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Case Report

Twin pregnancy with metastatic complete molar pregnancy and coexisting live fetus

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ABSTRACT

We present a case of a 34-year old G1P0 female with twin-gestation and positive prenatal screening. Initial ultrasounds demonstrated a normal live fetus with an indeterminate but persistent placental lesion. The patient presented at 23 weeks of gestational age with vaginal bleeding. On examination, a 2 cm vaginal lesion was identified. Further cross-sectional imaging demonstrated a normal appearing fetus with a mixed solid and cystic placental lesion as well as an additional lesion in the vagina. Metastatic workup revealed diffuse pulmonary metastases. Intravascular embolization was carried out to minimize the bleeding from the vaginal lesion, followed by the delivery of the fetus with an urgent Caesarean section and treatment with chemotherapy. Pathology and genetics testing confirmed diagnosis of a complete molar pregnancy with a coexisting live fetus. This case highlights the importance of any unexpected findings within the placenta or the uterus in a pregnant patient. The radiologist should maintain a high index of suspicion for gestational trophoblastic disease in such cases, communicate clearly with the clinical team and suggest appropriate additional imaging.

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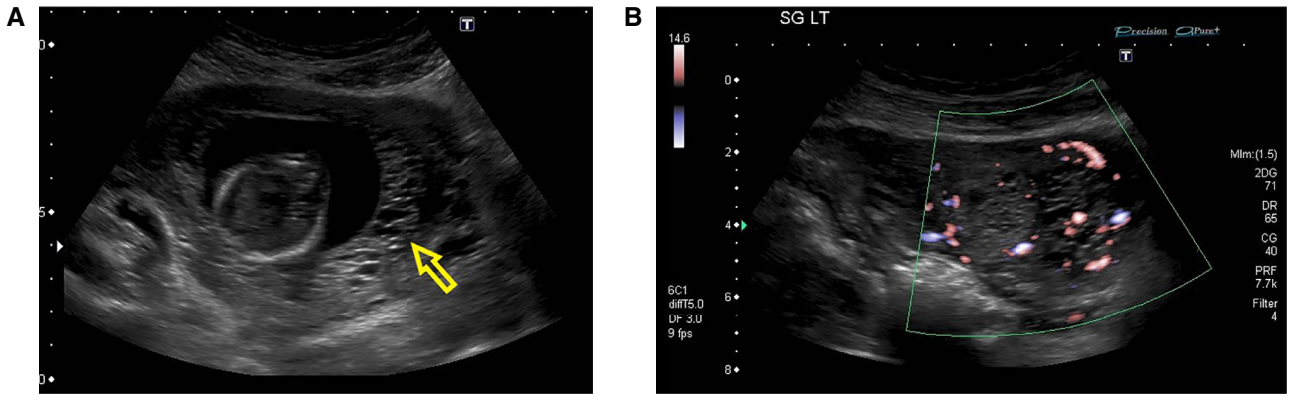

Fig. 1 – (A) A mixed solid and cystic lesion with somewhat "snowstorm" appearance next to the normal fetal placenta. (B) The lesion demonstrated color flow.

Case report

A 34-year-old G1P0 previously healthy female was initially seen by maternal fetal medicine for a possible molar pregnancy at 14 weeks gestation. She was also known to have a 1 in 200 risk of Down's syndrome based on first trimester screening as well as an elevated level of human chorionic gonadotropin (HCG) at 900,000 mIU/mL (normal 25,700-288,000 mIU/mL). She presented to the hospital for vaginal bleeding at 23 weeks of gestational age. Vaginal examination showed a 2 cm extremely friable lesion in the upper third of the right posterior vagina.

Patient had an amniocentesis earlier at 15 weeks of gestation that showed a normal Quantitative Fluorescence-Polymerase Chain Reaction (QF-PCR), ruling out a partial mole. However, there was an abnormal microarray with Xp22.31 microduplication of unknown clinical significance.

At presentation to the hospital, her beta-HCG (β-HCG) level was 83,000 mIU/mL (normal 4060-165,400 mIU/mL). Ultrasound examination demonstrated a viable fetus. There was also a mixed cystic and solid lesion with internal vascularity that appeared separate from the placenta (Fig. 1). There were no clear signs of twin pregnancy such as a twin-peak sign (triangular appearance of the chorion insinuating between the layers of the intertwin membrane suggesting a dichorionic twin pregnancy) or T-sign (absence of twin-peak sign appearing as a thing intertwin membrane suggesting a monochorionic twin pregnancy).

