An Unusual Cause of Confusion
Hepatic Encephalopathy in Hereditary Haemorrhagic Telangectasia

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ABSTRACT

This case report describes a 73 year old lady with a known Hereditary Haemorrhagic Encephalopathy (HHT) who presented with confusion. She had several previous self-limiting episodes over 3 months. She had known hepatic arterio-venous (AV) malformations. A urinary tract infection was detected and thought to be the cause of her confusion. However despite targeted antibiotic treatment her neurological state worsened (GCS 10/15) and she developed hepatic asterixis. Hepatic encephalopathy was confirmed with diagnostic EEG and elevated ammonia 211umol/l (<40). Laxative treatment had transient improvement but she was unsuitable for hepatic AV embolisation or liver transplantation. Hepatic encephalopathy is a rare complication of HHT with less than 10 previous documented cases.

Key words: *Confusion, hereditary haemorrhagic telangectasia, hepatic encephalopathy*

Konfüzyonun Nadir Bir Nedeni: ***Herediter Hemorajik Telenjiektazide hepatik Ensefalopati***

ÖZET

Bu olgu sunumunda konfüzyon nedeni ile başvuran herediter hemorajik ensefalopatili 73 yaşında yaşlı bir kadın sunulmuştur. Daha önceden 3 ay süren kendi kendine sınırlanan atakları vardı. Hastanın bilinen hepatik arterio-venöz malformasyonları vardı. Konfüzyon nedeni olarak idrar yolu enfeksiyonu düşünüldü. Antibiyotik tedavisine rağmen GCS kötüleşti ve hepatik asteriksis gelişti. Hepatik ensefalopati EEG ile tespit edildi ve amonyak düzeyi yüksekti (211umol/L). Laksatif tedavisi geçici düzelme sağladı, fakat hasta AV embolizasyon ve transplantasyon için uygun değildi. Hepatik ensefalopati herediter hemorajik ensefalopatinin nadir bir komplikasyonudur.

Anahtar kelimeler: *Konfüzyon, herediter hemorajik telenjiektazi, hepatik ensefalopati*

INTRODUCTION

Confusion is a very common non-specific disease in the elderly, often wrongly attributed to urinary tract infection. Delirium can have serious consequences in terms of long-term cognitive change, higher mortality and morbidity, and increased length of hospital-stay (1). It is important to find the cause of confusion as it can be reversible. Common causes include infection, electrolyte imbalance and medications. However, there are other causes which are less common and here we present the case of a 73 year old lady with a more unusual cause for her confusion.

CASE

We describe a case of a 73 year old lady with known Hereditary Haemorrhagic Telangiectasia (HHT) presenting to the medical admissions unit with an acute confusional state. HHT had been diagnosed 45 years previously. She was transfusion dependent secondary to chronic blood loss from gastric telangiectasia. She had ongoing history of a persistent right pleural effusion as a consequence of high out-put cardiac failure resulting from a large number of hepatic arterio-venous shunts, demonstrated by CT 6 months prior (Figure 1,2).

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Received: 21.06.2011, Accepted: 29.06.2011

