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M mode ultrasound and tissue Doppler imaging to assess diaphragm function in late onset Pompe disease

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Abstract

Late onset Pompe disease (LOPD) is an autosomal recessive lysosomal storage disease. Clinical features include skeletal muscles deficiency and diaphragm weakness. Clinical management relies on supportive treatment and mechanical ventilation in patents with chronic respiratory failure. M mode ultrasound and sniff tissue Doppler imaging can be used to assess and to follow diaphragm function.

Key words: LOPD, diaphragm; ultrasound

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Manuscript

Introduction

Late onset Pompe disease (LOPD) is an autosomal recessive lysosomal storage disease. This disease is in relation with a defect in the activity of the glycogen degrading lysosomal enzyme, the *alpha* 1-4 glucosidase enzyme (GAA), causing glycogen accumulation and muscles weakness (1). Clinical features include skeletal muscles deficiency and diaphragm weakness. Clinical management relies on supportive treatment that includes enzyme replacement therapy and mechanical ventilation. Respiratory muscle monitoring is essential in this disease, since respiratory insufficiency and sleep disordered breathing are frequent in patients with LOPD and an important cause of morbidity (2, 3). Diaphragm, the main inspiratory muscle, has a crucial role for breathing during sleep. Diaphragm weakness is often associated with sleep-disordered breathing. Recently, ultrasound has been used to assess diaphragm weakness in LOPD (4). Here, using M mode ultrasound and tissue Doppler imaging (TDI) (5) , we report diaphragm weakness attested by a paradoxical motion during a sniff test in a patient with LOPD.

Case report

A 64-year-old female patient was referred to our unit for a cardiorespiratory evaluation because of dyspnea and orthopnea. She was treated with enzyme replacement therapy since 10 years because of LOPD. She had limb girdle weakness with waddling gait. The Walton score was at 3.The other clinical parameters were as follow: Body mass index at 26kg/m2, systolic blood pressure at 109 mmHg, diastolic blood pressure at 65 mmHg, and diurnal oxygen transcutaneous saturation at 100%. Doppler Echocardiography showed a normal left ventricular ejection fraction (61%) with normal cardiac loading and subnormal systolic arterial pulmonary pressure (41 mmHg). We performed during the same exam a diaphragm exploration using ultrasound. From the subcostal view, we assessed the diaphragm motion using TM mode in rest and during a sniff maneuver, as previously described (5). We found a paradoxical diaphragm motion during a sniff maneuver of both the right (-11mm) and the left hemi diaphragm (-18 mm), with M mode (*figures 1 and 2*). Using tissue Doppler imaging, we also found a negative and reduced peak velocity of diaphragm during the sniff maneuver, measured on the right hemi diaphragm (- 6 cm/s) and on the left hemi diaphragm (- 4 cm/s) (*figures 3 and 4*). Diaphragm weakness was confirmed by the decrease of maximal inspiratory pressure (22 cmH20), the decrease of sniff inspiratory pressure (29 cmH2O) and the drop of the predicted value of respiratory forced vital

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capacity (VC) from upright to supine position (from 43% to 27%). In the meantime, with transcutaneous capnometry, the patient disclosed nocturnal hypoventilation attested by an increase of the transcutaneous PCO2 (82% of the registration time with pCO2>50mmHg) and a decrease of transcutaneous PO2 (39% of time with pO2<90%). Non-invasive nocturnal ventilation was introduced to manage the respiratory failure.

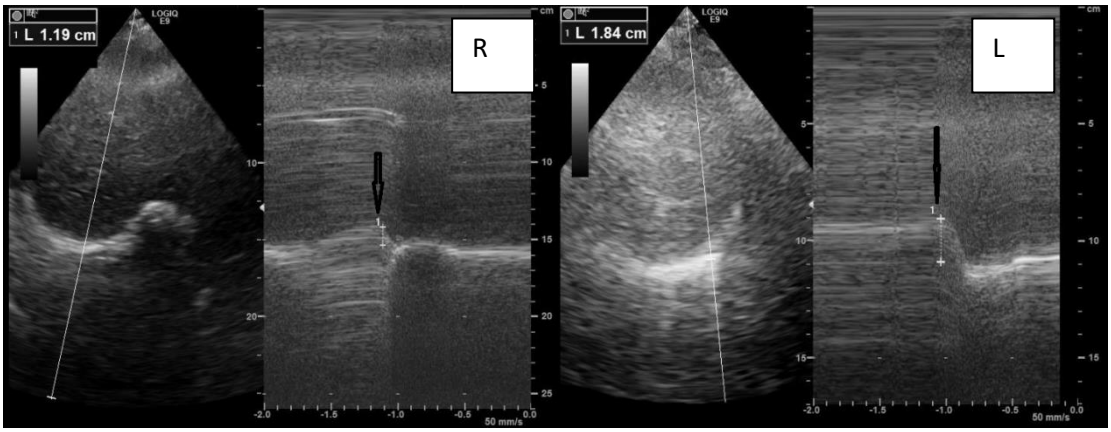

Figure 1 and figure 2: Right and left hemi diaphragm paradoxical displacement using M mode ultrasound during a sniff maneuver.