A fetal MRI demonstrated a normal appearing fetus. In correlation with the sonographic findings, there was a heterogeneous cystic lesion within the lower uterine wall near the placenta. This lesion was complex with T2 hyperintense and mixed T1 hypointense and hyperintense components (Fig. 2). In addition, there was a second similar lesion within the vaginal wall (Fig. 3), which was likely the culprit lesion for the vaginal bleeding.

The differential diagnosis at this point included a complete molar pregnancy with a coexisting live fetus (CMCF), a partial molar pregnancy, coexistence of a normal fetus, and a blighted ovum with hydropic changes to the placenta, an arteriovenous malformation or mesenchymal dysplasia.

A chest radiograph demonstrated multiple lung nodules, which were confirmed with a computed tomography scan (Fig. 4). There were no metastatic lesions within the abdomen, pelvis, or the brain.

The working diagnosis at this point was metastatic gestational trophoblastic disease (GTD). At this point, a discussion took place with the patient and her partner regarding the treatment options. One option would be to treat with chemotherapy during the pregnancy. However, case reports of successful outcomes with this option were scarce [1–3]. On the other hand, a delivered fetus at the early gestational age of 23 weeks would most likely not be viable. Colleagues from other services including maternal-fetal medicine, neonatology, and gynecological oncology from within and outside the institution were consulted. Finally, a consensus was reached to percutaneously embolize the vaginal lesion to control the bleed, followed by delivery of the fetus by Caesarean-section and subsequent treatment with the appropriate chemotherapy.

A live fetus was delivered but it did not survive past a few hours. The placenta was delivered with a small defect, which in retrospect was likely due to adhesion of the placenta with the adjoining molar gestational sac. Patient underwent chemotherapy with etoposide and methotrexate (EP) for 2 cycles followed by etoposide, methotrexate, actinomycin D, cyclophosphamide and vincristine (EMA-CO) for 7 cycles. Her β-HCG levels normalized 1-month post delivery.

On gross pathological assessment, the placenta measured 14.8 × 9.2 × 1.9 cm and weighed 132 g (less than the 10th percentile for weight expected for this gestational age). The umbilical cord exhibited eccentric insertion and the amniotic membranes exhibited marginal insertion. The maternal surface of the placenta disc contained a defect measuring 5.5 × 4.0 cm (Fig. 5A). Within this defect, there were grape like vesicular villi measuring up to 0.7 mm in diameter (Figs. 5B and C). Microscopic examination of the sections revealed 2 distinct populations of villi; hydropic villi, and histologically normal villi for the gestational age (Fig. 6A). Immunohistochemical analysis was carried out to confirm the diagnosis of complete hydatidiform mole with coexisting normal fetal placenta. Dilated villous (Fig. 6D) trophoblast cells were completely negative for P57 staining (Fig. 6E) and had