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3 This effusion had periodically required drainage previously for symptom relief. Over the preceding 3 months she had experienced episodes of mild confusion & affect change, noted by friends and relatives. Each episode was self limiting and lasted 1 -2 days. However one such episode required hospital admission, where despite thorough investigation (including MRI to exclude cerebral AV malformations) no cause was isolated. There was no history of any alcohol use. On admission she was afebrile with stable vital signs. Clinical examination was consistent with mild cardiac failure and a moderate right-sided pleural effusion, subsequently confirmed on chest radiograph. There was no focal neurological deficit and her Glasgow Coma Score (GCS) was 14 (V4) with mild confusion & inattention consistent with delirium. Full blood count revealed a chronic normocytic anaemia (Hb 7.9d/dl) and liver function showed a mildly chronically raised alkaline phosphotase. C reactive protein and urea and electrolytes were all within normal limits. CT brain demonstrated small vessel disease but no other abnormality. Urine culture grew Escherichia coli and Enterococcus sp. Oral trimethoprim was commenced and two units of red cells were transfused. Whilst there was clinical improvement & her GCS returned to normal there remained mild affect change, as noted by close relatives. On day 7 of admission worsening confusion was noted, and the subsequent morning she had deteriorated further with the GCS being 10/15. Bloods and clinical examination were unchanged except for the presence of a hepatic asterixis. Blood glucose and arterial blood gas analysis showed the known mild hypoxia, which despite correction with supplemental oxygen did not improve her confusional state. Repeat CT brain imaging revealed no new intracerebral event. A diagnosis of hepatic encephalopathy secondary to porto-systemic shunts as a complication of HHT was postulated. This was substantiated by diagnostic electroencephalogram confirming metabolic encephalopathy and further supported by a significantly elevated ammonia level of 211umol/l (<40). Treatment was commenced with rifaximin, movicol™ (Macragol) and lactulose with resolution of confusion within 48 hours, which corresponded with bowel opening. Concordance with treatment fluctuated due to drowsiness and oral intake and her GCS fell again 5 days later to 12/15 (E3, M5, V4). Her bowels had been open only once in 3 days and her ammonia level was again raised at 191umol/l. 2 days of higher-dose lactulose administration via nasogastric tube resulted in resolution of her confusion and return to GCS 15. Specific treatment for this hepatic encephalopathy, namely hepatic embolisation had been previously considered as treatment for persistent pleural effusion but was deemed to carry too high a risk of liver necrosis. Unfortunately hepatic transplant was contraindicated due to her comorbid disease burden and age. Despite ongoing specific treatment with aperients and rifaximin she continued to experience mild transient encephalopathic episodes of increasing frequency. She was discharged with palliative support to continue laxatives at her informed discretion.

DISCUSSION

Hereditary Haemorrhagic Telangiectasia (HHT), or Osler-Weber-Rendu disease, is a rare autosomal dominant disorder with a prevalence of 1 to 2 cases per 100 000 people (2). The disease is characterised by angiodysplastic lesions (telangiectasiae and arteriovenous malformations) that affect organs including the skin, lungs, gastrointestinal tract and brain (3). Hepatic involvement is thought to be uncommon, with reported prevalence of between 8% to 31% (2). However, the exact prevalence of hepatic arteriovenous malformation (AVM) is still unknown (2). Intrahepatic arterioportal shunts consist of abnormal communications between the hepatic arteries and the portal veins; in HHT they represent a congenital vascular malformation (4). In patients with HHT and symptomatic liver involvement, the typical clinical presentations include high-output heart failure, portal hypertension, and biliary disease (3). Clinical manifestations of liver involvement fluctuate, possibly as a result of changing shunting patterns or other underlying pathology such as anaemia or cardiac failure (3). Presentation with hepatic encephalopathy secondary to porto-systemic shunting resulting from AVM caused by HHT is rare with less than 10 reported cases in the literature (2-5). Hepatic encephalopathy is a complex neuropsychiatric syndrome with many causes, the most common of which being chronic liver disease, but also acute liver disease, inherited disorders of urea cycle, (6) or intra-hepatic portosystemic shunting either iatrogenic or spontaneous as in this case (6). The clinical manifestation of hepatic encephalopathy can range from subtle abnormalities to coma. Mechanisms in the pathogenesis of this syndrome include the accumulation of unmetabolised ammonia and most proven treatment is based on this ammonia hypothesis (6). Proven treatments of hepatic encephalopathy include dietary protein restriction (during acute episode), carbohydrate enemas,

