Natural Resources for Human Health
eISSN: 2583-1194

Original Research

Received 16 May 2026
Revised 18 June 2026
Accepted 09 July 2026

Natural Resources for Human Health 2026, Vol. 6 (7s): 723–730

KEYWORDS:
McCune–Albright syndrome, retained products of conception, pregnancy failure, ovarian cysts, reproductive health

Pregnancy Failure and Retained Products of Conception in a Patient with Mccune–Albright Syndrome: A Case Report

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ABSTRACT: Introduction: McCune–Albright syndrome (MAS) is a rare mosaic disorder characterized by postzygotic activating mutations in the GNAS gene, leading to constitutive Gsα signalling and autonomous endocrine activity. Gonadotropin-independent precocious puberty due to autonomous ovarian cyst formation is the most frequent endocrine manifestation in affected females. As patients with MAS increasingly reach reproductive age, pregnancy outcomes and gynaecological morbidity have emerged as important clinical considerations, though published data remain limited.

Case Presentation: We report a 19-year-old female with a history of MAS, diagnosed in childhood with precocious puberty, recurrent ovarian cysts, polyostotic fibrous dysplasia and café-au-lait pigmentation. After medical termination of an early pregnancy failure at about six weeks' gestation, she presented with persistent vaginal bleeding and lower abdominal discomfort. Transvaginal ultrasonography revealed a thickened endometrium, 17 mm, heterogeneous echogenic content and internal Doppler vascularity suggestive of retained products of conception (RPOC). She underwent surgical uterine evacuation under anaesthesia with suction curettage. Histopathological examination confirmed products of conception with no evidence of gestational trophoblastic disease. Her post-procedural recovery was uneventful, with resolution of bleeding and no complications.

Discussion: The case highlights where MAS-related ovarian dysfunction and early pregnancy failure overlap with RPOC. This cyst-driven estrogen excess of MAS is likely to create a proliferative and highly vascular endometrial environment that could theoretically predispose to persistent post-termination tissue. As of now, evidence indicates spontaneous conception is possible in MAS, but women with MAS have raised risks of abnormal uterine bleeding, infertility and pregnancy-related complications. Structured reproductive surveillance, early imaging after pregnancy loss, and multidisciplinary endocrine–gynaecological coordination are key to optimising outcomes.

Conclusion: This report highlights the need for heightened clinical awareness of post-pregnancy complications in women with MAS and supports recommendations for protocolised reproductive follow-up in this population.

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INTRODUCTION

McCune–Albright syndrome (MAS) is a rare, non-inherited mosaic disorder resulting from postzygotic activating mutations in the GNAS gene, which encodes the Gsα subunit of the stimulatory G protein. These mutations result in constitutive activation of the cyclic AMP signalling pathway, which leads to autonomous endocrine hyperfunction in affected tissues [1]. The classical phenotypic triad is composed of polyostotic fibrous dysplasia, café-au-lait macules and endocrine hyperfunction but is expressed markedly depending on the composition of mutated cells [2,3].

Ovarian involvement is among the most clinically significant endocrine manifestations in affected females. Autonomous activation of ovarian follicles through unregulated peripheral estrogen production leads to gonadotropin-independent precocious puberty, typically presenting with recurrent ovarian cysts, intermittent vaginal bleeding and advanced bone age [3,4]. The natural history of ovarian function in MAS is characterised by fluctuating estradiol levels, episodic cyst formation and variable ovulatory activity. While some patients achieve near-normal reproductive function, others experience persistent ovarian autonomy, anovulatory infertility and abnormal uterine bleeding into adulthood [5,6].

More and more patients with MAS have achieved reproductive age as the population increases due to improved recognition and multidisciplinary care, and the clinical importance of fertility and pregnancy outcomes has thus progressed [6,7]. Yet published pregnancy data in MAS is scant and mostly case-based. Recurrent functional cysts, hormonal instability, and the effect of related endocrinopathies, such as growth hormone excess and thyroid disease, on gestational course have all been reported [7,8].

