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Case Report

Heterotopic Mesenteric Ossification After a Ruptured Abdominal Aortic Aneurism: Case Report With a Review of Literatures

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Heterotopic mesenteric ossification (HMO) is a rare disease that results in intra-abdominal ossification of unknown origin. An 88-year-old man developed an intestinal obstruction 2 weeks after undergoing an operation for a ruptured abdominal aortic aneurysm, resulting in intestinal obstructions those did not improved concervatively. During relaparotomy performed 30 days after the first operation, hard adhesions of the small intestine and mesentery were found; these adhesions were difficult to separate without damaging the serosa of the small intestine. We removed 240cm of the small intestine and performed a jejuno-ileo anastomosis. Microscopically, trabecular bone tissue had increased irregularly in the fat tissue of the nodules with fibrosis, which were partially lined with osteoblasts. Accordingly, we histopathologically diagnosed the patient as having HMO. The patient was treated with NSAIDs and cimetidine to prevent the recurrence of HMO. No signs of recurrence have occurred as of one year after the second operation.

Key words: Heterotopic mesenteric ossification – Ileus – Obstruction – Small bowel – Aortic aneurysm

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Heterotopic mesenteric ossification (HMO) is a rare disease resulting in intra-abdominal bone formation of unknown origin that can lead to serious complications, such as intestinal obstruction, enterocutaneous fistulation, intestinal perforation, sepsis, or even death. These complications may require surgical therapy. Here, we report an extreme, rare case of HMO that occurred after an operation for a ruptured abdominal aortic aneurysm (AAA), with a review of the literature.

Case Presentation

An 88-year-old man was admitted to our hospital because of abdominal bloating and a consciousness disorder. His past medical history included hypertension and benign prostatic hypertrophy. An AAA had been recognized in 2008, and his primary physician had followed up on his condition. A computed tomography (CT) scan had demonstrated the rupture of the AAA, which measured 77 × 83 mm in diameter, and the patient had undergone an abdominal aortic repair. The histopathology of the excised abdominal aortic wall had shown an inflammatory aneurysm of the abdominal aorta.

Two weeks after the operation, he complained of severe constipation and was diagnosed as having an intestinal obstruction. An ileus tube was inserted into the jejunum, and conservative therapy was initiated. An abdominal X-ray showed a distended jejunum with abnormal intestinal gases. About 70 to 400 mL of intestinal fluid was collected daily. A CT scan showed the dilation of the small bowel, but no other abnormality was observed (Fig. 1). Because his clinical symptoms did not improve, the patient underwent a second operation 30 days after the initial operation. During the second operation, severe fibrosis and adhesions were seen at the small intestine, especially at between 30 cm from the Treitz ligament and 120 cm from the terminal ileum. The mesenterium of the small intestine and the transverse colon also had severe adhesions, and small nodules of calcification were palpable in some areas. Consequently, the small bowel was tortuous and obstructed at many locations. As the adhesions could not be easily separated, we removed 240 cm of the small intestine and performed a jejuno-ileal anastomosis. After the resection, the remnant small bowel was about 120 cm in length.

The macroscopic findings of the resected specimen showed severe adhesions of the serosa of the small intestine. The caliber inside the small intestine was narrowed or obstructed. Hard nodules were palpated in some areas, but mainly at the sites of severe adhesion. No abnormal changes in the surface mucosa of the resected specimen were noted. Microscopically, trabecular bone tissue had increased irregularly in the fat tissue of the nodules with fibrosis, which were partially lined with osteoblasts (Fig. 2). Accordingly, two weeks after the second operation, we histopathologically diagnosed the patient as having HMO, at which point the patient was treated with nonsteroidal anti-inflammatory drugs (NSAIDs) and cimetidine to prevent the recurrence of the intestinal obstructions. No symptoms of intestinal obstruction were evident a year after the second operation.

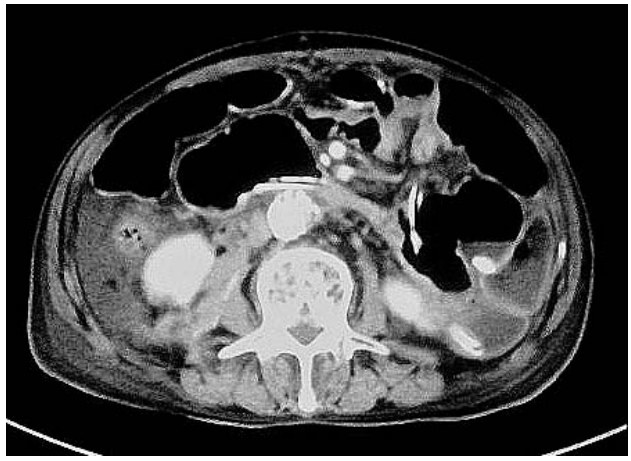

Fig. 1 A CT scan showed the dilation of the small bowel. Intra-abdominal ossifications could not be detected. No other abnormal sign was observed.

