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Reversed halo sign in pulmonary zygomycosis

We read with interest the article ‘The atoll sign’ by Walsh and Robertson¹ in the November issue of *Thorax*. The authors report a case of cryptogenic organising pneumonia with the atoll sign, also called the reversed halo sign. As mentioned by the authors, this CT sign was first described in

cryptogenic organising pneumonia and was initially considered to be specific for this disease.² It was subsequently reported in a variety of pulmonary diseases, including paracoccidioidomycosis (South American blastomycosis), tuberculosis, pulmonary sarcoidosis, lymphomatoid granulomatosis, Wegener’s granulomatosis, lipoid pneumonia and pneumococcal pneumonia.^{3–5}

We would like to highlight another important cause of the reversed halo sign: invasive pulmonary fungal infections, particularly pulmonary zygomycosis (PZ) (figure 1). In immunosuppressed patients, the presence of the reversed halo sign on CT should be considered as invasive fungal disease until proven otherwise. It is an early sign that is more frequently seen in patients with PZ than invasive pulmonary aspergillosis (IPA).⁶

Early institution of high-dose antifungal therapy is associated with improved outcomes; therefore, early recognition of invasive fungal disease is important. Moreover, because the therapy for presumed fungal pneumonia in this population is often aimed at IPA due to its higher incidence and the preferred antifungal agent for IPA is voriconazole, which is not effective against PZ, it is important to differentiate between the two entities. The presence of the reversed halo sign can be used to optimise antifungal therapy to cover PZ.

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Serum 25-hydroxy vitamin D and exercise capacity in COPD

Janssens and colleagues¹ have recently reported that vitamin D deficiency is very common in patients affected by chronic obstructive pulmonary disease (COPD) and that vitamin D status correlates with lung function. In the same issue of *Thorax*, Quint and Wedzicha² discuss potential effects of vitamin D deficiency and supplementation

Figure 1 Pulmonary zygomycosis in a 24-year-old woman undergoing chemotherapy for recurrence of acute myelogenous leukaemia, 1 year following allogeneic stem cell transplantation, with a 2-week history of fever and dry cough. (A) Chest CT shows a focal round area of ground-glass attenuation surrounded by a ring of consolidation in the right lower lobe, consistent with the reversed halo sign. (B) Photomicrograph of the specimen from a transthoracic biopsy of the lesion shows pauciseptated hyphae with non-parallel walls and 90° branching, characteristic of *Zygomycetes* species, which is confirmed by culture. (C) One-month follow-up CT shows cavitation of the lesion, which eventually resolved under antifungal therapy.

Table 1 Demographics, parameters of pulmonary function and exercise capacity of participating male COPD patients

Parameter	
Participants, n	79
Age, years	71.6±7.8
Weight, kg	73.7±15.9
Height, cm	164.6±7.9
BMI, kg/m ²	27.0±4.4
Smokers, (n) %	(10) 12.6
FEV ₁ , l	1.2±0.6
FEV ₁ , % predicted	49.8±19.3
VC, l	2.5±0.8
VC, % predicted	80.5±19.3
FEV ₁ /VC	0.5±0.1
TLCO, ml/min/mm Hg	14.9±6.3
TLCO, % predicted	67.1±27.7
VO _{2 peak}	1.35±0.59
VO _{2 peak} , % predicted	75.4±28.7
25(OH)D, ng/ml	30.7±25.5

Values are mean±SD.

in COPD with special focus on immunomodulatory function. However, they do not consider a potential impact of the hormone on muscle mass and function, and consequently on exercise capacity in these patients.³

Since exercise limitation is a very common complaint and a significant contributor to the poor quality of life in COPD,⁴ we studied the relationship between maximal aerobic capacity (VO_{2 peak}) evaluated by an incremental bicycle ergometry until exhaustion, circulating levels of 25(OH) vitamin D and respiratory function (forced expiratory

volume in 1 s, FEV₁; carbon monoxide transfer factor in a single breath method, TLCO) in a cohort of 79 stable male COPD patients (table 1).

Serum 25 (OH)D levels below the lower limit of the normal range (30 ng/ml) were found in 50 patients (63.3%), values between 30 and 12 ng/ml in 24 (30.4%) and values below 12 ng/ml in 26 patients (32.9%). In agreement with Janssens *et al*,¹ we report a correlation between 25(OH)D levels and FEV₁ ($r=0.504$, $p<0.001$), taking into account the differences in age, body weight and height. Further, 25(OH)D correlated with TLCO ($r=0.496$, $p<0.001$) and VO_{2 peak} ($r=0.247$, $p<0.05$). A stepwise linear regression analysis, using VO_{2 peak} as outcome measure and 25(OH)D levels, FEV₁ (% of predicted), TLCO (% of predicted), age, weight, and height as possible determinants, revealed 25(OH)D, TLCO, age and body weight to be significantly and independently associated with exercise capacity ($R^2=0.567$, $SEE=0.418$ l/min, $p<0.001$). In other words, our data indicate that low serum 25(OH)D levels are associated with poor exercise capacity in COPD while the degree of resting airflow limitation does not significantly add to the accuracy of the prediction of VO_{2 peak} in this model.

In conclusion, we agree with Quint and Wedzicha that attention should be paid to traditional values of pulmonary function and respiratory exacerbation, when evaluating the effect and benefits of D hormone supplementation in COPD patients. However, a more holistic approach claims to consider muscle health and exercise capacity as further potential targets of D hormone

treatment in this multidimensional, disabling and progressive disease.

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