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## Heterotopic ossification within the gallbladder – First reported Australian case

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### ABSTRACT

**INTRODUCTION:** We report the rare and unusual case of heterotopic ossification within the gallbladder secondary to chronic calculi debris. Presentation of case. A 35-year-old female underwent routine laparoscopic cholecystectomy for recurrent intermittent right upper quadrant pain which had persisted for three months and was worse post prandial with associated nausea. Abdominal ultrasound prior to surgery was reported by a consultant radiologist as demonstrating a thin-walled gallbladder and cholelithiasis, without features of cholecystitis. At four-week review, she had recovered well with no concerns. The histopathology report revealed fibromuscular hyperplasia and patchy chronic inflammation. Rokitansky-Aschoff sinuses were present and cholesterosis was noted. Additionally, there was a focus of eroded mucosa showing adherent microlithiasis with an incidental focus of heterotopic ossification within the mucosa, there was no evidence of dysplasia or malignancy.

**DISCUSSION:** Gallbladder heterotopic ossification is exceedingly rare, with few cases reported. To our knowledge this is the first reported case in Australia.

**CONCLUSION:** In conclusion, we report the rare and unusual finding of heterotopic ossification of the gallbladder, and suspect that inflammation secondary to calculous debris initiated the ossification. Current technical limitations preclude diagnosis prior to surgery. Appropriate follow-up is unclear, but we feel a single report associated the finding with adenocarcinoma was sufficient to warrant follow-up.

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### 1. Presentation of case

A 35-year-old female was referred to our public tertiary hospital general surgery outpatient clinic for assessment of recurrent intermittent right upper quadrant pain which had persisted for three months. It did not radiate elsewhere. The patient reported her pain to be worse after meals and she had associated nausea but had not vomited. She denied fevers or rigors and there were no changes in her urine or faeces.

She had undergone a single anastomosis gastric bypass four months earlier for weight loss. In that time, she had steadily lost 16 kg. Her medical history was migraine for which she took chlorpromazine as required. She never smoked and only rarely drank alcohol. She reported an allergy to penicillin as a child but was unsure of the adverse effect.

COVID restrictions at the time had resulted in most outpatient clinics (including this one) being completed via telephone rather than in-person review, so formal physical examination was impossible. An abdominal ultrasound had been performed prior

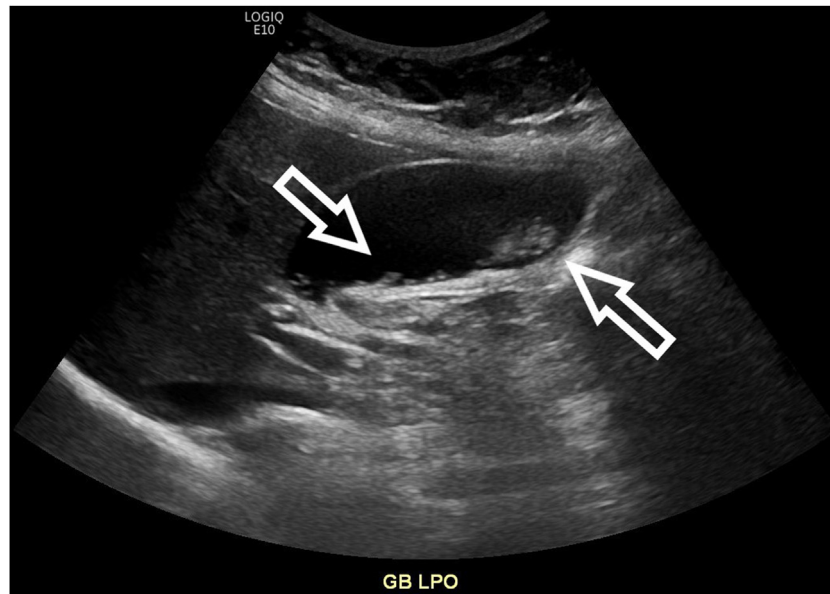
to attending our outpatient clinic and was reported by a consultant radiologist as demonstrating a thin-walled gallbladder and cholelithiasis. There were no features of cholecystitis (Fig. 1). A full blood count and liver function tests were unremarkable. Due to the recurrent nature of her pain and nausea, she was offered a laparoscopic cholecystectomy. The relevant risks and benefits were discussed prior to her giving verbal consent to allow her procedure to be booked. She provided written consent on the morning of her admission.

Dr Laurens, a surgical Registrar performed a routine laparoscopic cholecystectomy under general anaesthesia. Intra-operative findings included minimal omental adhesions to the thin-walled opaque gallbladder and a normal intra-operative cholangiogram (which we perform routinely in our hospital). A sizeable posterior branch of the cystic artery and a presumed duct of Luschka were both dissected and clipped during resection. She recovered well and was discharged the following morning with simple analgesia.

