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Internal hemipelvectomy is a safe procedure and provides a satisfying outcome for pelvic chondrosarcoma with coexisting pregnancy

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1. Introduction

Chondrosarcoma is one of the most commonly occurring pelvic tumors, with others being Ewing sarcoma, plasmocytoma and osteosarcoma.[1] Except for some rare forms (e.g., mesenchymal chondrosarcoma), these tumors are generally regarded as refractory to radiation or chemotherapy. Therefore, surgical treatment remains the most promising approach.

In the last 25 years, only 10 cases of gestational chondrosarcomas have been reported in the literature. Surgical intervention during pregnancy is not always feasible and present its own difficulties due to the location and potential complications it brings.[2]

This case report presents the role of internal hemipelvectomy in the management of high grade pelvic chondrosarcoma with coexisting pregnancy. We proposed that such approach is safe and provide satisfying results without the need for termination of pregnancy.

2. Case report

A 22-year old woman presented to our hospital with a one-year history of lump and pain on her right hip that had worsened over the last three months. Patient also complained of difficulty in walking. She denied any history of trauma, weight loss or prolonged cough. She initially came to the hospital with the same complaint four months ago but decided to seek alternative therapy. She was 16-weeks pregnant at the time of presentation.

Physical examination revealed lump on the right inguinal extending to the medial side of right pubic that was tender to touch. The lump was 10 × 10 cm in size with ill-defined margin, soft consistency and fixed to surrounding structures. The range of motion of the right hip is 10–110°. There are no sign of lymph node enlargement, nor symptoms of pulmonary metastases.

Laboratory investigations revealed elevated erythrocyte sedimentation rate (76.4; normal value: <20) and C-reactive protein (6.62; normal value: 0.00–5.00). Serum alpha-fetoprotein was 52.10 (normal value: <5.8) while other tumor markers were within normal limits.

Plain pelvic radiographs revealed extensive calcification over the right pubis and ischium with ill-defined margin. Bone destruction was minimal (Fig. 1). Pelvis Magnetic Resonance Imaging with contrast revealed a multilobulated 9.8 x 11.4 × 13 cm soft tissue mass on the right pubic bone, extending towards the right acetabulum and hip joint. The mass appeared to be pushing the surrounding soft tissue towards the left lateral side (Figs. 2 and 3). Chest X-Ray showed no evidence of distant metastases.

Open biopsy was performed and microscopic examination revealed malignant chondroid matrix producing tumor gravitating towards high grade chondrosarcoma.

A few weeks later, internal hemipelvectomy with en bloc surgical excision was performed (Fig. 4). Patient underwent spinal anesthesia followed by exploration and resection of the mass. The duration of the operation was 10 hours with total bleeding of 1500 cc. The high-grade cancer was seen extending beyond the bone.

Post-operative condition was unremarkable and patient was hemodynamically stable. No residual tumor was found on histopathological analysis of the surgical specimen (Fig. 5). An

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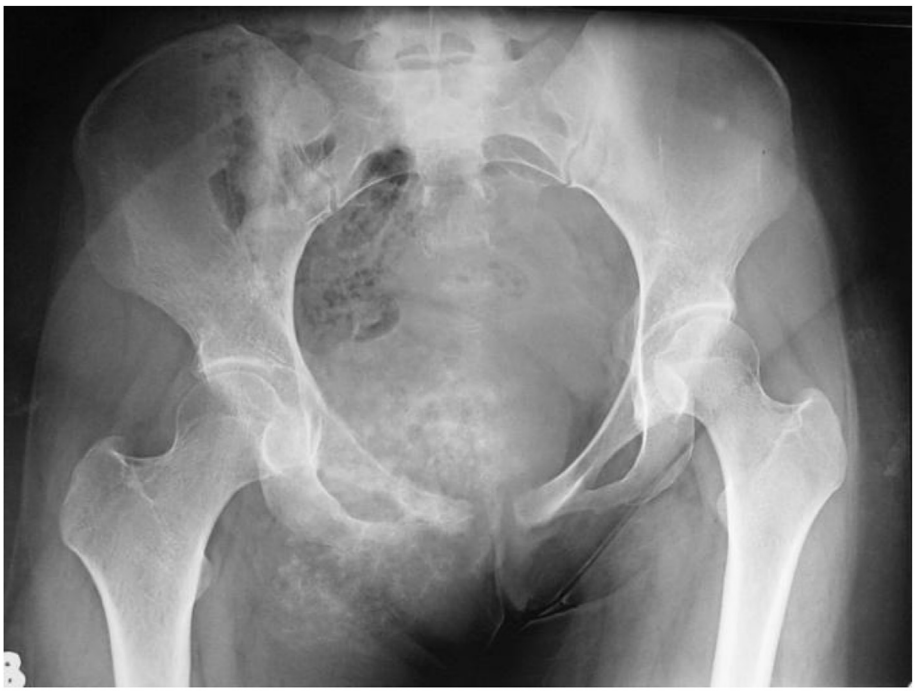