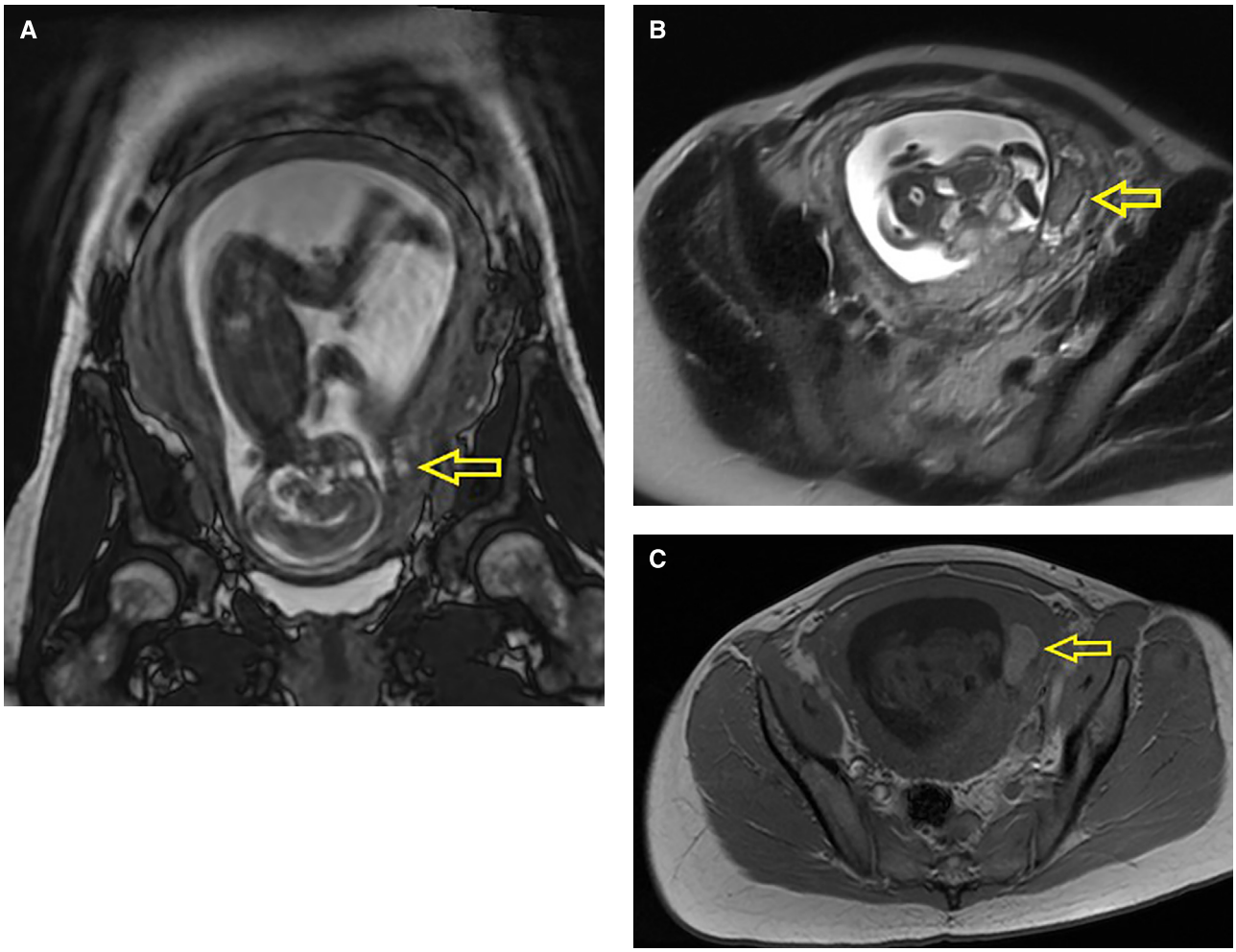

Fig. 2 – (A) A heterogenous lesion was noted adjacent to the placenta containing a viable fetus. (B) The lesion demonstrated peripheral T2 hyperintense nodular cystic components, which later correlated with vesicular grape-like villi. (C) The lesion demonstrated central T1 hyperintensity content, suggestive of hemorrhagic components.

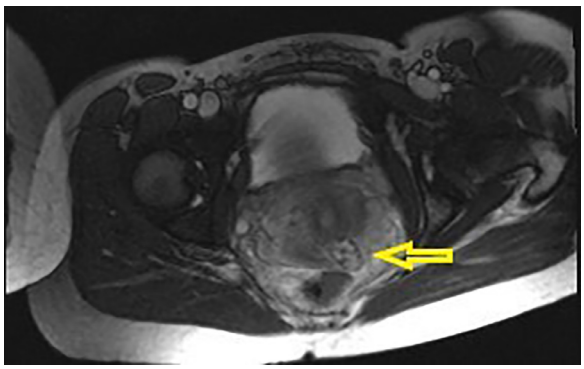

Fig. 3 – There was another lesion in the lower cervix demonstrating T2 hyperintense components.

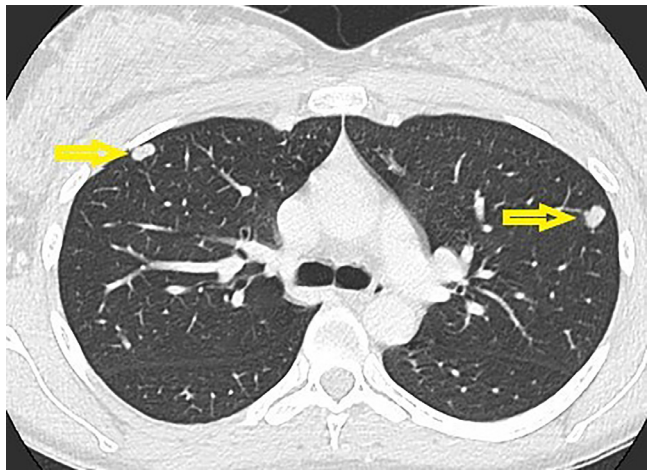

Fig. 4 – A CT of the Chest, abdomen, and pelvis demonstrated multiple scattered rounded nodules in bilateral lungs in keeping with metastatic foci. No metastatic lesions were noted in the abdomen or pelvis.