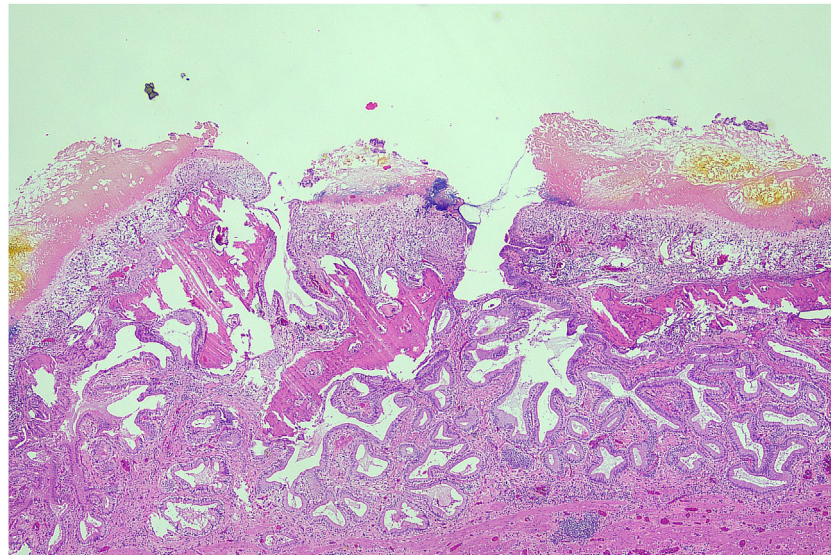
At her routine follow-up appointment four weeks later, she was well with no concerns. The histopathology report described an intact 85 mm × 20 mm gallbladder with maximal wall thickness of 2 mm (after formalin fixation). Macroscopically, the mucosa was described as velvety with yellow flecks and despite the sono-

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**Fig. 1.** Ultrasound. Gallbladder, left posterior oblique positioning. Showing echogenicity reported as cholelithiasis.



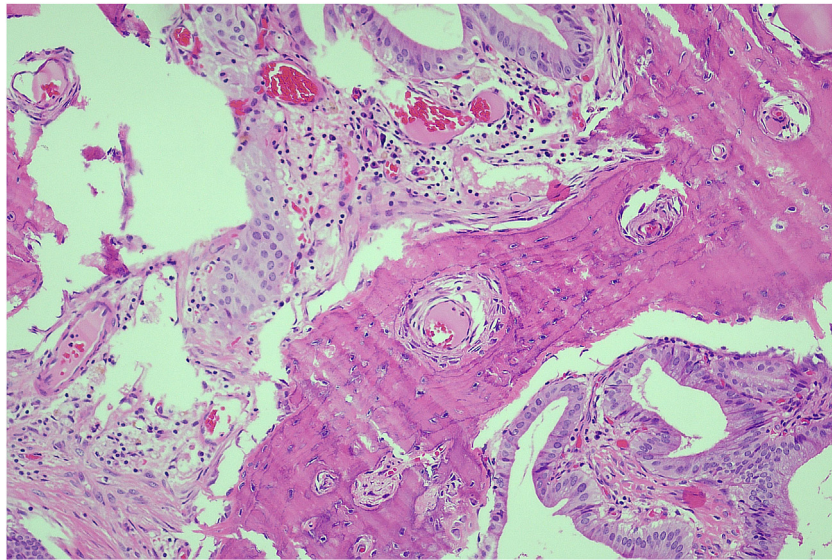
**Fig. 2.** H&E slide 40 $\times$ . There are features of chronic cholecystitis including a lymphocytic infiltrate, fibrosis and thickening of the muscularis. Heterotopic ossification is present in the lamina propria. The surface epithelium is denuded with a bile and stone remnants on the surface.

graphic findings, calculi were not found. Microscopic examination revealed fibromuscular hyperplasia and patchy chronic inflammation. Rokitansky-Aschoff sinuses were present and cholesterosis was noted. Additionally, there was a focus of eroded mucosa showing adherent debris (microlithiasis) with an incidental focus of metaplastic/heterotopic ossification within the mucosa. There was no evidence of dysplasia or malignancy (Figs. 2 and 3).

