Surgical management of ovarian fibromas in young patients with Gorlin syndrome: a case series and review of the literature

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Objective: To characterize the presentation and surgical management of ovarian fibromas among a case series of pediatric and adolescent patients with Gorlin syndrome.
Design: Retrospective case series.
Setting: Tertiary-care hospital.
Patient(s): Patients aged 18 years and younger with a diagnosis of Gorlin syndrome who underwent surgical care of ovarian fibromas at a single tertiary children's hospital from 1990 to 2022.
Exposure: Surgical management of ovarian fibromas.
Main Outcome Measure(s): Clinical characteristics, surgical treatment outcomes, ovarian conservation, surveillance imaging, and recurrence after surgical management of ovarian fibromas.
Result(s): Four patients, aged between 5 and 18 years, underwent surgical resection of one or more ovarian fibromas. Dominant fibromas ranged in size from 4 to 9 cm, and most cases had multiple fibromas. Three patients underwent transverse laparotomies, and one patient had a laparoscopic approach. Unilateral oophorectomy was performed in three patients, two of whom presented with adnexal torsion. Among those with surveillance imaging, two patients with prior oophorectomy had a recurrence in the remaining contralateral ovary, one of whom underwent a second surgical procedure.
Conclusion(s): Ovarian fibroma presentation and treatment varied widely among pediatric patients with Gorlin syndrome, and the presence of multiple and bilateral ovarian lesions raises important considerations regarding the optimal surgical approach and surveillance. Ovarian conservation should be prioritized in patients with Gorlin syndrome, because they are at risk of iatrogenic oophorectomy with their initial or repeat surgical management. (F S Rep® 2024;5:430–8. ©2024 by American Society for Reproductive Medicine.)
Key Words: Fertility, fibroma, Gorlin syndrome, ovarian mass, ovarian torsion

INTRODUCTION

Gorlin syndrome, also known as nevoid basal cell carcinoma syndrome, is a rare genetic multisystem disorder with an estimated prevalence of 1/50,000 to 1/250,000 (1, 2). The syndrome is most commonly inherited in an autosomal dominant pattern with high penetrance and is characterized by a predisposition to various benign and malignant tumors often diagnosed at a young age, including multiple basal cell carcinomas, odontogenic cysts, calcification of the falx cerebri, skeletal and craniofacial abnormalities, medulloblastoma, and ovarian or cardiac fibromas (Table 1) (1, 2).

Recent literature estimates that ≤25% of women with Gorlin syndrome will develop ovarian fibromas (3, 4), which may be identified after a diagnosis of nevoid basal cell carcinoma syndrome or as the presenting finding. Although fibromas are the most common sex cord-stromal tumor in adult women, they are a rare diagnosis in children and adolescents, accounting for only 1.5% of pediatric ovarian tumors (5). In Gorlin syndrome, multiple fibromas are often present and frequently occur bilaterally (6, 7), raising the risk of oophorectomy in young patients early in their reproductive lifespan. Minimal data exist on surgical management of ovarian fibromas associated with Gorlin syndrome, and data are further sparse within the pediatric, adolescent, and young adult population. In this case series, we present four pediatric and adolescent patients

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diagnosed with Gorlin syndrome who received surgical management of ovarian fibromas at a single institution.

CASE REPORT

We conducted a retrospective cohort study of female patients aged 18 years and younger with a diagnosis of Gorlin syndrome who received care at a single tertiary-care children's hospital from 1990 to 2022. Inclusion criteria included patients with a diagnosis of Gorlin syndrome confirmed either before or after surgical management of an ovarian fibroma. Electronic medical records of all patients meeting inclusion criteria were reviewed for patient demographics and clinical characteristics at time of presentation, treatment outcomes, and any fibroma recurrence. Operative characteristics, including surgical approach, procedure type, tumor number, and size, were also gathered from operative and surgical pathology reports. Written consent from the patients was obtained for use of de-identified data in research, and this study was approved and deemed exempt by the Institutional Review Board.

A selective literature review was conducted in PubMed to identify additional recent reports of surgical management of ovarian fibromas in young patients with Gorlin syndrome. Studies were included if written in English, published between 2000 and 2023, and described patients aged 25 and younger with confirmed Gorlin syndrome either before or after surgical management of fibromas. Four patients underwent surgical resection of one or more ovarian fibromas during the study period (Table 2).