Fig. 1. Plain pelvic radiographs showing extensive calcification overlying the right pubis and ischium.

immunohistochemistry test done on the sample revealed negative estrogen and progesterone receptor.

The pregnancy was continued and followed up until full term. During the entire pregnancy, patient was prescribed bed rest but was allowed to sit. At 38 weeks of pregnancy, she underwent cesarean section and gave birth to a healthy baby boy with Apgar score of 8–9, birth weight of 2590 g and birth length of 49 cm. Pelvic radiograph taken at 6 months post operatively showed pseudoarthrosis of right femur and wide resection of right ilium (Fig. 6). One year after the operation, the patient is doing well with no evidence of recurrence. Physical examination showed a leg length discrepancy of 3 cm and patient is currently ambulating using crutches. The functional outcome was measured using Musculoskeletal Tumor Society (MSTS) score. At 12-months follow up, her MSTS score was calculated to be 80% (Pain = 5, Function = 3, Emotional = 5, Support = 3, Walking = 4, Gait = 4).

3. Discussion

Although originating from cartilaginous tissue, chondrosarcomas have been shown to exhibit microvascularity that has been associated with aggressive clinical behavior and a higher potential for metastasis. In 2011, a study involving 58 conventional chondrosarcomas found that microvessel densities in chondrosarcoma tumors correlate with histological grade and subsequently prognosis, suggestive of a role for neovasculature in the clinical behavior of chondrosarcoma. Vascular Endothelial Growth Factor (VEGF) is essential for the neovascularization required to sustain and propagate a tumor.[11]

There is still a vagueness related to the role of sex hormones which is highly presented during pregnancy, i.e. estrogen and progesterone, with chondrosarcoma.[3–6] The chondrosarcoma specimen in this report has negative result for estrogen nor progesterone receptor, yet the progressivity is markedly increased after the gestation. One possible explanation is the relationship between VEGF receptor, which present in high amount in high-grade chondrosarcoma,[11] and the hormone estrogen, which is highly expressed during pregnancy. The rapid increase of the tumor in this case may be an indirect effect of highly-expressed estrogen during pregnancy, via the VEGF receptors.

Estrogen could promote angiogenesis via combination with estrogen receptor-α to up-regulate the expression of VEGF-A in Hemangioma-derived stem cells, promoting proliferation of infantile hemangiomas.[12] A recent study indicate the importance of estradiol effect on VEGF expression, which is an important growth factors that have been involved in proliferation and angiogenesis processes in epithelial ovarian cancer.[13] 17β-estradiol is known to increase VEGFR-2 expression on human myometrial microvascular endothelial cells (MEC) promoting endothelial cell proliferation, an effect that varies between subjects and appears to be mediated primarily by ERα.[14] Another study also shows that estrogen replacement treatment (ERT) leads to an increase in serum VEGF levels.[15] Thus, the rapid increase of the tumor size might be indirectly resulted due to highly-expressed estrogen during pregnancy, via VEGF receptor in the chondrosarcoma.

