

SARCOIDOSIS INVOLVEMENT OF THE DIAPHRAGM LEADING TO RIGHT DIAPHRAGMATIC ELEVATION: A CASE REPORT

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ABSTRACT. A 69-year-old male Caucasian presenting with dyspnea on exertion related to unilateral diaphragmatic dysfunction as caused by sarcoidosis is described. First, right diaphragmatic elevation was unexplained, while the patient presented with a restrictive pattern in lung function testing using bodyplethysmography and with reduced global and diaphragmatic respiratory muscle strength as evidenced by respiratory pressures. Subsequently, surgical diaphragm plication was performed, unfortunately, without any clinical improvement. Microscopic examination of diaphragm sections revealed a lymphocytic myositis with granulomatous pleuritis showing multiple non-caseating epithelioid granulomas. Accordingly, a lymphocytic alveolitis (26% lymphocytes) with an elevated CD4/CD8 T cell ratio of 8.0% and elevated serum parameters (neopterin and sIL-2 receptor) were established. Consequently, the diagnosis of pulmonary sarcoidosis with diaphragm involvement but without extrapulmonary involvement has been established. Therefore, sarcoidosis needs to be considered in any patient presenting with unilateral diaphragmatic dysfunction. The optimal treatment strategy, however, needs to be established in the future.

KEY WORDS: Sarcoidosis, Lymphocytic myositis, Diaphragmatic paresis, Non-caseating epithelioid granulomas

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INTRODUCTION

Sarcoidosis is a systemic non-caseating granulomatous disease of unknown etiology (1). Sarcoidosis most frequently affects the lungs and the lymph

nodes, but extrapulmonary organ involvement is also common in the skin, eyes, liver, kidneys, heart and the central nervous system. Even though sarcoidosis is also known to affect the skeletal muscles, respiratory muscle involvement is only rarely described by case reports (2-8).

On the other side, respiratory muscle dysfunction is a common clinical finding in patients presenting with dyspnea. Here, the underlying conditions are diverse, but may eventually remain undetected. This is particularly true for unilateral diaphragmatic dysfunction; in this scenario, many patients are classified with idiopathic diaphragmatic paralysis, as the reason for this condition frequently remains undetermined.

In the current case presentation, we report - for the first time - on a patient with inspiratory muscle

weakness based on unilateral diaphragmatic dysfunction, which was related to sarcoidosis.

CASE REPORT

A 69-year-old male Caucasian presented with dyspnea on exertion. The chest x-ray revealed right diaphragmatic elevation and a poorly inflated right lower lobe (Figure 1). Bodyplethysmography showed reduced lung volumes with a total lung capacity of 4.7 L (64% predicted) and a forced vital capacity of 2,3 L (51% predicted) indicating pulmonary restriction. In contrast, there was no evidence of airway obstruction (FEV_1/FVC 86%). Subsequent respiratory muscle function testing indicated a decreased global inspiratory and expiratory respiratory muscle strength (PI_{max} 3.8 kPa, PE_{max} 6.5 kPa), while the effective inspiratory impedance was normal ($P_{0,1} \times T_1/TV$ 0.27 kPa*s/l). Maximal nasal sniff pressures (Sn_{pna} 5.2 kPa) more specifically suggested a weakness of the diaphragm. Thus, right hemidiaphragmatic paralysis was suggested, as symptoms also aggravated in the supine position. Mediastinal lymphadenopathy was evident on the CT scan, but this was suggested not to impact on the current findings. Rather, neither conditions potentially affecting the right phrenic nerve nor any other potential reasons for diaphragmatic dysfunction were diagnostically evident. Following, the patient was started on respiratory muscle training using inspiratory threshold loading, but this was unsuccessful as

dyspnea on exertion persisted and lung function testing did not improve. Following, surgical diaphragm plication was performed. Unfortunately, there were no clinical improvements following surgery, while lung function testing even showed a deteriorated restrictive pattern: total lung capacity 4.1 L (57% predicted), forced vital capacity 2.1 L (49% predicted).

Interestingly, microscopic examination of several diaphragm sections revealed a lymphocytic myositis with granulomatous pleuritis showing multiple non-caseating epithelioid granulomas (Figure 2). From this data, the diagnosis of sarcoidosis was suggested. Subsequent diagnostic evaluation including bronchoscopy showed the following: a lymphocytic alveolitis (26% lymphocytes) with an elevated CD4/CD8 T cell ratio of 8.0%, a serum ACE (Angiotensin converting enzyme) of 35.1 U/L (normal 16-85 U/L), a serum neopterin of 12.4 nmol/L (normal <10 nmol/L) and an sIL-2 (soluble interleukin-2) receptor of 851 U/mL (normal 223-310 U/mL). Consequently, the diagnosis of pulmonary sarcoidosis with diaphragm involvement has been established. Following, completion of diagnosis did not provide evidence of any other organ involvement.

Following steroid treatment starting with 40 mg prednisolone per day with a subsequent reduction of the daily dosage of 10 mg each month, dyspnea subjectively improved, while lung function measured two months following initiation of treatment started to improve: total lung capacity 4,6 L (64% predicted), forced vital capacity 2,5 L (56% predicted).