Discussion

HMO is a rare disease resulting in intra-abdominal ossifications that can lead to severe complications. HMO was first reported by Hansen *et al*[1] and Lemeshev *et al*[2] in 1983. Wilson *et al*[3] concluded that HMO is an exuberant reaction to trauma in a predisposed individual. To date, only 33 cases have been reported, based on a review of the world literature (Pub Med). All these previous cases, together with the present case, are summarized in Table 1. Thirty-one of the 33 cases occurred in men. The mean patient age at the time of development of HMO was 53.1 years (range, 21–80). The presently reported case represents the oldest patient with HMO to date. HMO has caused intestinal obstructions (21 cases, 63.6%); abdominal mass formation (3

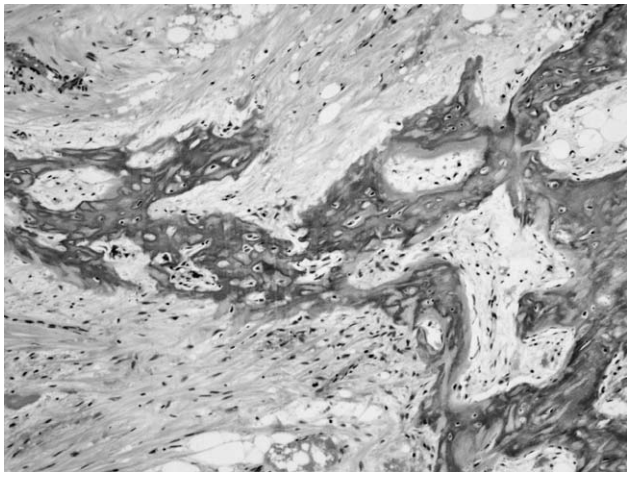

Fig. 2 Microscopic findings (hematoxylin-eosin stains, ×100). Trabecular bone tissue had increased irregularly in the fat tissue of the nodules with fibrosis, which were partially lined with osteobla.

cases, 9.1%); fistula formation (4 cases, 12.1%); and intra-abdominal inflammations such as cholelithiasis, pancreatitis, and peritonitis (2 cases, 6.1%). Surgical therapy is usually required in order to cure it. The clinical symptoms usually appear 2 or 3 weeks after abdominal trauma or surgery (range, 4 days to 2 years). The present case is the third case to occur following an operation for AAA. Ossification occurs mainly in the mesentery (28 cases, 84.8%). Some cases occurring in the omentum have been reported (7 cases, 21.2%). The intra-abdominal ossifications were detected using a CT scan in 10 cases.[4–12] Additional therapy to prevent HMO after the histological HMO diagnosis was performed in 4 cases.[6–8,13] In two cases, the patient was administrated NSAIDs; in others, cimetidine.[7,13]

A preoperative diagnosis is often difficult. In some cases, the ossifications were detected by the CT scan.[4–12,14] In the present case, intra-abdominal ossifications could not be detected using a CT scan preoperatively because the ossifications were too small. FDG PET-CT and Tc-99m bone SPECT are considered to be useful for identifying intra-abdominal ossifications.[8,15] However, in general, these examinations are not routinely performed for patients suffering from intestinal obstruction. These examinations should be performed in cases with intestinal obstruction in which HMO is being considered as a possible cause.

Some laboratory abnormalities have been reported. Some reports have suggested that an elevation in alkaline phosphatase (ALP) may reflect the activity of osteoblasts and heterotopic bone formation.[16–18] In cases with high ALP levels, Tc-99m bone SPECT can detect ossifications earlier than abdominal X-ray examinations.[15] High carbohydrase antigen-125 values have also been reported in patients with HMO, but the significance of this finding is unknown.[7,18] The preoperative laboratory data did not show any specific abnormalities in the present case. Postoperative laboratory data showed a continuously high C-reactive protein level and an elevation in serum parathyroid hormone (PTH) activity. However, our patient did not have any symptoms of hyperparathyroidism.