Retained products of conception (RPOC) is a well-recognised complication following spontaneous pregnancy loss, medical termination or delivery, defined as the persistence of placental and/or fetal tissue within the uterus [9]. Sonographic features supporting RPOC include increased endometrial thickness, heterogeneous intrauterine echogenic material and demonstrable Doppler vascularity, which improves diagnostic specificity over grayscale findings alone [10,11]. The estrogen-excess state characteristic of MAS may theoretically modify endometrial vascularity and post-pregnancy resolution, though direct evidence is lacking [12]. We report a case of early pregnancy failure and subsequent RPOC in a young woman with MAS, highlighting the reproductive implications of this rare disorder and the importance of coordinated endocrine–gynaecological follow-up.

PATIENT INFORMATION

The patient was a 19 year old Asian woman with a recognized diagnosis of McCune – Albright syndrome that began in childhood. She had been evaluated about six years of age for premature thelarche, early vaginal bleeding and accelerated growth. The diagnostic work-up that occurred observed suppressed gonadotropins (follicle stimulating hormone around 0.23 mIU/mL; luteinising hormone around 0.13 mIU/mL) with detectable estradiol (about 33 pg/mL) and advanced bone age relative to chronological age. Skeletal imaging showed polyostotic fibrous dysplasia involving multiple sites, and on physical examination, café-au-lait pigmentation was observed. She had no known thyroid dysfunction, and her thyroid profile was within reference range.

Her medical history was otherwise unremarkable. There was no history of diabetes mellitus, hypertension or other chronic illnesses. She had no known drug allergies. She reported irregular menstrual cycles throughout late adolescence, consistent with her underlying ovarian dysfunction. The current pregnancy was spontaneous and unplanned.

Clinical Findings

On presentation to our gynaecology service, the patient reported persistent vaginal bleeding of moderate volume and lower abdominal discomfort that had continued for approximately one week following medical termination of pregnancy performed at an outside facility on 3 December 2025. The termination had been undertaken for early pregnancy failure diagnosed at approximately six weeks' gestation.

She was haemodynamically stable: blood pressure 118/72 mmHg, heart rate 78 beats per minute, respiratory rate 16 breaths per minute and afebrile at 36.7°C. Abdominal examination revealed mild suprapubic tenderness on palpation, with no guarding or rigidity. Pelvic examination demonstrated bleeding through os, normal-sized uterus with mild cervical motion tenderness; adnexal examination was unremarkable bilaterally. There were no clinical signs of pelvic sepsis—no fever, no purulent vaginal

discharge and no significant peritoneal signs. Cutaneous examination revealed characteristic café-au-lait macules over the trunk and extremities, consistent with her known diagnosis of MAS.

Timeline

Date/Period	Event
Age ~6 years	Presented with precocious puberty; diagnosed with McCune–Albright syndrome based on gonadotropin-independent precocious puberty, polyostotic fibrous dysplasia and café-au-lait pigmentation
Late adolescence	Irregular menstrual cycles; periodic endocrine follow-up
November–December 2025	Spontaneous conception confirmed
Early December 2025	Ultrasound at ~7 weeks 6 days gestation: intrauterine gestational sac (MSD 29.3 mm) with yolk sac but no fetal pole or cardiac activity; consistent with early pregnancy failure (anembryonic pregnancy).
3 December 2025	Medical termination of pregnancy performed at outside facility
~10 December 2025	Persistent vaginal bleeding and lower abdominal discomfort prompted reassessment; outside ultrasound suggested retained products of conception
Presentation	Referred to our gynaecology service for further management
Day 1 (presentation)	Clinical assessment, transvaginal ultrasonography confirming RPOC (endometrial thickness 17 mm with internal Doppler vascularity); decision for surgical evacuation
Day 2	Uterine evacuation under anaesthesia (suction evacuation with gentle curettage); specimens sent for histopathology
Days 3–7	Post-procedural recovery: bleeding decreased substantially within 24 hours and resolved over subsequent days; no complications
Follow-up (2 weeks)	Repeat ultrasound: no evidence of retained products; patient asymptomatic; histopathology confirmed products of conception without trophoblastic disease

DIAGNOSTIC ASSESSMENT

Initial Pregnancy Ultrasound

Ultrasound at 7 weeks 6 days' gestation demonstrated a single intrauterine gestational sac measuring 29.3 mm (MSD). A yolk sac was visualized, but no fetal pole or embryonic cardiac activity was identified. The right ovary appeared normal, while the left ovary showed a haemorrhagic cyst measuring 2.5 × 2.4 cm. In the context of a positive pregnancy test, these findings are consistent with early pregnancy failure (anembryonic pregnancy/non-viable pregnancy).

