Rare disease

Hibernoma with metabolic impact?

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Summary

A hibernoma is a benign tumour of brown adipose tissue (BAT). BAT is also present in physiological depots, previously considered residual. However, in 2009 functional BAT in adults was reported. Metabolically active BAT is suggested to significantly influence the energy balance and increasing BAT activity could possibly treat obesity. This strongly increased the interest in BAT in man and currently more research is conducted. We describe the case of an intramuscular hibernoma and illustrate the pathophysiology of the observed hibernoma in relation to recent insights on physiological BAT. Immunofluorescence staining of the hibernoma showed the presence of uncoupling-protein-1, a protein specific for active BAT. This suggests that this hibernoma contains BAT that could possibly contribute to the human energy balance.

BACKGROUND

Brown adipose tissue (BAT) is currently a worldwide-recognised target to combat obesity and diabetes due to the (re)-discovery of functional BAT in adult humans.¹ Since then the scientific interest in the physiology of BAT increased rapidly. Here we report our recent observation of a rare hibernoma and place this clinical case presentation in the light of the recent developments in BAT physiology. We think this pathophysiological observation, in perspective of the recent uprise of knowledge in the physiology of BAT, is very appropriate as a case report.

CASE PRESENTATION

We present the case of a 55-year-old man who underwent a CT scan of the abdomen for upper abdominal complaints. The patient's medical history consisted of a Nissen fundoplication for gastro-oesophageal reflux disease, dyslipidaemia and depression. The family history was negative for malignancies. The patient used paroxetine 30 mg and simvastatin 40 mg, both once per day. Patient's weight was

105 kg, length 186 cm and body mass index 30.4 kg/m², blood pressure was 140/95 mm Hg and pulse 68 beats/min.

INVESTIGATIONS

The CT scan revealed no abdominal abnormalities, but the left gluteus maximus muscle contained a mass reported as a lipoma by the radiologist. Following the Dutch oncology guideline for soft-tissue tumours (www.oncoline.nl/wekdelentumoren (in Dutch)), additional MRI was carried out for local tumour staging. This confirmed the presence of an intramuscular mass of approximately 11×7×5 cm with an inhomogeneous signal intensity and central vascularisation (figure 1). Injection of intravascular gadolinium contrast showed dispersed uptake within the tumour, which is suggestive of a significant blood supply (figure 1). This is uncommon for classical benign lipomatous masses. After consideration of the case in the multidisciplinary oncology committee it was decided to take an ultrasound-guided biopsy of the lesion. The biopsy showed both univacuolar and multivacuolar adipocytes, characterised as white adipose tissue (WAT)

Figure 1 MRI of intramuscular hibernoma. (A) Coronal MRI survey image showing the presence of an intramuscular mass with lipomatous intensity. (B) Transversal T1-weighted MRI showing a well-defined mass with a slightly hypo-intense signal compared to the subcutaneous adipose tissue. (C) Coronal T1-weighted image with fat suppression (SPIR; self-consistent parallel imaging reconstruction) and gadolinium contrast, showing a central vessel and irregular aspect of tumour.

and BAT, respectively. Since hibernomas are benign and the patient did not experience any discomfort, the patient was treated conservatively. Ten months later, the patient presented with complaints of discomfort from the gluteal mass during his occupation as a railroad engineer. To define growth of the mass MRI was repeated. The mass had not increased in size, but because of the patient's discomfort the tumour was resected.

OUTCOME AND FOLLOW-UP

Resection revealed a lipomatous mass of 17×9×5 cm (figure 2). H&E-stained slides showed the clear presence of brown adipocytes (figure 3). Additional immunofluorescence staining for the BAT-specific uncoupling-protein-1 (UCP-1) was positive, confirming the presence of stimulative BAT (figure 3).

DISCUSSION

Hibernomas comprise 1.6% of benign lipomatous masses and are reported in different anatomic locations throughout the body. After extensive study of 170 cases, Furlong *et al*² concluded that the most common site is the thigh (55/170; 32% of cases).

Active BAT expresses UCP-1, the BAT-specific mitochondrial membrane protein that facilitates thermogenesis. Immunofluorescence for UCP-1 has been used to show that active BAT on FDG-PET-CT-imaging was indeed present in these depots.¹ The resected hibernoma in this case showed a clear and large amount of UCP-1 on immunofluorescence, resembling active physiological BAT.¹ Whether the BAT of the resected hibernoma was

active in this case is not known, since we were not able to perform FDG-PET-CT-imaging during cold exposure. Nonetheless, a PET-CT-positive hibernoma has been reported before,³ suggesting this is indeed possible. A functional hibernoma could significantly influence energy metabolism. It is suggested that 100 g of functional BAT can increase the basal metabolic rate by 5% or more.⁴

Figure 2 Hibernoma after resection. Formalin-fixed resected preparation of 17×9×5 cm³. The black-and-white bar displayed left indicates 1-cm sections.

Figure 3 (A) Formalin-fixed 4 µm H&E (×10)-stained slides show the clear presence of multivacuolar brown adipocytes, located adjacent to univacuolar white adipocytes. (B) HE slides in comparable magnification (×20) with slides of hibernoma with positive immunofluorescence staining for uncoupling-protein-1 (UCP-1) ((C), 5 µm, ×20). UCP-1 is stained green, nuclei are stained with 4',6-diamidino-2-phenylindole (blue) and laminin is used for cell membranes (red). BAT, brown adipose tissue; WAT, white adipose tissue.

In conclusion, we report an intramuscular hibernoma containing BAT comparable to the recently discovered functional BAT in other anatomical locations. The positive UCP-1-immunofluorescence staining in the hibernoma shows active BAT was present and could have had a role in the patient's energy balance. Future studies are needed to estimate this contribution by application of methods used in recent studies on the physiology of functional BAT.

Learning points

- ▶ Hibernomas are rare and comprise 1.6% of benign lipomatous masses.
- ▶ The most common site of a hibernoma is the thigh.
- ▶ A hibernoma contains brown adipose tissue (BAT), comparable to the recently discovered functional BAT in other anatomical locations.
- ▶ If activated, BAT in a hibernoma could possibly have a role in the body's energy balance.

Competing interests None.

Patient consent Obtained.

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