The histopathological features consist of mature lamellar bone formation with hypercellular fibrous connective tissue. Trabeculae of osteoid material are rimmed by a layer of active osteoblasts separated by fibrous septa. Spindle-shaped cells form fascicles and exhibit a morphology resembling that of activated fibroblasts, but without neoplastic cytologic features. This manifestation is called *zone phenomena*. HMO can be distinguished from malignant diseases that result in ossification in the extraskeletal soft tissues, such as osteosarcoma, based on the presence of mature trabeculae, the grade of nuclear polymorphism, the level of cellularity, and the number of mitoses, as well as the recognition of it being a reactive process.[3,4]

Various theories about heterotopic bone formation have have been supported in the literature. External irritation factors such as trauma and operation may have a strong relation. The symptoms of HMO are shown after a laparotomy or abdominal injury in 16 cases.[1,3,4,6,7,9–11,13,19–22] In 3 cases reported, heterotopic bone formation was observed along an abdominal midline incision, which was thought to have led to the HMO.[2,7,10] However, this hypothesis may be incorrect, as 7 cases reported had not experienced an operation or abdominal injury prior to developing HMO.[3,5,8,18,23] Ebrahim *et al*[24] reported a case of heterotopic bone formation in a burn patient and mentioned that the ingestion of more than 150 g of protein per day facilitated the heterotopic calcification. In recent years, HMO has been considered a reactive process to various stimuli, such as trauma, surgical invasion, ischemia, and inflammation; in this reactive process, immature pluripotent mesenchymal cells differentiate to osteoblasts or chondroblasts, resulting in heterotopic bone formation.[8,10,11,25,26]

Table 1 Summary of the previously reported cases of HMO

Article number (year)	Age	Sex	Primary disease/operation	Onset	Clinical history	CT	Site	Primary therapy	Additional therapy
1 (1983)	55	Male	Coloprotectomy	2 wk	SBO	−	M	OP	ND
2 (1983)	44	Male	SBO	12 d/24 d/2 wk	SBO/SBO/fistula	−	M/IS	OP	ND
29 (1989)	57	Male	ND	-	SBO	−	M	OP	ND
3 (1999)	75	Male	AAA	10 d	SBO	−	M	OP	ND
	76	Male	Sigmoid colon cancer, AAA	11 d	SBO	−	M	OP	ND
	43	Male	None	-	SBO	−	M	OP	ND
	80	Male	None	-	Cholelithiasis, pancreatitis	−	M	OP	ND
	43	Male	Incarcerated umbilical hernia	7 d/14 d	SBO/SBO	−	M	OP/OP	ND
19 (2000)	25	Male	Fire-gun injury	2 wk	SBO	−	M	OP	ND
4 (2001)	50	Male	Trauma	1 y	Fistula	+	M	OP	ND
22 (2002)	36	Female	Right ovary teratoma	-	Discomfort of abdomen	−	O	OP	ND
23 (2004)	64	Male	None	-	SBO	−	M	OP	ND
	76	Female	None	-	Abdominal mass	−	M	OP	ND
5 (2004)	70	Male	None	-	Right flank pain	+	M	OP	ND
18 (2004)	76	Male	None	-	SBO	−	M	OP	ND
7 (2005)	74	Male	Umbilical hernia, Cholecystectomy, prostatectomy	4 d/10 d	SBO, renal failure	−	M, O	OP	ND
30(2006)	51	Male	ND	-	SBO	−	M, O	OP	ND
	21	Male	ND	-	Peritonitis	−	O	OP	ND
	65	Male	ND	-	SBO	−	M	OP	ND
	62	Male	ND	-	SBO	−	M	OP	ND
	22	Male	ND	-	SBO	−	M	OP	ND
	72	Male	ND	-	SBO	−	M	OP	ND
6 (2006)	25	Male	Trauma	7 d/14 d	SBO	+	M	OP/OP	Observation
7 (2007)	60	Male	Diverticulosis of colon	1 mo	Stenosis of ileum stoma	+	M, IS	OP	NSAIDs
25 (2008)	42	Male	Watermelon stomach	-	Septic fever	−	O	OP	ND
8 (2008)	69	Male	None	-	Abdominal mass	+	M	OP	Observation
9 (2008)	51	Male	Gun shot injury	3 mo	Abdominal mass	+	RP	OP	ND
13 (2009)	40	Male	Trauma	ND	SBO	−	M	OP	NSAIDs, Cimetidine
10 (2009)	40	Male	Ventral hernia after traffic injury	2 y	Incisional hernia, SBO	+	M, IS	OP	ND
11 (2010)	50	Male	Gastric bypass, cholecystectomy	12 d	Fistula	+	M, O	OP	ND
	42	Male	Gastric bypass	ND	Fistula	+	M	OP	ND
12 (2011)	56	Male	SBO	3 wk	SBO	+	M	OP	ND
20 (2011)	39	Male	Descending colon cancer	2 wk	SBO	−	O	OP	ND
Our case	88	Male	AAA	2 wk	SBO	+	M	OP	NSAIDs, Cimetidine

AAA, abdominal aortic aneurysm; CT, the diagnosis of ossification by CT scan; IS, incision site; M, mesentery; ND, not described; NSAIDs, nonsteroidal anti-inflammatory drugs; O, omentum; OP, operation; RP, retroperitoneum; SBO, small bowel obstruction.