Case 1

A previously healthy 5-year-old presented with acute abdominal pain, fever, nausea, and vomiting. Pelvic ultrasound revealed appendiceal enlargement and inflammation concerning for appendicitis, in addition to a separate, lobulated, and calcified heterogeneous midline pelvic mass measuring 4.3 cm in diameter with internal vascularity. Pediatric surgery was consulted, and a diagnostic laparoscopy was performed given concern for torsion of a complex adnexal mass. Intraoperative findings demonstrated a large calcified pelvic mass with extensive adhesions to the abdominal wall. The approach was then converted to a transverse laparotomy, which confirmed acute appendicitis in addition to a calcified and necrotic-appearing right adnexal mass involving the ovary and fallopian tube, which was torsed three times. It was unclear if the appendicitis primarily occurred or was reactive to the necrotic adnexa. A right salpingo-oophorectomy and an appendectomy were performed by pediatric general surgeons. Pathology revealed a necrotic adnexa containing a fibroma. This pathology led to the patient later receiving a diagnosis of Gorlin syndrome and subsequently undergoing surveillance imaging to assess for other associated tumors and recurrence of ovarian fibromas.

The patient remained asymptomatic and progressed through normal pubertal development and menarche at age 12 with regular menses. At age 17, a surveillance ultrasound revealed a 5.3-cm complex solid and cystic left ovarian mass with scattered calcifications. Tumor markers—including cancer antigen 125, lactate dehydrogenase, α-fetoprotein, β-human chorionic gonadotropin, inhibins A and B—were negative and antimüllerian hormone (AMH) was 0.29 ng/mL. Given concern for potential recurrent asynchronous torsion and loss of the remaining ovary, the gynecology service recommended cystectomy. A repeat transverse laparotomy was performed to optimize the removal of all nine fibromas of varying size, shape, and location within the multilobular ovary although conserving the surrounding normal ovarian tissue. Pathology confirmed the masses as fibromas. A pelvic ultrasound 6 months later revealed a normal appearing right ovary without masses. Postoperatively, the patient continued to have regular menses and has been without known recurrence for 5 years.

Case 2

A 14-year-old postmenarchal female was previously diagnosed with Gorlin syndrome after treatment for recurrent basal cell carcinoma and identification of jaw cysts. A right adnexal mass was incidentally found during ultrasound imaging of the urinary tract. Pelvic ultrasound characterized a 4.7-cm homogenous and vascular mass adjacent to the right ovary. Tumor markers were negative. The patient was asymptomatic, but given the mass complexity and vascularity, the gynecology service recommended surgical removal. A transverse laparotomy was performed and identified an exophytic, solid right ovarian mass measuring 6 cm, which was removed via cystectomy. Pathology confirmed the specimen as a fibroma without atypia. The patient has been without fibroma recurrence over the past 9 years.

Case 3

A 13-year-old postmenarchal female diagnosed with Gorlin syndrome after diagnosis of maxillofacial fibromas, basal

TABLE 1

Diagnostic criteria for nevoid basal cell carcinoma [Gorlin] syndrome.

- Diagnosis of NBCCS requires two major or one major and two minor criteria
  - Major criteria
    - More than two basal cell carcinomas, or one basal cell carcinoma in a patient younger than 20 y
    - Odontogenic keratocysts of the jaw bone
    - Three or more palmar or plantar pits
    - Calcification of the falx cerebri
    - Bifid, fused, or markedly splayed ribs
    - First-degree relative with NBCCS
  - Minor criteria
    - Ovarian fibroma
    - Medulloblastoma
    - Macrocephaly
    - Craniofacial malformations: cleft lip or palate, frontal bossing, coarse facial features, hypertelorism
    - Skeletal abnormalities: Sprengel deformity, pectus deformity, syndactyly
    - Radiologic abnormalities: bridging of the sella turcica, vertebral anomalies (i.e., hemivertebrae, fusion or elongation of the vertebral bodies), modeling defects of the hands and feet (i.e., flame-shaped lucencies of the hands or feet)

Note: NBCCS = nevoid basal cell carcinoma [Gorlin] syndrome.

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TABLE 2

Clinical and surgical characteristics of pediatric patients with Gorlin syndrome undergoing surgical management of fibromas (N = 4).