R= right; L=left

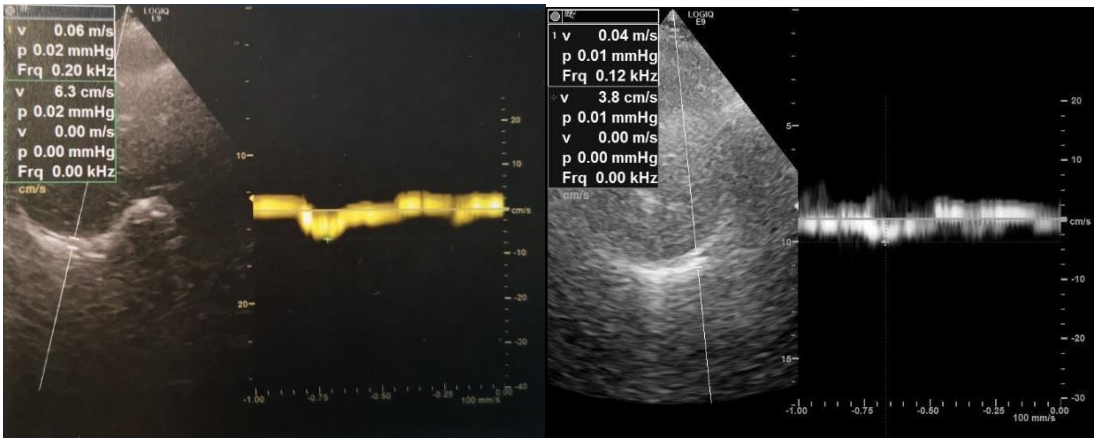

Figure 3 and figure 4:

Right peak negative velocity (- 6 cm/s) and left peak negative velocity (- 0.4 cm/s) using tissue Doppler imaging coupled to a sniff maneuver.

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Discussion

We report this case, in which bedside diaphragm evaluation by ultrasound allowed to suspect diaphragm weakness with nocturnal hypoventilation as the cause of dyspnea and orthopnea, in a patient with LOPD. In LOPD, clinically relevant diaphragm weakness may develop even in patients with little peripheral muscular impairment, causing nocturnal hypoventilation, supine dyspnea aggravation, daytime hypercapnia, fatigue and excessive daytime sleepiness (3). Diaphragm weakness is often associated with limb girdle weakness (6). NIV has been shown to normalize gas exchange and improve respiratory status and symptoms, in this context (1,7). Respiratory involvement in LOPD can be subtle and it is essential to monitor patients with repeated respiratory function tests, measuring vital capacity, maximal inspiratory pressure, and maximal expiratory pressure. The disease can affect not only the diaphragm, but also the upper airways and the other respiratory muscles (1). Classically, the drop of the VC from upright to supine is an indirect marker of diaphragmatic weakness (8). To assess the inspiratory muscle strength, sniff inspiratory nasal pressure and maximal inspiratory mouth pressure can be used. Sniff maneuver coupled with ultrasound can be used to selectively assess diaphragm function (5,9). Regular respiratory function monitoring is crucial in LOPD. In fact, LOPD patients with a supine VC <60% of predicted value have frequently sleep disordered breathing and nocturnal hypoventilation is frequent when VC is below 40% (10). M mode ultrasound and Tissue Doppler imaging may be applied in patients with LOPD to assess and monitor the diaphragm function, with the advantage of being applicable at the bedside, without the need of lung function facilities. In this case report, the paradoxical motion and the negative velocity of the diaphragm during the sniff manoeuver gave the clue to further investigate respiratory function, allowing to depict the presence of nocturnal hypoventilation. This finding highlights the potential application of ultrasound to monitor diaphragm in LOPD. Current guidelines recommend to introduce noninvasive ventilation in patients with LOPD relying on the values of blood gas exchange, MIP, FCV and sleep studies. Future studies will be necessary to assess the additive value of diaphragm ultrasound in this field.

Conclusion

In LOPD, bedside ultrasound may be used to screen for diaphragmatic dysfunction. In the presence of a diaphragm paradoxical motion or a negative TDI velocity during a sniff maneuver, nocturnal transcutaneous capnometry should be performed.

Conflicts of interest: none

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