Efficacy of intravenous immunoglobulins in severe scleromyxedema dysphagia assessed by oesophageal scintigraphy

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Scleromyxedema is a rare chronic mucinous disorder of unknown origin characterised by infiltrative skin lesions due to abnormal proliferation and activation of fibroblasts. Skin sclerosis is frequently associated with extracutaneous manifestations, the most common being monoclonal gammopathy and oesophageal dysmotility with severe dysphagia (1, 2). Scleromyxedema is therefore a chronic and disabling condition with high morbidity and mortality. Moreover, oesophageal involvement is often assessed invasively, while oropharyngoesophageal scintigraphy (OPES) represents a valid alternative for a non-invasive, accurate and safe evaluation that has already demonstrated its utility in the assessment of patients with chronic severe dysphagia (3). OPES involves the swallowing of liquid and semi-solid marked boluses, then obtaining for both a functional and a semi-quantitative evaluation of the transit time and the percentage of retention index in the oropharyngeal (OTT and OPRI) and oesophageal (ETT and ERI) regions (Supplementary material).

So far, no definitive therapeutic guidelines are published. However, in the literature intravenous immunoglobulins (IVIG) are reported as the most used first-line therapy given their efficacy derived mainly from case reports and their generally well tolerated nature (4). The vast majority of evidence supporting IVIG efficacy in scleromyxedema is based on clinical descriptions. A recent study investigated their action also at a cellular and molecular level, observing a reduction in circulating Tc17 cells and a decreased gene expression of transforming growth factor-β and interferon-related pathways in skin samples from scleromyxedema patients treated with IVIG (5). Herein we used OPES to obtain an imaging and instrumental demonstration of IVIG efficacy in a case of life-threatening dysphagia secondary to scleromyxedema.

In 2020 we evaluated a 72-year-old male scleromyxedema patient who was diagnosed for the presence of diffuse skin thickening (mucinous findings in skin biopsy), monoclonal gammopathy IgGλ and no thyroid disorders. After an initial treatment with methotrexate that had been beneficial on cutaneous involvement, he developed progressively worsening dysphagia which was complicated by two episodes of aspiration pneumonia resulting in discontinuation of methotrexate and that finally led to a severe malnutrition. Despite the presence of a nasogastric tube, the clinical picture was so severe to receive the indication for percutaneous endoscopic gastrostomy surgery. At that time liquid bolus OPES showed a slowdown in both OTT and ETT and high percentages of retention (18% OPRI and 50% ERI). Semi-solid bolus OPES presented a similar pathological increase in OTT and ETT and even higher retention indexes (32% OPRI and 79% ERI). Functionally, there were signs of inhalation and tracer retention throughout the oesophagus. IVIG were then started at the dose of 2 g/kg for 3–4 days every month achieving a dramatic clinical improvement of the dysphagia, with no more episodes of aspiration and the removal of nasogastric tube. Liquid bolus OPES repeated after one year of IVIG showed both OTT and ETT within normal range and a significant decrease in both OPRI and ERI (9% and 20%, respectively). Semi-solid bolus OPES values were still pathological but significantly improved (16% OPRI and 41% ERI) (Fig. 1). Functionally, no signs of inhalation were detected, and tracer retention was noted only in the lower-third of the oesophagus.

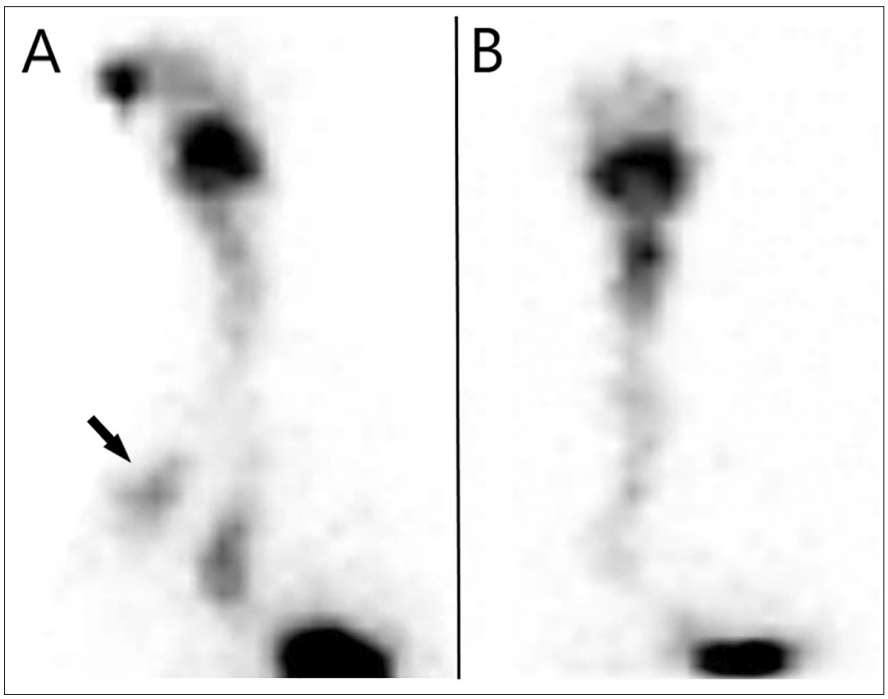

Fig. 1. Functional oesophageal comparison at OPES for semi-solid bolus between baseline (**A**) and post-IVIG treatment (**B**). Note the inhalation of the tracer at baseline (arrow), no more visible after IVIG.

In conclusion, IVIG are confirmed as an effective therapy in the treatment of a rare, insidious and severe complication such as oesophageal dysmotility due to scleromyxedema. OPES emerges as a useful tool for the non-invasive assessment and monitoring of dysphagia.

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References

1. RIGHI A, SCHIAVON F, JABLONSKA S *et al.*: Intravenous immunoglobulins control scleromyxoedema. *Ann Rheum Dis* 2002; 61(1): 59-61. https://doi.org/10.1136/ard.61.1.59
2. KULCZYCKI A, NELSON M, EISEN A, HEFFERNAN M: Scleromyxoedema: Treatment of cutaneous and systemic manifestations with high-dose intravenous immunoglobulin. *Br J Dermatol* 2003; 149(6): 1276-81. https://doi.org/10.1111/j.1365-2133.2003.05682.x
3. DI BATTISTA M, GROSSO M, DA RIO M *et al.*: Is oropharyngoesophageal scintigraphy the method of choice for assessing dysphagia in systemic sclerosis? A single center experience. *Esophagus* 2023; 20(3): 567-72. https://doi.org/10.1007/s10388-023-00995-0
4. HABER R, BACHOUR J, EL GEMAYEL M: Scleromyxedema treatment: a systematic review and update. *Int J Dermatol* 2020; 59(10): 1191-201. https://doi.org/10.1111/ijd.14888
5. MECOLI CA, TALBOT CC, FAVA A *et al.*: Clinical and molecular phenotyping in scleromyxedema pretreatment and posttreatment with intravenous immunoglobulin. *Arthritis Care Res* 2020; 72(6): 761-7. https://doi.org/10.1002/acr.23908