Post-Termination Ultrasound

On referral, transvaginal ultrasonography revealed the uterus to be 7.2 × 3.5 × 4.5 cm in size, while the endometrial contents were heterogeneous. Endometrial thickness measured 17 mm with internal Doppler vascularity identified within the endometrial cavity. Around the fundus, a focal echogenic intrauterine area of around 2.4 × 1.4 cm was observed. Minimal free fluid was seen in the pouch of Douglas. The right ovary was about 4 × 2.6 cm in size with an associated cyst of about 2.5 × 2.6 cm; the left ovary measured approximately 2 × 1.5 cm and appeared unremarkable.

The presence of a thickened, heterogeneous endometrium with a focal echogenic lesion and demonstrable Doppler vascularity was highly suggestive of retained products of conception. An endometrial thickness threshold of >1.49 cm has been shown to

aid in diagnosing RPOC, and Doppler flow enhances diagnostic value in symptomatic patients [10,11]. The vascularity within the intrauterine contents favoured retained trophoblastic tissue over inactive debris or organised blood clot.

Differential Diagnosis

The primary diagnostic consideration was retained products of conception (RPOC), supported by the temporal sequence of persistent bleeding beyond the expected post-termination period and characteristic sonographic findings. The differential diagnosis included:

- **Incomplete abortion**: Clinically overlapping with RPOC, this represented the same pathological spectrum and would warrant similar management—completion evacuation in a symptomatic patient.
- **Organised intrauterine blood clot**: Clots can appear echogenic on ultrasound; however, the presence of internal vascularity made this less likely, as blood clots typically lack Doppler flow.
- **Gestational trophoblastic disease**: Persistent bleeding after pregnancy failure raised the possibility of trophoblastic disease, including hydatidiform mole or invasive mole. Histopathological confirmation was therefore planned to exclude this entity.
- **MAS-related endometrial changes**: Chronic or intermittent estrogen excess from autonomous ovarian activity could produce a proliferative, vascular endometrial environment [12]. While this was considered a contributing background factor, it was insufficient to explain a focal vascular intrauterine lesion.
- **Post-procedural endometritis**: This was clinically unlikely in the absence of fever, significant uterine tenderness or systemic features of infection.

Childhood Endocrine Records

Review of childhood records confirmed suppressed gonadotropins with detectable estradiol, consistent with gonadotropin-independent precocious puberty. Bone age was advanced relative to chronological age. Prior skeletal imaging demonstrated polyostotic fibrous dysplasia. These findings established the diagnosis of MAS according to established clinical criteria [1,2].

Summary of Diagnostic Context in MAS

To contextualise the patient's presentation against known reproductive phenotypes, **Table 1** summarises the key reproductive and pregnancy outcomes reported in recent studies and case series of MAS, which guided the diagnostic framework and prognostic counselling for this patient.

Table 1. Summary of Reported Reproductive and Pregnancy Outcomes in Women with McCune–Albright Syndrome (Contextual Diagnostic Benchmark)

Author(s) & Year	Study Type / Cohort	Number of Women / Pregnancies	Key Reproductive Findings	Reported Pregnancy Complications / Outcomes
Boyce et al. (2019) [6]	Retrospective cohort	39 women; 25 pregnancies (in 14 women)	Abnormal uterine bleeding (77%); Infertility (43%). Spontaneous conception possible despite ovarian dysfunction.	No clear worsening of skeletal disease during pregnancy; one case of preterm labour reported.
Ferris et al. (2021) [5]	Longitudinal natural history	42 women	Fluctuating estradiol levels; 62% had evidence of ovulatory cycles; regular menses in a subset.	Miscarriage reported in a subset of patients; detailed gestational outcomes not systematically quantified.

Salenave et al. (2020) [7]	Review / Single-center series	Patients with GH excess/acromegaly	Highlighted risk of elevated GH/IGF-1 impacting reproductive function and pregnancy.	Recommended rigorous multidisciplinary monitoring during pregnancy due to potential tumour expansion and metabolic changes.
Tan et al. (2025) [13]	Case report	1 patient	MAS with GH excess; pegvisomant continued throughout pregnancy.	Uncomplicated pregnancy; delivery of a healthy neonate. Demonstrated safety of continuing GH antagonist therapy.
Present Case (2026)	Case report	1 patient	Early pregnancy failure following spontaneous conception.	Retained products of conception with vascular endometrial features; successfully managed with surgical evacuation and good recovery.