HMO can recur, but additional therapy to prevent recurrence is controversial, as no obvious evidence proving the effectiveness of such therapies exists. According to previous reports, NSAIDs, cimetidine, diphosphonates, and prophylactic radiation therapy have been recommended for the prevention of HMO recurrence in symptomatic patients.[7,11,13,16,18,23,27,28] We found only 4 reports describing the use of additional therapy.[6–8,13] Two authors followed up with conservative observation if no symptoms of recurrence were present.[6,8] Lai *et al*[7] used NSAIDs as an additional therapy after surgery, while Hayashi *et al*[13] used NSAIDs and cimetidine. However, each method has both advantages and disadvantages. NSAIDs suppress inflammation but are associated with a risk of gastric or duodenal ulcers and perforations. Cimetidine was reportedly effective in cases of hyperparathyroidism to normalize the serum PTH and calcium levels and to prevent heterotopic ossification.[13] Diphosphonates are contraindicated in cases involving vitamin D deficiency after an intestinal or gastric bypass operation, because of the malabsorption of calcium. Radiation causes intestinal wall fibrosis and ischemia, possibly leading to ulceration and anastomotic leakage.[11] Recently, new methods with fewer side effects and greater therapeutic values have been investigated. Baird and Kang *et al*[28] reported the use of three therapies: noggin (a bone morphogenetic protein inhibitor), pulsed electromagnetic fields, and free radical scavengers in the form of allopurinol and N-acetylcysteine. These therapies are expected to have fewer side effects and better control of heterotopic bone formation and should be evaluated as alternative methods. We used NSAIDs and cimetidine in the present case because our patient showed a continuous elevation of C-reactive protein, suggesting an ongoing inflammatory reaction, and although the patient was asymptomatic, his serum intact PTH level was high. At this writing, 1 year and 7 months after the second operation, no signs of recurrence have been noted. We need more long-term follow up to confirm the preventive effect of NSAIDs and cimetidine against HMO.

In summary, we reported a rare case of HMO that developed after an operation for a ruptured AAA. It seems difficult to draw a conclusive therapeutic strategy for HMO based on this case report. However, since there have not been enough sufficient collective data regarding HMO, we believe that the literature review in this paper will help to provide useful information about clinical features and optimal therapy for this rare disease.

References

1. Hansen O, Sim F, Marton PF, Gruner OP. Heteritipic ossification of the intestinal mesentery. Report of a case following intraabdominal surgery. *Pathol Res Pract* 1983;**176**(2–4):125–130
2. Lemeshev Y, Lahr CJ, Denton J, Kent SP, Diethelm AG. Heterotopic bone formation associated with intestinal obstruction and small bowel resection. *Ala J Med Sci* 1983;**20**(3): 314–317
3. Wilson JD, Montague CJ, Salcuni P, Bordi C, Rosai J. Heterotopic mesenteric ossification (intraabdominal myositis ossificans): report of five cases. *Am J Surg Pathol* 1999;**23**(12): 1464–1470
4. Hakim M, McCarthy EF. Heterotopic mesenteric ossification. *Am J Roentgenol* 2001;**176**(1):260–261
5. Bosker RJ, Eddes EH. A mesenteric lymphangioma showing calcification and ossification. *Dig Surg* 2004;**21**(3):182–183
6. Gouello JP, Auvray L, Bouix A, Vazelle F, Guinard N, Hermes D. Early post-traumatic heterotopic mesenteric ossification: report of a case. *Intensive Care Med* 2006;**32**(6):950–951
7. Lai HJ, Jao SW, Lee TY, Ou JJ, Kang JC. Heterotopic mesenteric ossification after total colectomy for bleeding diverticulosis of the colon—a rare case report. *J Formos Med Assoc* 2007; **106**(2)(suppl):s32–s36
8. Deryk S, Goethals L, Vanhove C, Geers C, Vandenbroucke F, VanHove K. Imaging characteristics of heterotopic mesenteric ossification on FDG PET and Tc-99m Bone SPECT. *Clin Nucl Med* 2008;**33**(7):496–499
9. Como JJ, Yowler CJ, Malangoni MA. Extensive heterotopic mesenteric ossification after penetrating abdominal trauma. *J Trauma* 2008;**65**(6):1567
10. Morrison JE, Brizendine JB, Yost MJ, Fann SA. Massive ventral hernia with extensive heterotopic ossification: the honeycomb-abdomen. *J Trauma* 2009;**66**(4):1234–1237
11. Yushuva A, Nagda P, Suzuki K, Llaguna OH, Avgerinos D, Goodman E. Heterotopic mesenteric ossification following gastric bypass surgery: case series and review of literature. *Obes Surg* 2010;**20**(9):1312–1315
12. Hashash JG, Zakhary L, Aoun EG, Refaat M. Heterotopic mesenteric ossification. *Colorectal Dis* 2012;**14**(1):e29–e30
13. Hayashi Y, Takamura H, Nakamura Y, Fujita H, Ninomiya I, Nishimura M. A case of heterotopic mesenteric ossification after multiple pelvic bone fracture. *Jpn J Gastroenterol Surg* 2009;**42**(10):1621–1625
14. Shepherd TM, Idakoji IA, Pampalori MH. Incidental detection of gastrointestinal stromal tumor by Tc-99m MDP bone scan. *Clin Nucl Med* 2012;**37**(2):198–199
15. Jacobs JE, Birnbaum BA, Siegelman ES. Heterotopic ossification of midline abdominal incisions: CT and MR imaging findings. *Am J Roentgenol* 1996;**166**(3):579–584
16. Haas ML, Kennedy AS, Copeland CC, Ames JW, Scarboro M, Slawson RG. Utility of radiation in the prevention of