increased mitotic index by Ki67, almost staining 100% of the cytotrophoblasts (Fig. 6F). This confirmed that the villi were of complete mole pregnancy. Whereas, the stromal cells of the small and normal looking villi (Fig. 6G) were positive for P57

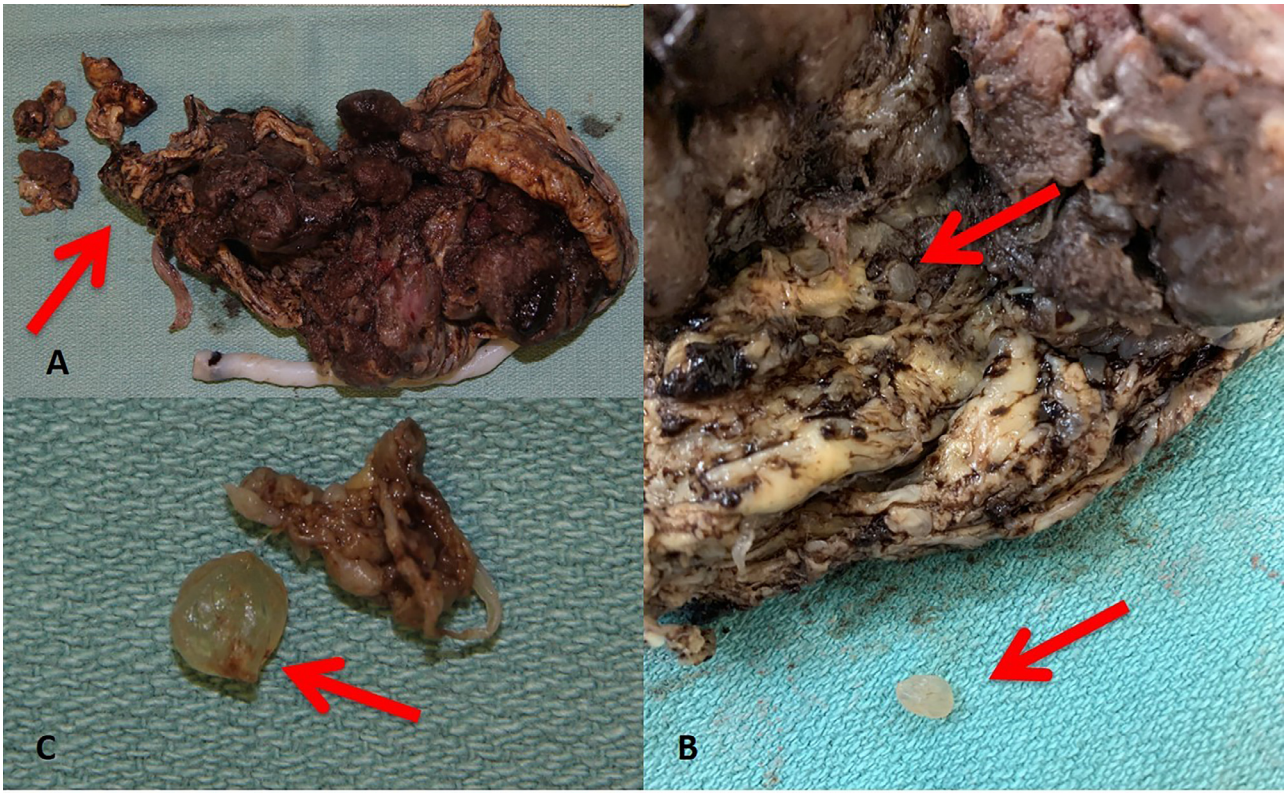

Fig. 5 – Gross appearance of a complete hydatidiform mole with a coexisting fetus placenta. (A) A single placenta with defective area at the margin. (B) Vesicular grape like villi seen in the incomplete area and as single (arrow). (C) A separate vesicular villous.

and the cytotrophoblasts had low mitotic index, less than 25% (Figs. 6H and I).

