

1           **Localisation of an occult thyrotropinoma with <sup>11</sup>C-Methionine PET-CT before and after**  
2   **somatostatin analogue therapy**

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18   **Abbreviated title:** Detection of occult TSHoma with <sup>11</sup>C-Methionine PET

19   **Key words:** <sup>11</sup>C-Methionine PET, pituitary, TSHoma

20   **Word Count:** text 298; figure 1.

21 A 75-year-old woman presented with tiredness, palpitations and enlargement of a longstanding  
22 goitre. Unexpectedly, thyrotropin (TSH) was not suppressed [6.3 mU/L; reference range (RR) 0.35–  
23 5.5] despite markedly raised thyroid hormones [free thyroxine (FT4) 89.1 pmol/L (RR 10–19.8); free  
24 triiodothyronine (FT3) 11.7 pmol/L (RR 3.0–6.5)]. Following exclusion of laboratory assay  
25 interference, a thyrotropin-releasing hormone (TRH) test showed an attenuated response (TSH 0  
26 minutes 6.1 mU/L, 20 minutes 6.8 mU/L, 60 minutes 8.5 mU/L), raising suspicion of a  
27 thyrotropinoma (TSHoma). However, pituitary MRI was reported as normal. The patient was  
28 referred for further evaluation. On repeat MRI the pituitary gland was noted to show mild  
29 asymmetry (right>left) (figure A). Functional imaging with <sup>11</sup>C-Methionine PET-CT (Met-PET)  
30 demonstrated intense tracer uptake (denoting active peptide synthesis) on the right side of the sella  
31 (figure A – red ‘hot spot’). Treatment with depot somatostatin analogue (SSA) led to resolution of  
32 symptoms and normalization of thyroid function (TSH 0.6 mU/L, FT4 12.5 pmol/L, FT3 3.8 pmol/L).  
33 Repeat Met-PET showed absence of the right-sided focal ‘hot spot’ (figure B). Fourteen months into  
34 treatment, the patient developed hypoglycaemic episodes, which resolved following discontinuation  
35 of SSA. However, thyrotoxicosis recurred (TSH 4.3 mU/L, FT4 38.1 pmol/L, FT3 11.6 pmol/L), and  
36 repeat Met-PET revealed reappearance of the right-sided ‘hot spot’ (figure C). At pituitary surgery a  
37 micro-TSHoma was resected from the right side of the gland (figure D). The patient remains in  
38 clinical and biochemical remission 14 months post-surgery and is eupituitary.

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40 To our knowledge, this is the first example of a microTSHoma being unmasked by functional imaging  
41 before and after endocrine manipulation (in this case SSA therapy). As MRI does not reliably detect  
42 all pituitary microadenomas (e.g. Cushing’s; microprolactinoma), we believe this novel ‘endocrine  
43 switch’ approach could find wider application in the management of such occult tumours.

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47 **Contributors**

48 OK, PE and MG collected the data. All authors contributed to the writing of the report. OK, AH and  
49 MG performed the image analysis. NA and HC interpreted the imaging studies. KA reviewed the  
50 histopathology. ND & RJM performed the surgical procedure.

51 The patient gave her written informed consent for publication of this case report.

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53 **Declaration of interest**

54 OK and MG are supported by an unconditional award from Ipsen Ltd.

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56 **Figure legend**

57 **Figure: Imaging and histopathological findings**

58 **(A)** SE (Spin Echo) MRI (top panel) and <sup>11</sup>C-methionine PET-CT co-registered with SPGR (Spoiled  
59 Gradient Recalled Acquisition) MRI (bottom panel) at presentation. Repeat imaging **(B)** during, and  
60 **(C)** following discontinuation of, SSA therapy. **(D)** Microscopic appearance (top panel) and positive  
61 TSH immunohistochemistry (bottom panel) of resected adenoma.

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