heterotopic ossification following repair of traumatic acetabular fracture. *Int J Radiat Oncol Biol Phys* 1999;**45**(2):461–466
17. Burtis WJ, Lang R. Chemical abnormalities. *Orthop Clin North Am* 1984;**15**(4):653–669
18. Bovo G, Romano F, Perego E, Franciosi C, Buffa R, Uggeri F. Heterotopic mesenteric ossification ("intraabdominal myositis ossificans"): a case report. *Int J Surg Pathol* 2004;**12**(4):407–409
19. Marucci G, Spitale LS, Piccinni DJ. Heterotopic mesenteric ossification. A case report. *Pathologica* 2000;**92**(5):331–334
20. Shi X, Zhang W, Nabieu PF, Zhao W, Fu C. Early postoperative heterotopic omental ossification: report of a case. *Surg Today* 2011;**41**(1):137–140
21. Androulaki A, Chatzoulis G, Kalahanis N, Lazaris AC. Heterotopic mesenteric ossification: a rare reactive process. *J Gastroenterol Hepatol* 2005;**20**(4):664–666
22. Bhardwaj S, Bal A, Mohan H. Heterotopic omental ossification in response to spilled contents of a mature cystic teratoma: an unusual reaction. *Histopathology* 2002;**41**(6):561
23. Comperat E, DeSaint-Maur PP, Kharsa G, Flejou JF. Ossification heterotopique du mesentere: une cause rare d'occclusion post-operatoire. *Gastroenterol Clin Biol* 2004;**28**(2):188–189
24. Ebrahim MK, Kanjoor JR, Bang RL. Heterotopic calcification in burn scars and non-healing ulcers. *Burns* 2003;**29**(5):461–468
25. Vlachos K, Archontovasilis F, Karameris A, Tsiambas E, Lagoudiannakis E, Manouras A. Heterotopic mesenteric ossification after gastrectomy for watermelon stomach. *J Gastrointestin Liver Dis* 2009;**18**(2):229–231
26. Cohly HH, Buckley RC, Pecunia R, Das SK. Heterotopic bone formation: presentation of an experimental rat model and a clinical case. *Biomed Sci Instrum* 2003;**39**:446–453
27. Chantraine A, Minaire P. Para-osteo-arthropathies. A new theory and mode of treatment. *Scand J Rehabil Med* 1981;**13**(1): 31–37
28. Baird EO, Kang QK. Prophylaxis of heterotopic ossification—an updated review. *J Orthop Surg Res* 2009;**4**:12
29. Myers MA, Minton JP. Heterotopic ossification within the small-bowel mesentery. *Arch Surg* 1989;**124**(8):982–983
30. Patel RM, Weiss SW, Folpe AL. Heterotopic mesenteric ossification: a distinctive pseudosarcoma commonly associated with intestinal obstruction. *Am J Surg Pathol* 2006;**30**(1):119–122