Case		Age (y)	Past medical history	Clinical symptoms	Imaging findings	Surgery (y)	Pathology: Intraoperative findings	Pathology: Largest size (cm)	Pathology: No. of lesions	Recurrence
1	a	5	None	Pain, concern for torsion	Lobulated 4.3 cm calcified midline mass with heterogenous vascular soft tissue	Laparotomy, RSO, appendectomy (2005)	Acute appendicitis; calcified right ovarian mass with necrotic adnexal torsion	4.3	1	Yes, see 1b
	b	17	GS diagnosed after ovarian fibroma	Asymptomatic	Left 5.3 cm complex cystic-solid ovarian mass with scattered calcifications	Laparotomy, left ovarian cystectomy (2017)	Hard, 6 cm left ovarian mass	4.5	9	No
2		14	Known GS; BCC x2, odontogenic cyst	Asymptomatic	Right 4.7 cm hypoechoic vascular paraovarian mass	Laparotomy, right ovarian cystectomy (2014)	Exophytic 6cm solid right ovarian mass	6	1	No
3		13	Known GS; BCC, maxillofacial fibromas, medulloblastoma	Pain, concern for torsion	Multiple masses, largest 9.3 cm with hemorrhage and necrosis	Laparoscopic RSO, left ovarian cystectomy (2019)	Multilobulated 15 cm ovary; 2 cm left ovarian mass	9	3	Yes, multiple (largest 4 cm)
4		18	Known GS; BCC x2, embryonal rhabdomyosarcoma	Asymptomatic	Right 7 cm paraovarian mass with enhancing fibrous tissue; left ovary with multiple <1 cm hyperechogenic lesions	Laparotomy, RSO (2022)	Solid, irregular right ovarian mass with no discrete borders; normal left ovary	7.6	3	No

Note: BCC = basal cell carcinoma; GS = Gorlin syndrome; RSO = right salpingo-oophorectomy.

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cell carcinoma, and medulloblastoma presented to gynecology because of bilateral adnexal masses incidentally found on abdominal imaging. Pelvic magnetic resonance imaging (MRI) was planned in conjunction with her other surveillance imaging and revealed multiple T2 hypointense bilateral adnexal masses of varying sizes, with the largest diameter of 5 cm. As the patient was asymptomatic and had regular menses, the gynecology service planned to observe the suspected fibromas with surveillance imaging, given the patient's medical comorbidities and concern for the inability to conserve ovarian tissue. An MRI 6 months later revealed interval enlargement of the masses, but the patient remained asymptomatic until presenting 3 months later with acute pelvic pain. MRI demonstrated interval growth of multiple, large solid and cystic pelvic masses measuring $\leq$9 cm each and notably containing hemorrhage and necrosis. Because of concern for possible adnexal torsion, the patient underwent surgical evaluation. Diagnostic laparoscopy revealed a grossly enlarged multilobulated 15 cm right ovary and a 2 cm pedunculated solid mass on the left ovary. There was no adnexal torsion, but given the inability to rule out malignancy and conserve normal ovarian tissue, a right salpingo-oophorectomy was performed and morcellated in a bag before removal. A left ovarian cystectomy was performed to remove the pedunculated left ovarian mass. Pathology confirmed ovarian fibromas without atypia.

The patient underwent a surveillance MRI 3 months later, demonstrating two presumed residual subcentimeter fibromas within the left ovary. Observation with surveillance imaging was performed and demonstrated stability in size. During this time, the patient underwent alkylating chemotherapy for a newly diagnosed radiation-induced high-grade poorly differentiated brain tumor. After completion of treatment, she developed oligomenorrhea. Laboratory evaluation revealed normal-range gonadotropins and estradiol but low AMH level at 0.010 ng/mL and later $<$0.003 ng/mL. The patient was counseled on the risk of iatrogenic primary ovarian insufficiency and diminished ovarian reserve after treatment with gonadotoxic agents in the setting of one remaining ovary with multiple remaining fibromas. The patient and family declined consultation with reproductive endocrinology and infertility specialists to discuss options for fertility preservation. Surgical intervention on the remaining ovary was not performed, given concern for further injury to the remaining ovary.