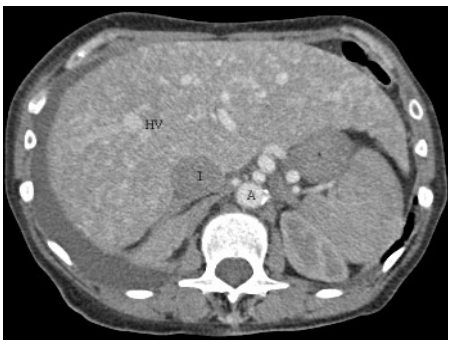

***Figure 1**. Arterial phase post IV contrast axial.*

oral lactulose, oral rifixamin. The treatment of hepatic encephalopathy as a result of portosystemic shunt (iatrogenic or spontaneous) is usually managed along conventional lines (6). For refractory encephalopathy such as this case further management options for symptomatic hepatic AVM are limited but include hepatic artery embolisation, or liver transplantation, the former remaining controversial given the risk of fatal hepatic necrosis (2,4). This case further builds on the literature reporting this unusual manifestation of HHT with less than 10 cases of hepatic encephalopathy secondary to portosystemic shunts as a complication of HHT reported in the literature (2-5). Although rare this case is of relevance to clinicians due to the common presentation of confusion in the elderly, it highlights the importance of seeking unusual yet potentially treatable causes of confusion when initial treatment fails, particularly in complex patients with pre-existing disease (6).

Acknowledgements

Conflict of Interest - None, Author Contributions; Dr Marianne Tinkler & Dr Eleanor Lyons joint 1st author. Contribution to construction of article Dr Emily Henderson Acknowledgement to: Dr Susan Wensley for Consultant supervision. Dr Sanjay Gandhi for images. North Bristol NHS Trust.

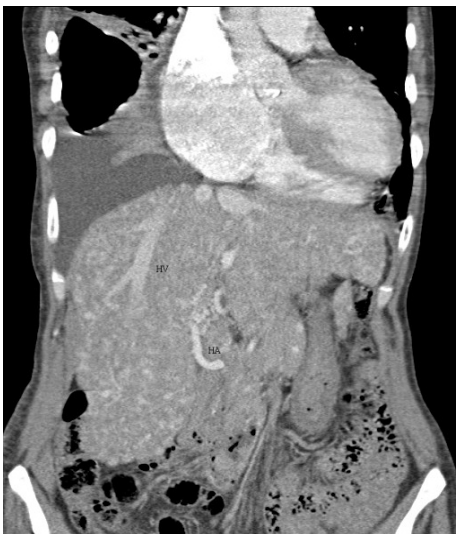

***Figure 2**. Arterial phase post IV contrast coronal CT images show aneurysmal dilatation of hepatic artery (HA). There is extensive shunting resulting in early filling of hepatic veins (HV) and a right basal pleural effusion. Note presence of contrast in the abdominal aorta (A), however, inferior vena cava (I) is unopacified at this stage.*

REFERENCES

1. *National Institute for Clinical Excellence. Delirium: diagnosis, prevention and management. NICE Clinical Guideline 103, July 2010.*
2. *Chan TL, Allen L, Loke, T, et al. Hereditary Haemorrhagic Telangiectasia - Osler-Weber - Rendu Disease - with Extensive Hepatic Arteriovenous Malformation. J HK Coll Radiol 2002;5:237-9*
3. *Garcia-Tsao G, Korzenik J et al. Liver Disease in Patients with Hereditary Haemorrhagic Telangectasia. New England Journal of Medicine 2000;343:931-6*
4. *Memeo, M, Stabile Ianora et al. Hepatic involvement in hereditary hemorrhagic telangiectasia: CT findings. Abdominal Imaging 2004;29:211-20.*
5. *Matsumoto S, Mori H, Yamada Y, et al. Intrahepatic portohepatic venous shunts in Rendu-Osler-Weber disease; imaging demonstration. European Radiology (2004) Vol 14. 4, 592-6*
6. *Riordan S, Williams R. Treatment of Hepatic Encephalopathy. New England Journal of Medicine 1997; 337:473-9*