THERAPEUTIC INTERVENTION

Given persistent symptomatic bleeding, significant endometrial thickening with internal Doppler vascularity and the risk of ongoing retention with potential complications (including infection, haemorrhage and future fertility compromise), active surgical management was preferred over expectant management or repeat medical therapy [9,11].

The patient was thoroughly counselled regarding the diagnosis, available management options (expectant, medical and surgical), procedural risks (including haemorrhage, infection, uterine perforation and Asherman syndrome) and the importance of histological confirmation to exclude trophoblastic disease. She provided written informed consent for the procedure.

She underwent uterine evacuation under general anesthesia by suction evacuation with gentle curettage to complete the cavity. Retained intrauterine tissue was removed in toto, as far as technically possible. Due to the patient's young age and the possibility of fertility in the future, a controlled instrumentation and gentle technique was adopted to minimise endometrial trauma.

Evacuated material was subjected to histopathological assessment to confirm products of conception and rule out trophoblastic pathology. The usual peri-procedural management was routine haemodynamic monitoring and prophylaxis (institution-based single-dose intravenous cefotaxim). No adnexal manipulation was necessary even though the underlying MAS-related ovarian cyst was found in the right ovary since it was asymptomatic and surgical management was not medically indicated at this time.

Follow-up and Outcomes

The post-procedural course was uneventful. Vaginal bleeding decreased substantially within 24 hours of the procedure and resolved completely over the following days. There were no clinical signs of infection, secondary haemorrhage or other complications. Vital parameters remained stable throughout the observation period.

Histopathological examination confirmed the presence of products of conception, including chorionic villi and decidual tissue, without evidence of gestational trophoblastic disease (no hydatidiform change, no atypical trophoblastic proliferation). This finding supported the adequacy of surgical evacuation and excluded the need for oncologic surveillance.

A repeat transvaginal ultrasound performed at two-week follow-up demonstrated a normal uterine cavity with no evidence of retained products. Endometrial thickness had normalised, and there was no abnormal vascularity. The patient was completely asymptomatic.

Given her underlying McCune–Albright syndrome, she was advised to continue multidisciplinary follow-up with endocrinology and gynaecology services. Counselling included discussion of:

- Menstrual variability and the likelihood of continued irregular cycles
- Risk of recurrent ovarian cyst activity
- Reproductive unpredictability associated with MAS
- Importance of early ultrasound confirmation and supervised monitoring in any future pregnancy
- Contraceptive options and preconception planning

Emotional support and reassurance were provided in view of the pregnancy loss occurring in the setting of chronic endocrine disease.

DISCUSSION

McCune–Albright syndrome is caused by postzygotic somatic activating mutations in the GNAS gene resulting in mosaic expression of constitutive Gsα signalling with autonomous endocrine activity in affected tissues. The clinical phenotype is highly variable reflecting the stochastic distribution of mutated cells during embryogenesis [1,3]. Ovarian involvement, manifesting as gonadotropin-independent estrogen production from autonomous cysts, is among the most clinically consequential endocrine features in affected females [4,5].

The natural history of ovarian function in MAS is characterised by intermittent, cyst-driven estrogen secretion rather than the predictable cyclical pattern of normal hypothalamic-pituitary-ovarian axis function. Fluctuations in ovarian cyst size result in corresponding fluctuations in plasma estradiol, leading to episodic advancement and regression of secondary sexual characteristics and irregular menstrual bleeding. Some longitudinal cohorts suggest that ovulatory cycles may eventually occur in a subset of patients, permitting spontaneous conception, though cycle unpredictability and anovulatory infertility persist in many [5,6].

The reproductive consequences of this ovarian dysfunction are significant. In a natural history study of 39 women suffering from fibrous dysplasia/McCune–Albright syndrome, abnormal uterine bleeding affected 77% of participants, with 9 women needing hysterectomy for bleeding control—including 67% at an unusually young age of less than 35 years. Infertility affected 43% of women who attempted pregnancy. Of these 14 women who achieved spontaneous pregnancies, 35% (8 of 25 pregnancies) were unplanned, demonstrating the inconsistency of fertility among this population [6].