Surveillance MRI had since demonstrated multiple new left ovarian fibromas and interval growth of the left fibromas $\leq$4 cm in diameter, with no normal ovarian tissue identified. The patient was asymptomatic from these ovarian fibromas and had return of regular menses. With shared decision-making, imaging surveillance has continued with deferment of surgical intervention that would risk leaving the patient agonadal and dependent on hormone replacement therapy.

Case 4

An 18-year-old female with Gorlin syndrome diagnosed after treatment of basal cell carcinoma and embryonal rhabdomyosarcoma presented with lower abdominal discomfort. A pelvic ultrasound and subsequent MRI revealed a lobular, heterogeneously enhancing, solid right ovarian mass measuring 7 cm in greatest diameter. There were no other findings concerning for malignancy, and tumor markers were negative.

Surgical removal via transverse mini-laparotomy was planned to increase the likelihood of complete resection although preserving normal ovarian tissue. Intraoperatively, the right ovary was described as a large, solid, irregular mass without discrete planes between the ovarian cortex and the fibroma. As the mass was not amenable to resection without compromising ovarian tissue, a right salpingo-oophorectomy was performed. The left ovary was visibly normal in appearance. Pathology confirmed multiple fibromas measuring $\leq$7.3 cm in diameter. A surveillance ultrasound 6 months later demonstrated a normal appearing left ovary without masses. The patient has been without recurrence on surveillance imaging for the past 2 years and continues to have regular monthly menses.

DISCUSSION

In this case series, surgical management of ovarian fibromas varied based on presentation and characteristics of the ovarian masses, and the presence of large, multiple, or bilateral ovarian lesions raised the likelihood of oophorectomy. Similar to our case series, a review of the literature demonstrated high frequency of large and bilateral ovarian masses commonly resulting in open laparotomy and oophorectomy (Table 3) (6–22). In contrast to prior reports, most cases in our series already had a known diagnosis of Gorlin syndrome before the identification of fibromas, suggesting increased identification of the syndrome before adnexal surgery is indicated. It is salient to note that in these patients with a known diagnosis of Gorlin syndrome, ovarian fibromas were either incidentally found on surveillance imaging for other malignancies or only after developing symptoms from the adnexal masses (6, 10). Although there is currently no universally recommended protocol for surveillance of the development of benign fibromas among patients with Gorlin syndrome, this case series raises the question of whether early identification of ovarian fibromas would alter surgical management and improve the chances of ovarian conservation.

Preoperative planning

This case series highlights the several challenges with conservative surgical management of ovarian fibromas. First, most of the cases had symptoms and imaging findings concerning for adnexal torsion, which may obscure the ability to rule out malignancy or conserve normal ovarian tissue in the acute setting (22). Second, imaging findings in general may be challenging to interpret and therefore increase the risk of oophorectomy because of concern for malignancy. Benign fibromas not associated with Gorlin syndrome are more often unilateral with absence of calcifications (19). In contrast, ovarian fibromas secondary to Gorlin syndrome are often bilateral (75%), calcified, with a nodular and solid appearance on imaging that imitates malignant features, and may even be misdiagnosed as uterine leiomyomata (19). Fibromas can also

TABLE 3

Published studies and case reports on surgical management of benign ovarian fibromas in Gorlin syndrome in patients 25 years and younger.