Beside VEGF and estrogen, there are still numerous other oncogenic pathways that are essential for aggressive behavior of cartilage cells in the biology of chondrosarcoma, such as phosphoinositide-3 kinase with MEK-extracellular signal-regulated kinase (ERK) signaling, peroxisome proliferator-activated receptor-gamma (PPAR-γ), Ephrin-A5 (EFNA5), hedgehog, p53, insulin-like growth factor, cyclin-dependent kinase 4, hypoxia-inducible factor, SRC, and AKT.[7]

The successful eradication of a malignant cartilage tumor depends on complete wide excision, if this is technically feasible. Surgery is the primary and most effective treatment for chondrosarcoma. Other modalities, such as irradiation and chemotherapy, play a minor role and only apply to high-grade chondrosarcomas.[7] Internal hemipelvectomy is an adequate therapeutic alternative in certain cases of pelvic tumors and should be considered whenever possible, since this procedure has a low recurrence rate if compared to other radical resections. In addition,

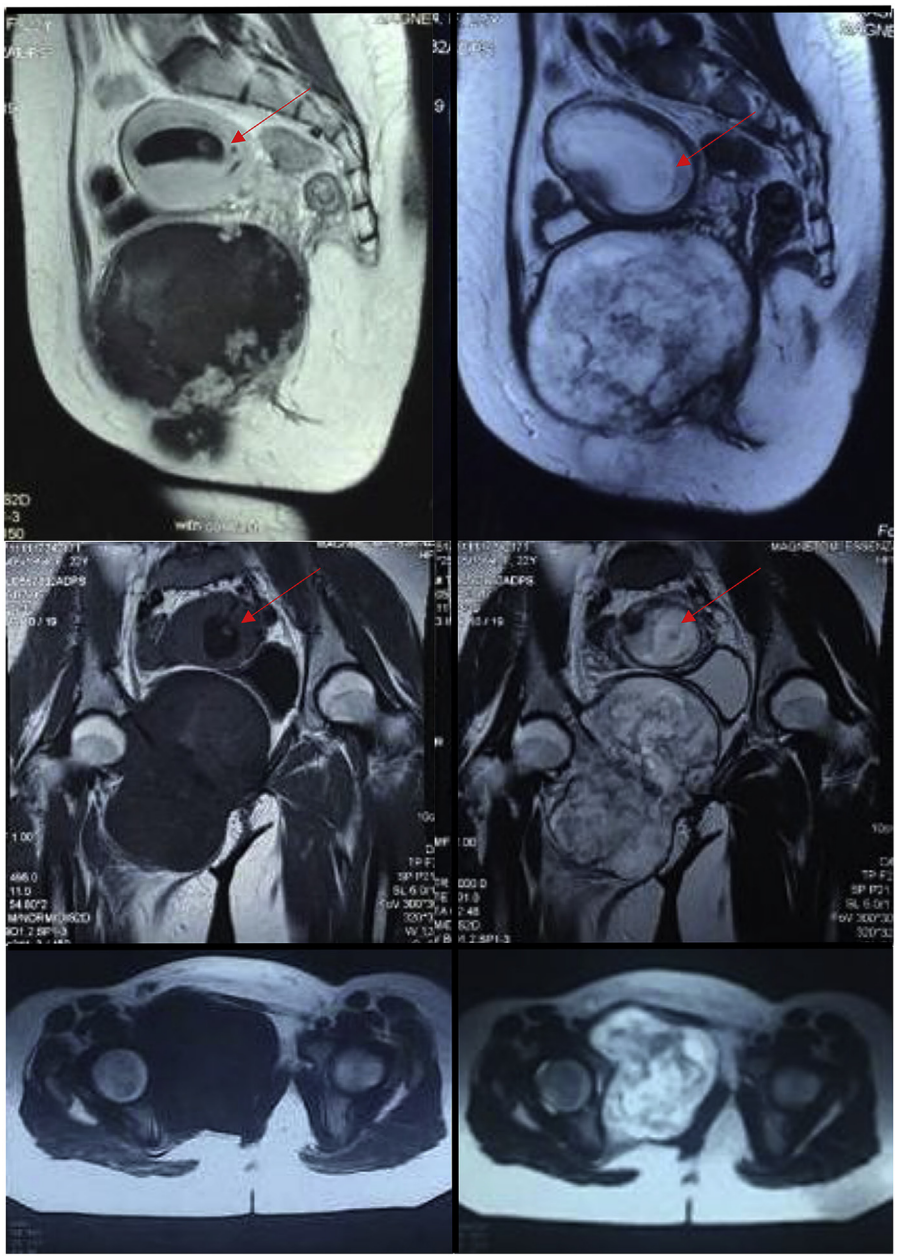

Fig. 2. Pelvic MRI at 2 months pre-operative. Incidental finding of gestational sac (red arrow).

