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Royal Cornwall Hospitals NHS Trust

MORVAN'S SYNDROME: COULD INSULIN LIKE GROWTH FACTOR-1 (IGF-1) BE A MARKER?

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INTRODUCTION

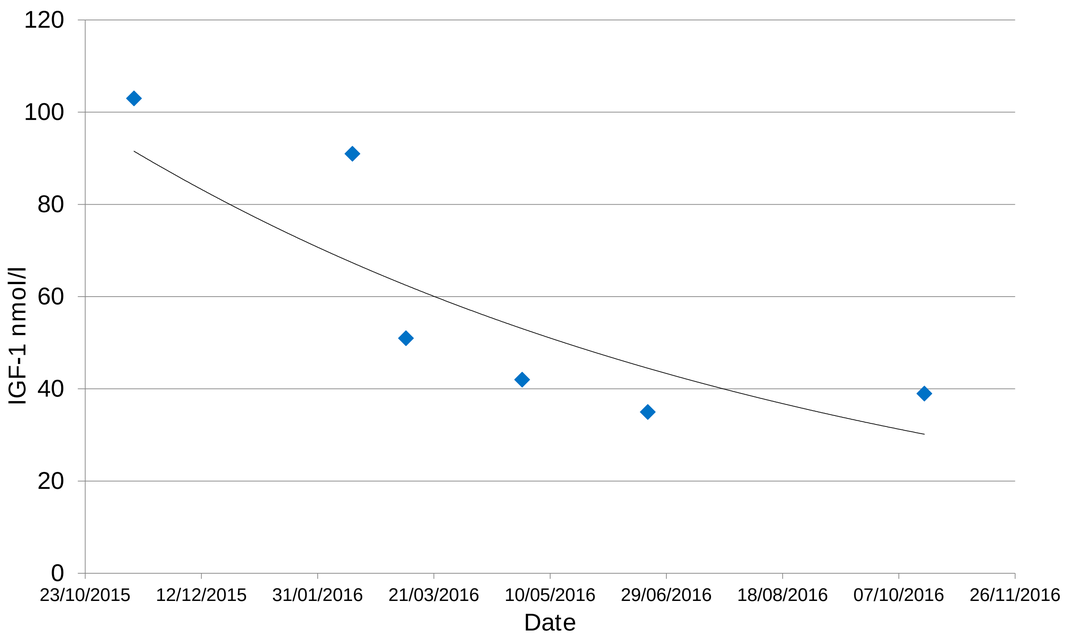
Morvan's syndrome is a rare autoimmune disease characterised by peripheral nerve hyper excitability, central nervous system symptoms and autonomic dysfunction which can manifest as hyperhidrosis, weight loss, neuromyotonia and insomnia[1]. It can mimic endocrinopathies and is associated with malignancy, in particular thymomas, suggesting paraneoplastic aetiology[2].
This case is the first to associate Morvan's with renal cell carcinoma and proposes insulin like growth factor 1 (IGF-1) as a marker of disease activity.

CASE REPORT

A 52 year old man presented to his general practitioner with non-specific symptoms including weight loss, diarrhoea, hyperhidrosis and paraesthesia. He had a past medical history of hypertension for which he took lisinopril but otherwise was previously fit and well.

Subsequently, he was extensively investigated and a Computed tomography (CT) scan revealed a 5.4 X 5.1cm left renal mass which was confirmed to be renal cell carcinoma following a curative nephrectomy. His symptoms persisted three months post-surgery and a phaeochromocytoma, carcinoid tumor, thyrotoxicosis and Cushing's syndrome were all excluded after referral to the endocrine outpatient clinic.

Furthermore, he had a normal positron emission tomography (PET) scan that ruled out metastatic spread or a secondary malignancy.
Interestingly, his IGF-1 was found to be elevated at 103nmol/L (normal range 8-39nmol/L) which persisted on subsequent testing (although he had a normal oral glucose tolerance test excluding acromegaly). Voltage gated potassium channel (VGKC) antibodies (diagnostic of Morvan's) were positive at 843pM (normal <100pM) confirming the diagnosis. He received an immunoglobulin infusion and high dose prednisolone with significant improvement of his symptoms and stepwise reduction in his IGF-1 (Figure).
He is presently under joint neurology and endocrinology follow up, doing well on low dose prednisolone.



DISCUSSION

There are very few documented cases of Morvan's and the natural history varies from spontaneous remission to chronic presentations[1,3]. The pathogenesis is not fully understood but is believed to be paraneoplastic, hence the resolution of symptoms following thymectomy in some patients with associated thymomas[2,4]. VGKC antibodies also play a role and the treatment options include plasmapheresis, immunoglobulins, steroids and symptomatic relief with anxiolytics[5, 6].

IGF-1 is synthesized primarily in the liver under the influence of growth hormone (GH), which also regulates its secretion into the systemic circulation[7]. It is a small peptide that is about 99% protein bound and exerts its effects via activation of IGF-1 receptors found on multiple target tissues[8]. It is uncertain what connection Morvan's has with IGF-1 but based on our investigations it is unlikely to cause acromegaly which results from persistent hypersecretion of GH.

A possible hypothesis is that Morvan's might result in increased secretion of IGF-1 into the peripheral circulation as some mesenchymal cells play a role in IGF-1 secretion. This is the first documented case of Morvan's associated with renal cell carcinoma and we propose IGF-1 as a marker of disease as the patient's levels progressively improved with treatment and resolution of symptoms.

CONCLUSION

Standard clinical practice should not necessarily be changed based on these findings, but further research into the role of IGF-1 in Morvan's syndrome should be considered. We are presently looking into analysing IGF-1 levels in established cases of Morvan's to determine any correlation with disease progression.

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