First author	Year	Country	Age (y)	Clinical presentation	Mass characteristics	Surgical management	Follow-up for recurrence
Seracchioli et al. (8)	2001	Italy	17	Known GS; abnormal menses	Multiple, bilateral, calcified ovarian masses; largest 15cm diameter	Laparoscopic bilateral ovarian cystectomies	Return of regular menses; recurrence 5 y later: multiple, bilateral ovarian masses requiring laparotomy, bilateral cystectomies
Smith et al. (9)	2002	United States	12	Known GS; abdominal pain	Heterogeneous, 20 cm right ovarian mass	Laparotomy, right oophorectomy	Not reported
Aram et al. (7)	2009	Iran	22	Irregular menses	Bilateral, calcified ovarian masses, largest 10 cm diameter	Laparotomy, RSO, left ovarian cystectomy	Not reported
Ball et al. (10)	2011	Canada	15	Abdominal pain	Multiple, bilateral ovarian masses, largest 6 cm diameter	Laparoscopic bilateral ovarian cystectomies	Not reported
Morse et al. (11)	2011	United States	15	Known GS; irregular menses	Multiple, bilateral ovarian masses, largest 8 cm diameter	Laparotomy, bilateral ovarian cystectomies	Return of regular menses; no recurrence
Fedele et al. (12)	2012	Italy	21	Known GS; prior LSO for fibromas; abdominal pain	Multiple, right ovarian masses, largest 6 cm diameter	Laparoscopic right ovarian cystectomies	No recurrence
Finch et al. (13)	2012	Canada	22	Known GS; irregular menses	Calcified, 10 cm right ovarian mass	Laparotomy, RSO	Not reported
Pirschner et al. (6)	2012	Brazil	20	Known GS; abdominal mass	Calcified, 20 cm right ovarian mass	Laparotomy, RSO	Recurrence 1 y later: 20cm left ovarian mass requiring LSO
Jimbo et al. (14)	2014	Japan	6	Abdominal distention	Calcified, 13 cm left ovarian mass	Laparotomy, LSO	Not reported
Ono et al. (15)	2015	Japan	24	Abdominal pain, irregular menses	Multiple, bilateral, calcified ovarian masses, largest 20 cm diameter	Laparotomy, LSO, right ovarian cystectomy	No recurrence, two live births
Iwasaki et al. (16)	2016	Japan	14	Known GS; pleural effusion	Bilateral, solid ovarian masses, largest 16 cm diameter, adherent to omentum and appendix	Laparotomy, RSO, left ovarian cystectomy, appendectomy	Not reported
Chihara et al. (17)	2018	Japan	20	Known GS; prior RSO for fibroma	Recurrence of 6 cm left ovarian mass; low AMH	Oocyte cryopreservation x2, laparotomy, left ovarian cystectomy	2 oocytes cryopreserved; no recurrence
Khodaverdi et al. (18)	2018	Iran	25	Chronic abdominal pain	Multiple, bilateral ovarian masses; largest 5 cm diameter; 6 cm right endometrioma	Laparoscopic bilateral ovarian cystectomies	Not reported
Scalia et al. (19)	2018	Italy	25	Irregular menses	Multiple, bilateral, calcified ovarian masses, largest 7 cm diameter	Laparoscopic bilateral ovarian cystectomies	Not reported
Osaku et al. (20)	2021	Japan	24	Known GS; pelvic mass	Multiple, calcified right ovarian masses, largest 8 cm diameter	Mini-laparotomy, right ovarian cystectomies	Not reported

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TABLE 3

Continued.

First author	Year	Country	Age (y)	Clinical presentation	Mass characteristics	Surgical management	Follow-up for recurrence
Reitere et al. (21)	2021	Latvia	15	Known GS; primary amenorrhea	Multiple, bilateral, calcified ovarian masses, largest 16 cm diameter	Laparotomy, LSO, right ovarian cystectomies, appendectomy	Spontaneous menarche; no recurrence
Higashimoto et al. (22)	2022	United States	4	Pelvic pain, ovarian torsion	Multiple, bilateral, lobulated ovarian masses, largest 5 cm diameter; right adnexal torsion	Laparotomy, bilateral ovarian cystectomies	Not reported

Note: AMH = antimüllerian hormone; GS = Gorlin syndrome; LSO = left salpingo-oophorectomy; RSO = right salpingo-oophorectomy.

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demonstrate cystic degeneration or present as Meig syndrome with associated ascites (10%–15%) and pleural effusions (1%) (16, 23), further complicating the differentiation of benign fibromas from malignant lesions unsuitable for ovarian preservation. Although ovarian malignancies have not been reported specifically in association with Gorlin syndrome, differentiation of benign fibromas from malignant tumors may be difficult, and there are few cases of primary ovarian fibrosarcoma in children and adolescents (24, 25).

To mitigate the challenges of radiologic interpretation, MRI may be a helpful adjunct to pelvic ultrasound. The high-density connective tissue in ovarian fibromas presents as low-intermediate signal intensity on T1-weighted images and low signal intensity on T2-weighted images (19). The presence of normal ovarian tissue adjacent to the solid ovarian mass in question is a useful radiologic feature that suggests a benign exophytic lesions that may be more amenable to conservative management with cystectomy (19). Tumor markers may also be helpful to differentiate from malignancy, because fibromas have no associated tumor markers and are hormonally inactive. However, fibrothecomas that contain a mixture of fibroblastic tissue and hormonally active thecal tissue may occasionally demonstrate estrogenic or androgenic effects (26).