Molecular testing was conducted to confirm the diagnosis. In the normal villi sample, the usual disomic complement of chromosomes 13, 18, 21, and X and Y for a female fetus was observed. There was no evidence of trisomy detected in these samples. Maternal cell contamination was not detected. In the molar villi sample, amplification of a single allele was noted at all the loci assessed. Absence of a maternally derived allele was also noted at several loci (9/19 loci with amplified products, including loci on chromosomes 13, 18, 21, and X) indicative of paternal inheritance of the detected alleles. This result is suggestive of whole genome paternal uniparental isodisomy and consistent with a complete molar pregnancy. Overall, these molecular results suggest that there is a population of normal placental tissue having a disomic complement of chromosomes seen in 13, 18, 21, and X and a population of cystic cells with evidence suggesting whole genome paternal uniparental isodisomy (complete molar pregnancy).

Diagnosis

Twin pregnancy with a complete hydatidiform molar pregnancy with a coexisting live fetus complicated by metastatic deposits to the vagina and lungs.

Discussion

GTD is a spectrum of diseases that includes a partial hydatid mole (PHM), a complete hydatid mole (CHM), and gestational trophoblastic neoplasia (GTN). GTN primarily includes invasive mole, choriocarcinoma, and the rare placental site trophoblastic tumor and epithelioid trophoblastic tumor. A combination of clinical and radiological clues usually triggers a suspicion for GTD. Clinically, it presents with vaginal bleeding and pain as well as elevated β-HCG levels [4]. Radiologically, it most commonly presents with abnormal ultrasound appearances [5].

Ultrasound plays an important role in the assessment of a CHM. It classically demonstrates a snowstorm appearance. Sonographic appearances of a PHM are not very specific, although may show a dead fetus with cystic appearance. The typical treatment for partial and complete molar pregnancy is dilation and curettage. In approximately 15%-20% of CHM and less than 5% of PHM, there is post-molar progression to GTN [4,5].

A rather rare entity is the presence of a twin pregnancy with a molar pregnancy (either CHM or PHM) and coexisting fetus. Several case reports and series have been published in this subject matter [6–8], including metastasis during pregnancy [9,2] or after pregnancy [10–15]. A twin pregnancy with CHM can be differentiated from a twin pregnancy with PHM by the presence of viable fetus as in the latter case the fetus