Pregnancy in MAS is rarely reported but it is biologically plausible and has been documented in several case reports. One study found 25 spontaneous pregnancies among 14 women with MAS in 2019 [6]. More recent reports have reported successful pregnancy with in vitro fertilisation in a patient with bilateral ovarian involvement, and the safe continuation of pegvisomant during pregnancy for management of growth hormone excess [13]. But pregnancy loss remains a documented outcome— one IVF case resulted in pregnancy but unfortunately ended in an incomplete miscarriage. Early pregnancy failure is currently not consistently quantified in MAS but disordered folliculogenesis, luteal phase defects and changes in endometrial receptivity provide mechanistic plausibility [8].

Retained products of conception is a recognised complication of pregnancy loss or termination, and the reported incidence is influenced by gestational age, method of pregnancy termination and diagnostic criteria [9]. The sonographic features in favor of RPOC include endometrial thickness >1.49 cm, heterogeneous intrauterine echogenic material, and demonstrable Doppler vascularity. The presence of vascular flow within intrauterine contents improves diagnostic specificity compared to grayscale findings alone and favours retained trophoblastic tissue over inactive debris or organised clot [10,11]. In one study involving 225 women undergoing hysteroscopy for suspected RPOC, Doppler flow was significantly associated with RPOC presence in symptomatic patients, and endometrial thickness >1.49 cm demonstrated diagnostic utility [11].

In MAS, the chronic or intermittent estrogen excess may create a more proliferative and vascular endometrial environment. Estrogen promotes endometrial angiogenesis, increases vascular endothelial growth factor expression and enhances endometrial vascularity [12]. This theoretical mechanism could increase the likelihood of persistent post-termination tissue, prolonged bleeding or both, though direct evidence in the MAS population is sparse. The present case is clinically instructive because it links three intersecting domains—MAS-related ovarian dysfunction, early pregnancy failure and RPOC—highlighting the need for structured reproductive surveillance in affected women.

RPOC treatment in MAS should adopt appropriate parameters, with surgical procedures based on symptomatology, vascularity, bleeding threat and fertility prospective [9]. In this scenario, surgery was a favored surgical approach rather than expectant or repeat medical treatment for persistent symptomatic bleeding, significant vascularity on imaging, and possibility of continued retention. Histopathological confirmation in this patient is important to rule out gestational trophoblastic disease, which, while rare, must be considered in any patient with persistent bleeding after pregnancy loss.

STRENGTHS AND LIMITATIONS

There are multiple strengths of this case report. It offers a detailed, chronologically structured description of pregnancy failure and RPOC in a rare endocrine disorder patient, and adds to the relatively scarce clinical reports of reproductive outcomes in MAS. The work-up of diagnosis was an extensive series of ultrasonographic, Doppler, and histopathological checks and confirmations. The case additionally demonstrates the significance of interdisciplinary care coordination between gynaecology and endocrinology services.

Limitations include the single-case nature of the report, which precludes generalisation. The patient's MAS diagnosis was established clinically in childhood without molecular confirmation of the *GNAS* mutation, though the clinical triad of precocious puberty, polyostotic fibrous dysplasia and café-au-lait pigmentation is considered sufficient for diagnosis. Long-term follow-up data on this patient's reproductive outcomes are not yet available.

Clinical Implications

This case supports several practical recommendations for clinicians managing reproductive-age women with MAS:

1. **Early imaging follow-up after pregnancy loss**: Given the potential for persistent RPOC and the vascular endometrial environment in MAS, early post-termination ultrasound with Doppler assessment is advisable.
2. **Careful interpretation of vascular endometrial findings**: Doppler-positive intrauterine contents should raise suspicion for RPOC and prompt appropriate management.
3. **Multidisciplinary coordination**: Endocrine–gynaecological collaboration is essential for optimising reproductive outcomes, managing associated endocrinopathies and providing comprehensive preconception and contraceptive counselling.
4. **Protocolised reproductive surveillance**: Given the high prevalence of abnormal uterine bleeding and infertility in MAS, structured reproductive follow-up should be standard in this population.

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