Surgical approach

The majority of patients in our case series underwent laparotomy for removal of ovarian fibromas, either because of the large size or with the goal of resection without spillage and preservation of remaining normal ovarian tissue. Although a minimally invasive approach is preferred for ovarian cystectomy procedures, the decision to proceed with laparoscopy vs. an open laparotomy for resection of the fibromas should be balanced with the preoperative suspicion for malignancy and influenced by the surgeon's ability to safely resect multiple tumors without injuring surrounding ovarian tissue and maintaining hemostasis (18, 27). In cases where a surgeon considers a laparoscopic approach to not be technically feasible, a mini-laparotomy may provide a minimally invasive approach that offers adequate visualization for delineation of normal ovarian tissue, optimal resection of numerous fibromas, and possible intraoperative assessment and palpation of lymph nodes if there is suspicion of malignancy (20). The ability to palpate the contralateral ovary also allows for identification of small fibromas that would otherwise not be visualized during laparoscopy. However, as encountered in this case series, resection of the fibromas alone may not always be feasible as the borders between fibromas and ovarian cortex and stromal tissue are not always well delineated (9, 13–15, 21).

Assessment of ovarian function and reproductive potential

In accordance with recommendations by the American College of Obstetricians and Gynecologists, once patients with Gorlin syndrome begin menstruating, clinicians should regularly ask about menstrual patterns that may indicate a need

TABLE 4

Recommendations for surveillance and management of Gorlin syndrome-associated ovarian fibromas.

Persons with Gorlin syndrome without known ovarian masses
- Review menstrual patterns at each visit (at least annually)
- Pelvic ultrasound, annually

Preoperative planning for ovarian fibromas
- Pelvic ultrasound, consider MRI if concern for malignancy or for surgical planning
- Tumor markers (CA-125, LDH, AFP, β-hCG, inhibin A and B)
- AMH level

Surgical management of ovarian fibromas
- Surgical resection of fibromas with conservation of ovary
- Minimally invasive approach recommended if able to conserve normal ovarian tissue
- Removal of adnexal masses indicated if rapid enlargement or >5 cm diameter due to risk of torsion

Postoperative surveillance after resection of ovarian fibromas
- Review menstrual patterns at each visit
- Pelvic ultrasound in 3 mo, then every 6 mo for 1 y, then annually
- Postsurgical AMH level
- Referral to Reproductive Endocrinology and Infertility for fertility preservation counseling
- Referral to Genetics for preconception counseling

Note: AFP = α-fetoprotein; AMH = antimüllerian hormone; β-hCG = β-human chorionic gonadotropin; CA-125 = cancer antigen-125; LDH = lactate dehydrogenase; MRI = magnetic resonance imaging.

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for further investigation into potential health concerns (28). Similar to case 3, multiple case reports in our literature review identify menstrual irregularity as a common reason for gynecologic evaluation and identification of ovarian fibromas (Table 3) (7, 13, 15, 19). It is unknown if the presence of ovarian fibromas interfere with stromal sex-hormone production, but multiple case reports have described irregular menses as an initial complaint that leads to diagnosis of ovarian fibromas, with the notable return of normal menses after removal of the fibromas (8, 11, 21).

Attempted preservation of normal ovarian tissue is imperative in children and young women of reproductive age with Gorlin syndrome, because they are at high risk of iatrogenic menopause and infertility with surgical removal of ovaries, either because of the presence of numerous, large fibromas, or the need for repeat excision in the setting of recurrence. Even with use of ovarian conserving techniques, repeated adnexal surgeries may reduce remaining ovarian tissue and may compromise fertility (12, 17). Furthermore, as demonstrated in case 3, the presence of other Gorlin syndrome-associated malignancies increases the likelihood of a patient receiving gonadotoxic therapy that could further cause iatrogenic injury to the remaining ovarian tissue. Given the inability to predict if conservative surgical management is possible, preoperative counseling should include a discussion on the possibility of oophorectomy, as well as consideration of early referral to fertility preservation counseling.