it preserves the lower limb, which will in turn has a positive effect on patients' quality of life.[8]

A meticulous preoperative radiology assessment to identify surgical landmarks and identification of blood vessels in surgical area were formed. Using the MRI, the patient was accidentally also found to be in around 8-week pregnancy. Clinically the mass are also getting rapidly and progressively bigger, hence requiring multidisciplinary approach due to the rarity of the case. The operation was carried out after two in-depth discussions with the anesthesiologists, obstetricians, urologist, vascular surgeons, and digestive surgeons in our center.

Despite the report of sarcomas during pregnancy[16,17,18] there is paucity in literature regarding concurrent hemipelvectomy procedure as the treatment. Merimsky et al. reported a case of Ewing's sarcoma of pelvic bones in pregnant woman which was treated with chemotherapy. The baby was delivered with Cesarean section. Surgical option is barely chosen in these cases due to the morbidity it might impose on the mother and fetus when surgical area is adjacent to uterine.[19] Amorosa et al. reviewed the occurrence of pelvic injuries management in pregnancy and emphasized on avoidance of excessive insult to surrounding uterine environment when performing surgery around pelvic area. There was also recommendation to position the patient in left lateral decubitus,[20] which could not be performed in this procedure since hemipelvectomy was performed on the right part.

Studies appear to show that there is an increased risk of spontaneous miscarriage in patients who have been exposed to anesthesia and surgery during pregnancy. Studies looking specifically at

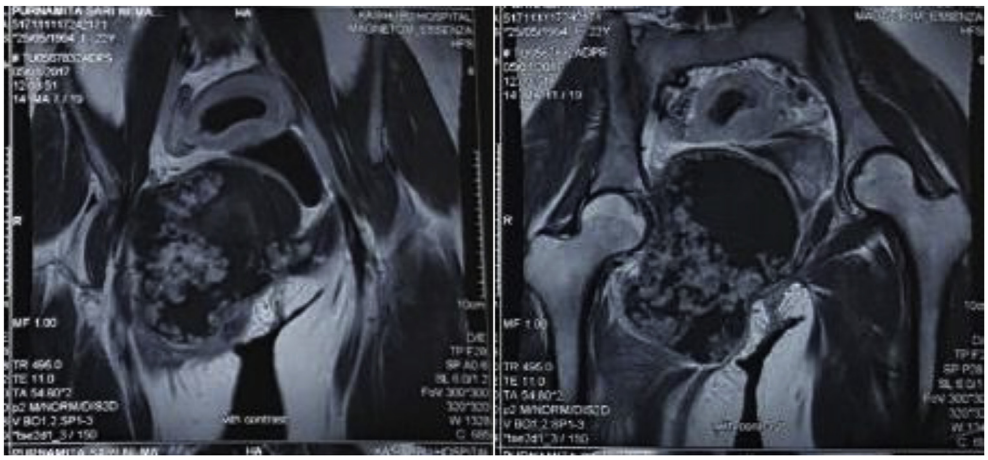

Fig. 3. T2-weighted coronal view of pelvic MRI with contrast at 2 months pre-operative.

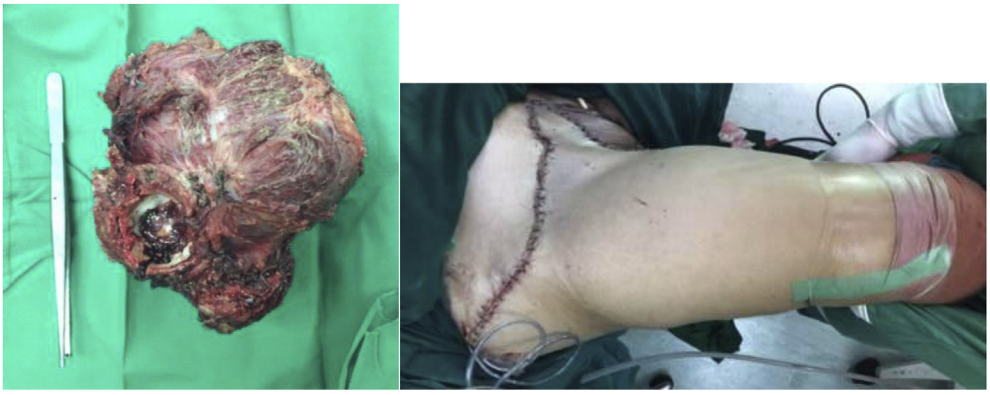

Fig. 4. Gross specimen post-wide excision (left) and post-operative clinical picture (right) showing the extend of excision.