## 2. Discussion

Both dystrophic calcification and heterotopic bone formation are forms of aberrant tissue repair associated with local or systemic insults including trauma, chronic inflammation, and surgery [1] and genetic mutations such as those causing Fibrodysplasia Ossificans Progressiva [2]. This process can occur at any site in the body but appears uncommon in the gastrointestinal tract [3]. It is even more

rare in the gallbladder, where it was first described by Huggins and Sammet [4]. Since then, few cases of heterotopic ossification within the gallbladder have been reported [5], with histological findings ranging from simple ossification within the mucosa [6] to polypoid cholesterosis [7] and gallbladder adenocarcinoma [8]. Heterotopic ossification may occur in isolation or within dystrophic calcification and is distinguished by lamella architecture, osteocytes, and marrow formation (fatty and/or haematopoietic) [1]. Dystrophic calcification when diffusely distributed is termed 'porcelain gallbladder'. Both dystrophic calcification and heterotopic ossification are strongly correlated with chronic cholecystitis and cholelithiasis [5,9]. Fibrosis and calcification may also occur at the site of neoplasia as a reactive process [10]; importantly, the causal relationship of calcification with malignancy is less clear when selection, sampling and publication bias are considered [9]. The long term sequelae of leaving an ossified gallbladder in situ are unknown due to the rarity of reported cases.



**Fig. 3.** H&E slide 200 $\times$ . Ossification within the lamina propria displays lamellar architecture and osteocytes within lacunae.

### 3. Conclusion

In conclusion, we report the rare finding of heterotopic ossification of the gallbladder and suspect that inflammation secondary to calculous debris initiated the ossification. Current technological limitations preclude reliable identification of heterotopic ossification prior to surgery. Appropriate follow-up of such a case is unclear, but we did not feel a single report associating the finding with adenocarcinoma was sufficient to warrant clinical or radiological follow-up. This case has been reported in line with the SCARE 2018 criteria [11].

### Declaration of Competing Interest

No conflicts of interest.

### Sources of funding

No sources of funding required for this case report.

### Ethical approval

No ethics approval was sought as this is a retrospective de-identified case report.

### Consent

Written informed consent was obtained from the patient for publication of this case report and accompanying images. A copy of the written consent is available for review by the Editor-in-Chief of this journal on request.

### Author contribution

Jason Laurens. Conceptualisation, investigation, writing original draft, writing review and editing.

Adam Frankel. Conceptualisation, supervision, writing review and editing.

Duncan Lambie. Investigation, writing review and editing.

### Registration of research studies

Not applicable.

### Guarantor

Jason Laurens.

### Provenance and peer review

Not commissioned, externally peer reviewed.

### References

- [1] C. Meyers, J. Lisiecki, S. Miller, A. Levin, I. Fayad, C. Ding, T. Sono, E. McCarthy, B. Levi, A.W. James, Heterotopic ossification: a comprehensive review, *JBMR Plus* 3 (4) (2019), e10172.
- [2] E. Shore, F. Kaplan, Role of altered signal transduction in heterotopic ossification and fibrodysplasia ossificans progressive, *Curr. Osteoporos. Rep.* 9 (2) (2011) 83–88.
- [3] S. Haque, R. Eisen, A. West, Heterotopic bone formation in the gastrointestinal tract, *Arch. Pathol. Lab. Med.* 120 (1966) 666–670.
- [4] C. Huggins, J. Sammet, Function of the gall bladder epithelium as an osteogenic stimulus and the physiological differentiation of connective tissue, *J. Exp. Med.* 58 (4) (1933) 393–400.
- [5] J. Ahn, S. Kim, K. Kim, S. Kim, Heterotopic ossification of the gallbladder, *J. Pathol. Transl. Med.* 51 (2) (2017) 185–186.
- [6] J. Indyk, E. Shipton, Heterotopic bone formation in the gall-bladder, *Med. J. Aust.* 44 (1957) 9–11.
- [7] C. Ortiz-Hidalgo, J. Baquera-Heredia, Osseous metaplastic in polypoid cholesterosis, *Am. J. Pathol.* 24 (2000) 895.
- [8] A. Cavazza, L. De Marco, Asioli, L. Pastore, G. Gardini, Stromal osseous metaplasia in metastatic adenocarcinoma of the gall-bladder, *Tumori* 85 (1999) 133–134.
- [9] T. Schnelldorfer, Porcelain gallbladder: a benign process or concern for malignancy? *J. Gastrointest. Surg.* 17 (6) (2013) 1161–1168.
- [10] H.U. Son, F. Borchard, B.S. Joel, Carcinoma of the gallbladder. Autopsy findings in 287 cases and review of the literature, *J. Surg. Oncol.* 28 (1985) 199–206.
- [11] R.A. Agha, T. Franchi, C. Sohrabi, G. Mathew, for the SCARE Group, The SCARE 2020 guideline: updating consensus surgical CAse REport (SCARE) guidelines, *Int. J. Surg.* 84 (2020) 226–230.

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