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EDITORIAL

Perception of health and cognitive dysfunction in acromegaly patients

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As therapeutic options improve for pituitary adenomas, we like to think we are capable of 'curing' patients with these diseases. However, in parallel to the availability of instruments to evaluate the patient's subjective perception of outcome of the disease, evidence is accumulating on residual morbidity despite endocrine control of hormonal dysfunction. Over the last few years, cognitive dysfunction has been identified as one of the most common co-morbidities of pituitary tumours. Why this occurs is still unclear and could be related to neurovascular decline, ageing, suffering a chronic disease, apart from hormone imbalance, either chronic hormone excess or deficiency (mainly GH or cortisol).

Evaluation of cognitive dysfunction in acromegaly has revealed contradictory findings. While Tiemensma et al. [1] reported normal cognitive function in patients with long-term cured acromegaly, several other studies showed deficits in attention, executive functions and memory [2–4]. In their paper, Yedinak and Fleseriu [5] show cognitive dysfunction in 10 patients with active acromegaly, 17 with controlled acromegaly (defined as normal IGF-I and GH after an oral glucose tolerance test of <1 ng/mL) and 14 non-functioning pituitary microadenoma (NFPA), which were prospectively enrolled over a 3 year period in a tertiary referral centre in the US. They evaluated self-perception of cognitive deficits and quality of life/health by selecting and modifying relevant questions of questionnaires, originally designed for other diseases. Certain questions (16 of the original 37) from the Functional Assessment of Cancer Therapy Cognitive Scale (FACT-Cog) were selected, which reflected subsets of cognition, like ability to learn, concentration and distractibility, mental agility, memory and recall and verbal recall.

Additionally, patients were asked to rate on a 1–5 scale how their health compared today with their desired health and to 12 months before. These questions are focused on patient perception, not objective cognitive measures, and this self-perception of cognitive function is influenced by the patient's goals, expectations, standards, concerns, personality, as well as life events. For example, increased psychopathology (mainly anxiety and depression), maladaptive personality traits or less effective coping strategies, all previously described in patients with controlled acromegaly, may determine how these questions are answered [1, 6, 7].

The main findings of Yedinak and Fleseriu were that prevalence of cognitive dysfunction, in parallel to severity score for each of the 5 subsets of questions, was higher in NFPA (69 %) than in both groups of acromegalic patients, with no difference in prevalence between the latter (54 % in controlled vs. 57 % in active acromegaly). When the five specific cognitive areas were analysed, significant differences were observed for each subset; NFPA expressed greater cognitive dysfunction for mental agility, memory/recall and verbal recall, but for ability to learn and concentration/distractibility, the group with active acromegaly expressed more problems and more severe dysfunction. This result is in line with previous studies that have reported attention and memory problems, and attenuation of electrophysiological brain activity in naïve acromegaly

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[8, 9]. Physiological IGF-1 levels maintain cognitive function in the adult brain, through its beneficial effects on synaptic structure and plasticity. On the other hand, IGF-1 excess can determine brain-insulin resistance which promotes tau hyperphosphorylation and amyloid accumulation leading to synaptic loss. These neurotoxic processes presumably contribute to cognitive dysfunction observed in active acromegaly. Accordingly, an earlier diagnosis to prevent long-term complications and good control of the disease and its co-morbidities may improve cognitive function in acromegaly. It could be hypothesized that pharmacological treatments (somatostatin analogues or pegvisomant) are able to promote benefits, directly or indirectly, on brain function. However, evidences are required to confirm this assumption.

Worse quality of life in active disease has persistently been observed in comparison to patients controlled after successful therapy, but impairment in quality of life persists in 'cured' acromegaly when compared to normal population or NFPA patients. Nevertheless, Yedikas's study has reported that active acromegaly patients have a positive perception about their current health in comparison to cured patients whose health perception was worse. This is somewhat surprising since in patients with active disease, their perception of current health is better, but they show more problems in learning and concentration. Thus, it would be interesting to explore the association between perception of cognitive function and health, and consider whether the patients' gender influences these variables; in other words, did the fact that 60–70 % of acromegalic patients were women versus only around 40 % of NFPA play a role on perception of health and cognitive function.

Furthermore, it would be methodologically desirable that the validity of the personalized selection of dimensions from the complete FACT-Cog questionnaire, an instrument developed for another disease situation, was proven; until then, the results of this pilot study may not be generalizable.

Certain degree of cognitive dysfunction perception was observed in all groups; however, this study shows higher perception of cognitive dysfunction in NFPA than in acromegalic patients. Interest in patient-related outcomes has led to the evaluation of well-being perception, which is complementary and not always concordant with endocrine, imaging or other clinical indicators. Indeed, patients with long-term remission of acromegaly show more negative illness perceptions than patients with acute illness (i.e. acute pain or vestibular schwannoma) [10]. To improve long-term prognosis, as well as offer the patient a realistic expectation with respect to the results of treatment, awareness on the lack of complete normalization of cognitive function outcome and impaired quality of life should be considered. These results advocate for patients with functional or non-functional pituitary tumours to be followed in specialized units, even after hormonal control.

In conclusion, this study adds to the evidence accumulating over the last years that hormonal 'control' of pituitary tumours does not mean complete reversal of co-morbidities and return to basal state/condition. Having suffered a pituitary tumour, even if dysfunction is controlled, confers a premature increase in health risks. The challenge for the future is how to improve outcome of pituitary patients, so that they can be nearer the concept of attaining a sufficient state of physical and mental well-being, to be considered healthy.

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