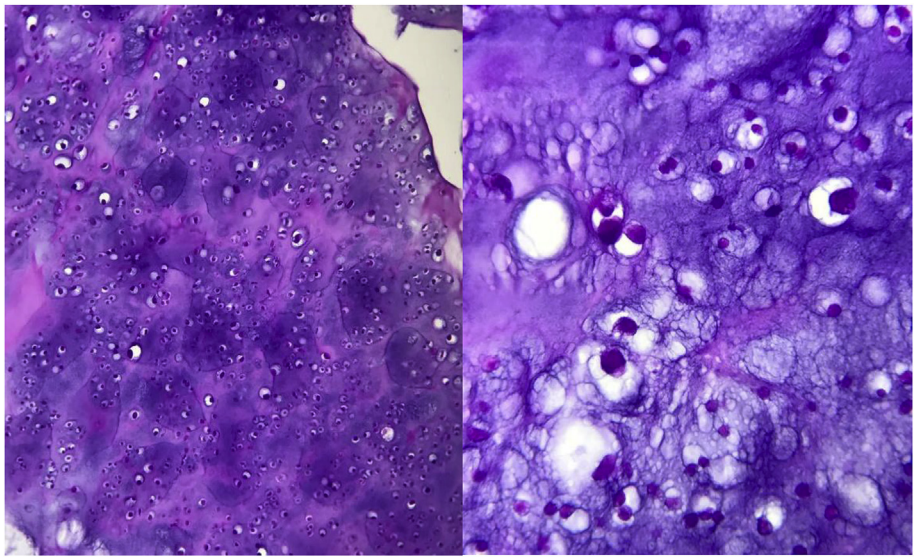

Fig. 5. Atypical chondroblastic cell embedded in chondroid matrix. Binucleus and mitotic figure can also be seen. (H&E, x100, x400).

appendicectomy in pregnancy have reported miscarriage rates of 13.3% and 26% in patients whose operation took place during early pregnancy.[21] One study reported a rate of 7.1% fetal loss, compared with 6.5% in controls who had no surgery, while the systematic review reported an incidence of 5.8% in all patients who underwent a surgical intervention in pregnancy, increased to 10.5% if the surgery occurred in the first trimester.[22] Yet the progression of the chondrosarcoma in this patient deemed the immediate resection of