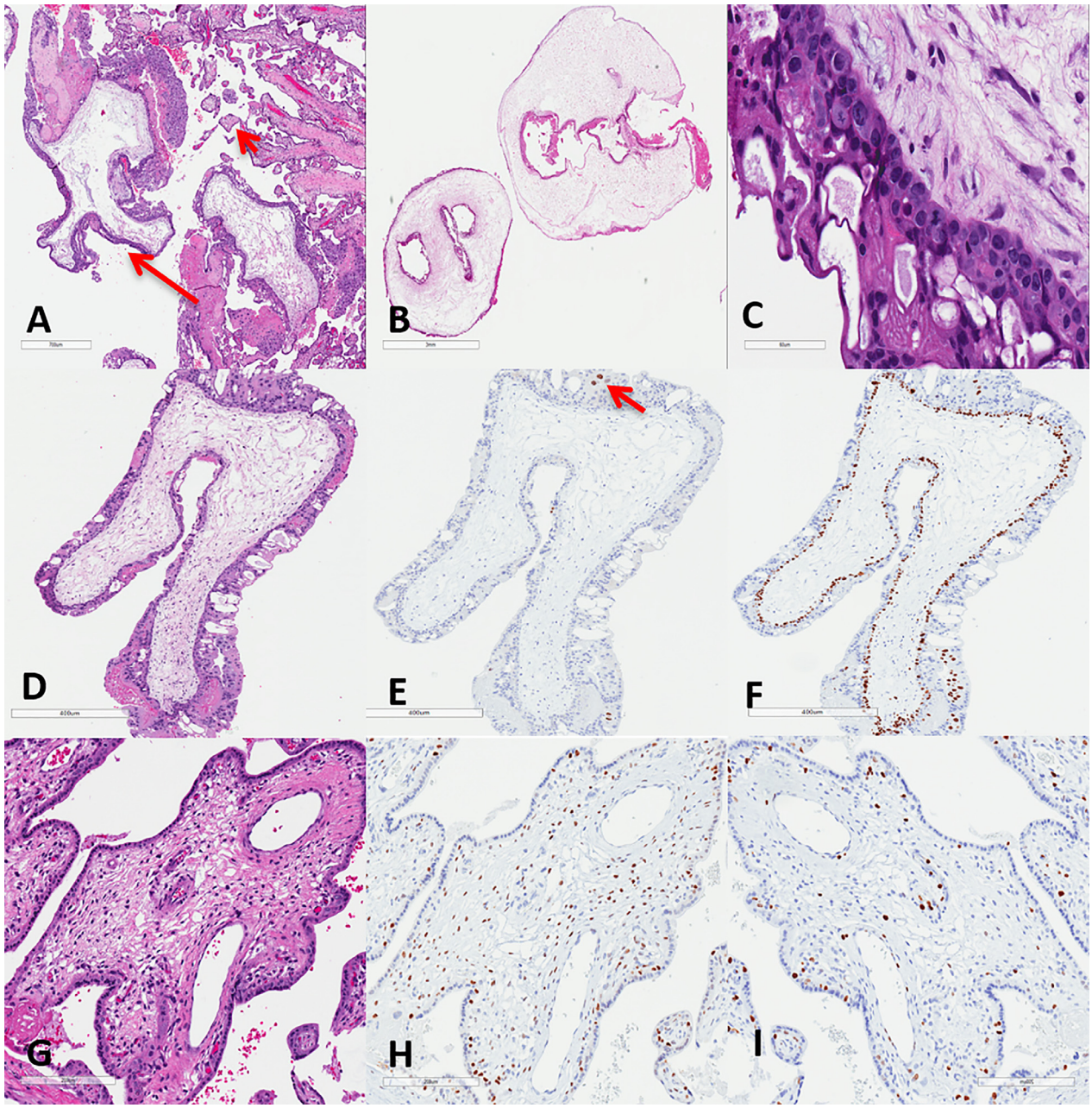

Fig. 6 – Microscopic findings in a complete hydatidiform mole with a coexisting fetus placenta H&E ×30. (A) Section showing complete hydatidfom villi (long arrow) and normal villi (short arrow). (B) Two vesicular villi recognized grossly H&E ×10. (C) Trophoblastic proliferation with atypia and 2 mitotic cells H&E ×400. (D) Enlarged hydropic villous containing containing a cistern and with circumferential proliferation of cytotrophoblasts and syncytiotrophoblasts H&E × 60. (E) Molar villous showing lack of P57 expression, it is expressed in the intervillous trophoblasts only (arrow) as internal control ×60. (F) Strong Ki67 immunostaining trophoblasts nuclei ×60. (G) Normal villous seen in proximity to the hydropic villi H&E ×140. (H) Normal villous showing strong P57 expression in cytotrophoblasts ×140. (I) KI67 staining occasional cytotrophoblasts in a normal villous × 140.

is usually anomalous or dead. Differentiation of a twin pregnancy with CHM from placental mesenchymal dysplasia (PMD) can be challenging but can be aided by the presence of color flow within the cystic lesion and location of the cystic lesion within the singleton placental sac in the case of PMD. In contrast, the cystic lesion is separated from viable placental sac in the case of twin pregnancy with CHM. In addition, the cystic spaces in CHM are caused by hydropic swollen villi and do not demonstrate vascularity [5].

In the present case, the initial ultrasound did not demonstrate clear signs of a twin pregnancy although the cystic lesions did have some resemblance to a “snowstorm” appearance. Furthermore, the presence of a normal appearing live fetus initially deterred one away from the diagnosis of GTN.

However, the suspicion was heightened by the confirmation of additional lesions within the vagina and the lungs with further cross-sectional imaging. The presence of a metastatic GTN while the fetus is in utero is certainly unusual as typically the metastatic disease develops post delivery [5].

The case was complicated by early gestational age of 23 weeks, which involved several challenges in the clinical management. Firstly, there was a need for acute management of the vaginal bleeding, which was accomplished by percutaneous embolization. Following this, a decision had to be made regarding whether to start chemotherapy with the fetus in utero or to deliver the fetus first with negligible chances of survival. After expert consultation and discussion with the patient, the decision was made to proceed with Caesarean-section delivery of the fetus, which is in line with prior literature review of 174 cases by Wee et al [1] who reported that 50% of patients elect termination of the pregnancy.

Conclusion

A case of twin pregnancy with complete molar pregnancy and a coexisting live fetus with development of in-utero metastatic disease is described.

The radiologist should be cautious about GTD in any pregnant patient with abnormal and unexpected placental or uterine mass. Differential considerations include twin pregnancy with complete/partial mole, arteriovenous malformation, or PMD. Appropriate β-HCG monitoring, amniocentesis, and karyotyping as well as imaging are key to appropriate and timely management. Further cross-sectional imaging should be considered in cases with persistent suspicion. Close and clear communication with the patient as well as the clinical team is key to ensuring optimal outcomes.

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