Reproductive life planning should be addressed with patients affected by Gorlin syndrome, particularly as life expectancy remains unchanged and case reports describe spontaneous pregnancy after conservative management of multiple and recurrent fibromas (7, 15). Fertility preservation measures such as oocyte cryopreservation have been reported as options for patients with this genetic syndrome, although may have poor yield of mature oocytes (17). Optimal timing and method of fertility preservation is unknown, and may need to be deferred until after ovarian conserving surgery if fibromas interfere with stimulation or retrieval of oocytes (11, 17). Ovarian tissue cryopreservation at time of surgery has not yet been described in the literature for patients with Gorlin syndrome, but may be an option for those who require oophorectomy or are unable to successfully undergo preoperative oocyte stimulation. However, this option may be limited by desire to retain ovarian tissue in situ for pubertal development. Patients must also be counseled on the inability to rule out ovarian malignancy at time of surgery, as well as the risk of fibroma recurrence in reimplanted ovarian tissue after cryopreservation.

Although low AMH levels were observed in this case series as well as in prior studies (17), the utility of AMH measurement and its relation to future fertility in this population is unknown. Prior research have suggested preoperative AMH levels are lower in individuals with endometriotic and nonendometriotic cysts, as well as after cystectomy (29); additional research is needed to elucidate if AMH measurement aids in identifying optimal timing of fertility preserving measures and counseling in those with Gorlin syndrome and ovarian fibromas. We recommend implementing presurgical and postsurgical AMH measurements and early referral to fertility preservation counseling after the first incidence of ovarian fibroma management. Most published studies regarding post-cystectomy AMH levels have reported short-term results with a small number of patients (29). If the postsurgical AMH is lower than pre-surgical levels, a repeat AMH level (such as a year later) may be helpful to allow for detection of possible late recovery of the ovarian reserve and guide clinical counseling. Patients diagnosed with Gorlin syndrome who are desiring pregnancy should also be referred for preconception genetic counseling and options for preimplantation genetic testing given the autosomal dominant inheritance pattern (9).

Recurrence and surveillance

Although ovarian-sparing surgery is desired for reproductive and hormonal function, conservative management of ovarian fibromas carries risk of recurrence in the remaining ovarian tissue that may lead to torsion or require oophorectomy. In our case series, half of the patients with prior oophorectomy had recurrence in the remaining contralateral ovary. After consideration and shared decision-making regarding the preservation of future fertility and ovarian function, one patient underwent a second surgical procedure, whereas the other continues with surveillance of the fibromas in the remaining ovary.

Limitations of this case series include its retrospective descriptive report on a small sample size over a limited period of time. Additionally, our findings of fibroma recurrence were

dependent not just on symptoms but also on surveillance, and there are no clear guidelines on the recommended frequency or duration of surveillance imaging. Although true recurrence rates of fibromas are difficult to ascertain due to the rarity of the disease, multiple case reports describe recurrent fibromas in the setting of conservative management (5, 8, 30). As described in Table 3, observation of fibroma recurrence is limited by variable reporting and follow-up at time of publication. Our institutional practice is to complete a pelvic ultrasound three months after surgery to assess if residual fibromas are present, followed by surveillance ultrasound imaging every 6 to 12 months to assess for recurrence and interval growth. We consider close surveillance because our pediatric and adolescent patients are early in their reproductive lifespan and to reduce the risk of serious sequelae such as ovarian torsion. The rate of fibroma recurrence may be underestimated if patients received care for recurrent fibromas at another institution. Because of the high likelihood of fibroma recurrence, preventative measures such as early detection, surgical management, and surveillance could be considered. Suggestions for pre- and postoperative surveillance are described in Table 4.

Ovarian fibromas are a rare diagnosis in the pediatric population, previously permitting only case reports on the prevalence and association with Gorlin syndrome in children and young women. To our knowledge, this is the first case series to describe the surgical management of ovarian fibromas among pediatric and adolescent patients with Gorlin syndrome. The clinical presentations and complex management decisions raise important considerations for gynecologic surgeons when determining optimal surgical approach and ovarian conservation. These cases should encourage awareness of the high prevalence and recurrence of benign fibromas among patients with Gorlin syndrome, further improving early identification, counseling, and approach to ovarian conservation.

CRediT Authorship Contribution Statement

Danielle T. Cipres: Writing – review & editing, Writing – original draft, Investigation, Data curation, Conceptualization. **Jessica Y. Shim:** Writing – review & editing, Supervision, Conceptualization.

Declaration of Interests

D.T.C. has nothing to disclose. J.Y.S. has nothing to disclose.

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