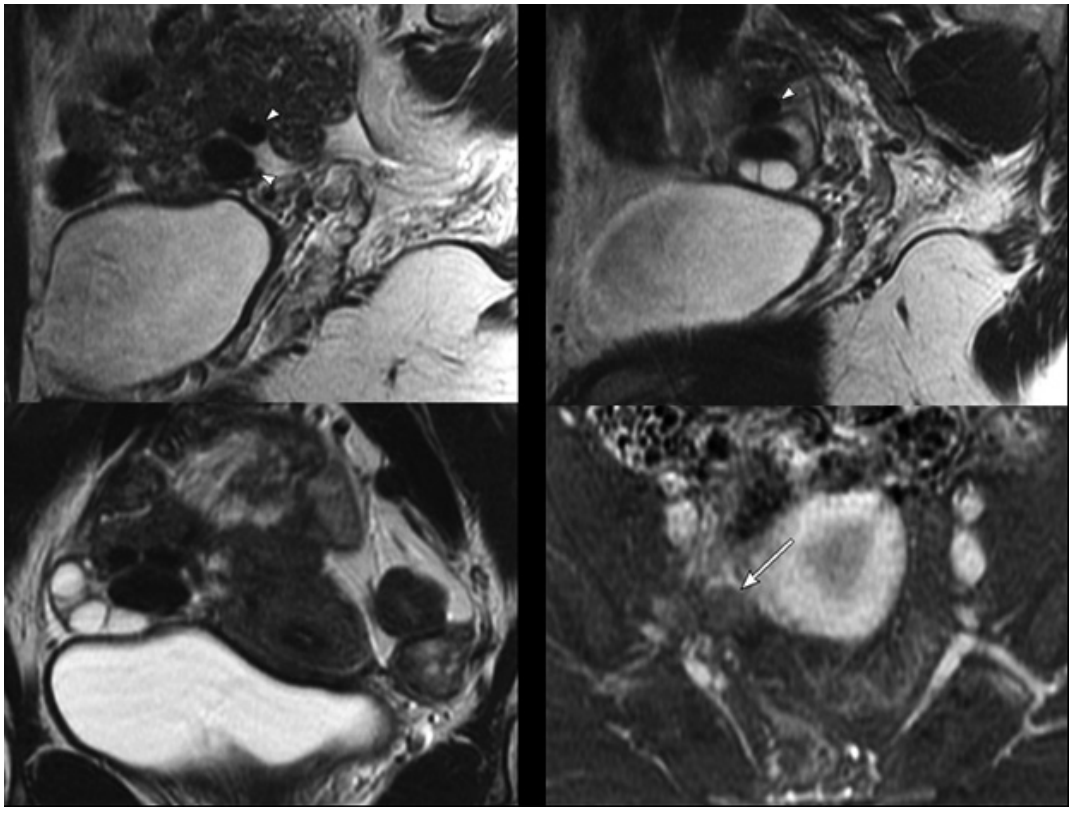

Figure 1B. Magnetic resonance imaging (MRI) demonstrates well-circumscribed T1-T2 hypointense nodular lesions (arrowhead) with heterogeneous enhancement on post-contrast sequences (arrow). Bilateral ovarian cysts were also noted

Ovarian cysts and fibromas are found in 25–50% of women with this syndrome, and they frequently occur bilaterally (75%) [8]. The patient presented with calcified right-sided ovarian fibromas and bilateral ovarian cysts. In the literature, epidermoid cysts have been discovered in 50% of the patients. Our patient had epidermoid cysts in the groin. BCC is found in 40 percent of black individuals and 90 percent of white patients with this syndrome [1]. Our patient had multiple BCC sites, some of which were surgically resected. In general, surgery for multiple basal cell carcinomas (BCCs) can result in disfigurement due to tissue defects and scarring. The increased radiation tumorigenesis in these patients makes radiotherapy contraindicated. In contrast to ablative therapies, photodynamic therapy (PDT) is a simple, repeatable procedure that causes minimal skin damage. BCCs of the skin that is superficial are now routinely treated with this method [9].

The diagnosis and management of Gorlin-Goltz syndrome depend on the identification of clinical and radiological manifestations as well as confirmation by genetic analysis of DNA.

Differential diagnosis includes large pedunculated subserosal uterine, thecoma, and fibrothecoma. In a large pedunculate subserosal uterine leiomyoma, a band of T2 hypointensity in fibroma separating the tumor from the uterus can be beneficial to differentiate the entities. Thecoma and fibrothecoma tend to have brighter signals on T2 weighted imaging given edema and cystic degeneration. Contrast-enhancement may be observed given the vascularization of the theca cells [10, 11].

Prognosis depends on multiple factors, although the symptoms of Gorlin syndrome may be milder in individuals with SUFU mutations than in those with PTCH1 mutations. SUFU mutations increase the risk of basal cell skin cancer by 90% in individuals with Gorlin syndrome. The risk of medulloblastoma (brain cancer) is as high as 33% in individuals with Gorlin's syndrome associated with SUFU. There is also a 2% risk of benign heart tumors (cardiac fibromas) in males and females with Gorlin syndrome. There is a 20% risk of benign ovarian tumors (ovarian fibromas) in women [12].

Furthermore, the type of interventions that the patient received, for example, patients who were treated using radical interventions for enucleation with shaving of surrounding bone or sometimes resection, might contribute to preventing recurrences and improving the prognosis [13].

A multidisciplinary approach is necessary for management. There should be particular attention paid to BCCs around the eyes and ears. An ophthalmologist, otolaryngologist, and plastic surgeon must be involved. Keratocysts are treated by surgical removal. BBCs are treated surgically when there are fewer lesions; alternative treatments include laser ablation, photodynamic therapy, and topical chemotherapy. The use of radiotherapy should be avoided. Vitamin A analog may contribute to preventing the development of new BCCs [1].

Until recently, there has been no approved therapy for advanced BCC. A breakthrough drug called vismodegib (Erivedge®) has been developed to treat advanced BCC [1–6]. US Food and Drug Administration (FDA) approval for vismodegib (Erivedge®) was obtained in January 2012. In July 2013, the European Medicines Agency (EMA) approved vismodegib (Erivedge®) for the treatment of adult patients with symptomatic metastatic BCC or locally advanced BCC that was not appropriate for surgery or radiotherapy. Vismodegib and sonidegib are considered promising treatments for patients with advanced or refractory cancer [14].

Early diagnosis of Gorlin-Goltz Syndrome is important to avoid fatal complications associated with the disease due to multiple neoplasms [15]. It is important to consider the prognosis of Gorlin-Goltz syndrome in patients who present with calcified ovarian fibroma, a history of multiple BCCs, and SUFU gene mutation. We present a case that demonstrates the role of radiological identification of features of this syndrome in establishing an early diagnosis which will provide a better prognosis. In addition to the multidisciplinary management of Gorlin syndrome, ovarian fibroma can be surgically or conservatively managed depending on a patient's symptom severity, future family plans, and the risk of a malignant transformation of the fibroma [4].

Conflict of interest

None declared.

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