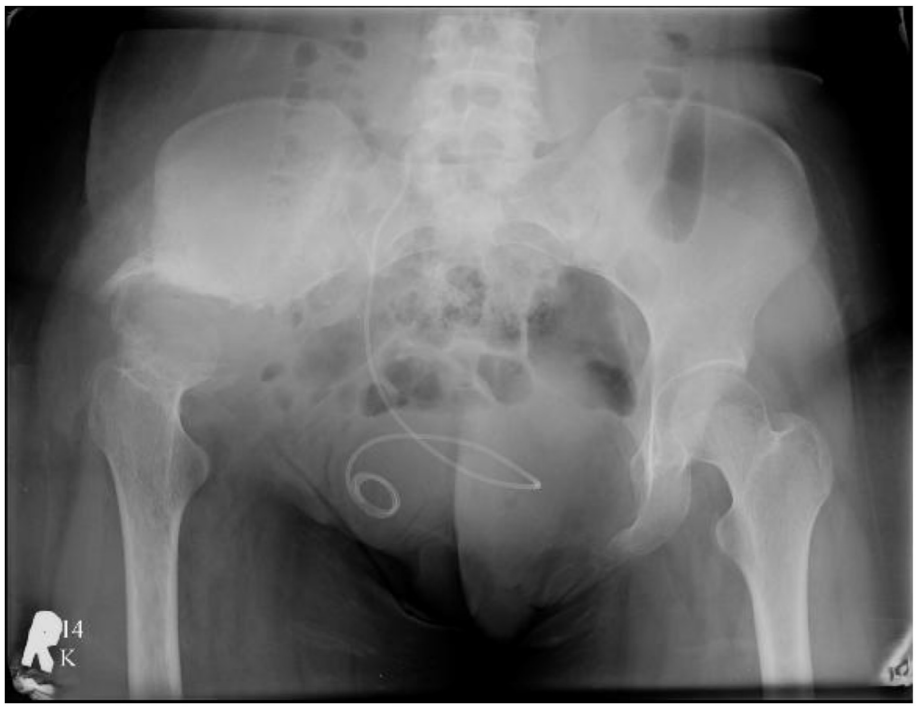

Fig. 6. Post-operative pelvic radiographs showing pseudoarthrosis of right femur and presence of double J stent.

the tumor by using internal hemipelvectomy. This procedure itself is associated with a high incidence of complications, while the high-volume of the tumor was also a distinct risk.[23] Therefore the surgery was done with the consent of high risk of fetal death.

The surgery began with the patient in supine position and using ilioinguinal incision. Double-J Stent was applied to both ureter to make it easier for ureter identification using finger palpation intraoperatively. After deep incision and meticulous hemorrhage control, the tumor was found to be strongly adhered to the bladder and rectum, so that both organ had to be partially excised and primarily sutured. Obturator neurovascular bundle and lumbosacral nerve trunk were meticulously preserved while the myocutaneous flaps are carefully retracted to expose the innominate bone. Origin of the hamstrings, adductors, and gracilis is transected. Osteotomy was done for the whole pubic until the periacetabular region (type II-III internal hemipelvectomy) to achieve 3-cm margin from the tumor, while taking a caution not to injure the sciatic nerve, and also femoral neurovascular bundle. Portion of the iliacus and gluteus medius muscles which lies against the ilium was resected en-bloc with the tumor. The remaining gluteus medius muscle is sutured to the abdominal wall musculature with the ipsilateral lower extremity in abduction. The suture line is also reinforced by oversewing the tensor fasciae lata and sartorius muscles. Wound closure is meticulously done with adequate drainage using vacuum tube is done until production of drain less than 50 ml. Perioperative intravenous antibiotics are continued until the drainage tubes are removed.

The prolonged surgical time, 1500-ml blood loss during surgery, the tumor proximity to the rectum and genitourinary tract, together with large dead space filled with a large amount of foreign material may contribute towards the high risk of infection, particularly after pelvic reconstruction.[9] We were able to manage these problems and a healthy full-term infant was delivered with Caesarean section at 38 week, because some studies have suggested cesarean section to avoid stressing the hemipelvectomy scar. The APGAR score were 8 at 1 minute and 9 at 5 minutes. The birth weight is 2590 g. There was no history of amniotic infection syndrome, nor any hints of circulatory disorders of the placenta and intrauterine hypoxia.

At her 6-month follow up, the Musculoskeletal Tumour Society (MSTS) score for this patient is remarkably good compared to the literature. The mean MSTS score of all survivors was 69.2%, after hemipelvectomy it was 37.6%, after internal hemipelvectomy with endoprosthetic replacement was 61.4%, and after continuity resection was 79.5%.[10] Meanwhile this patient, which undergone a substantial hemipelvectomy, has the MSTS score of 80% (Pain = 5, Function = 3, Emotional = 5, Support = 3, Walking = 4, Gait = 4). This might be due to postpartum contentment for the healthy male baby, and tremendous family support for the patient.

Further planned surveillance for possible recurrence and evolution of adverse effects involves a follow-up history and physical examination. Physical examination, and assessment of adverse effects were done at 6-month intervals for the year after, and at 12-month intervals thereafter.

In conclusion, chondrosarcoma is uncommon in pregnancy, but if it does occur in gestation, it presents a significant challenge to treat. In this case we were able to demonstrate that cautious and thorough planning is important and assist in achieving good functional and oncological outcome.

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Conflicts of interest

All authors have none to declare.

Authors' contributions

The author (I Gede Eka Wiratnaya) cared for the patient;

performed the surgery; and prepared the draft of the manuscript for finalizing this version to be published. The author read and approved the final manuscript.

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Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.jcot.2019.05.026.

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