DISCUSSION

In this case report, we report - for the first time - on a patient with unilateral diaphragmatic dysfunction related to sarcoidosis. Even though clinical experience suggests that respiratory muscle involvement is rare in sarcoidosis patients, the current case report teaches us the following:

Firstly, clinically relevant respiratory muscle involvement in sarcoidosis is possible, and clinicians should be aware of this when approaching a patient with dyspnea not otherwise explained (9). More importantly, this might also be true in unilateral diaphragmatic dysfunction. Here, it needs to be stressed that scientific evidence has suggested that respiratory muscle function is on average close to normal and only slightly reduced when compared to controls (8), even though few patients in this report had

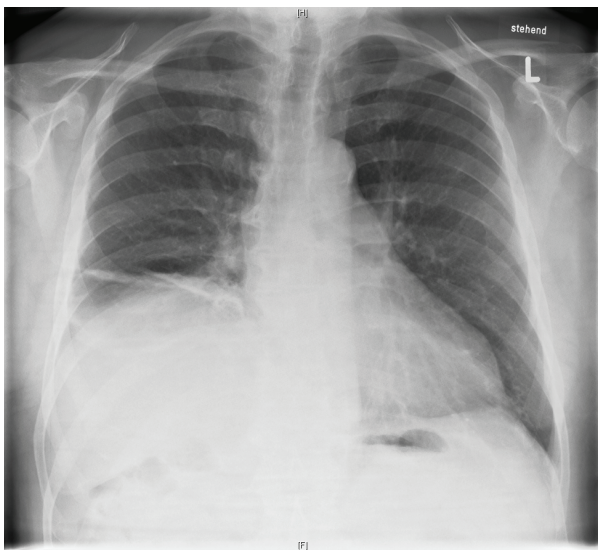


Figure 1. Chest x-ray. Right diaphragmatic paresis and poorly inflated right lower lobe.

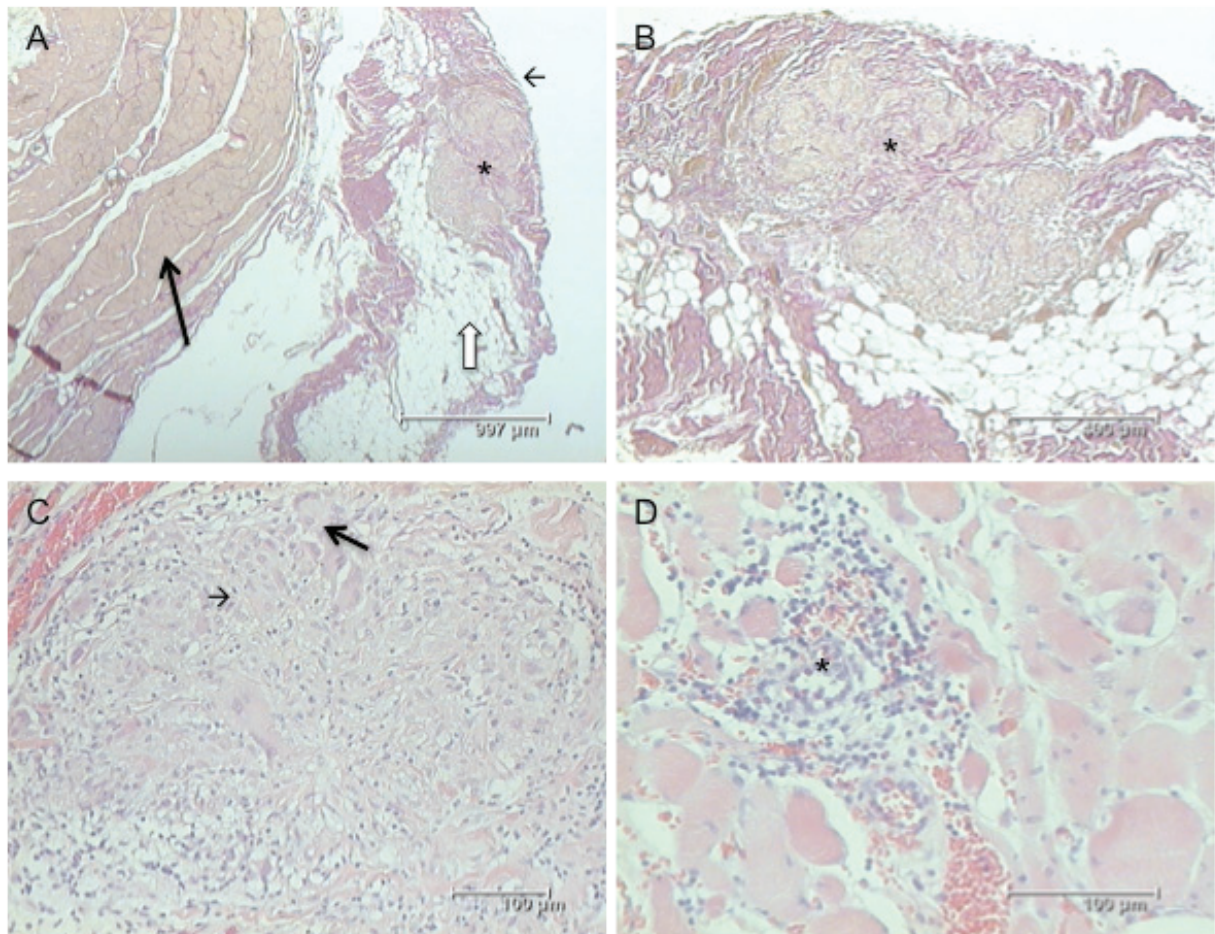


Figure 2. Hematoxylin and eosin (H&E) stain of diaphragm sections. (A) The section shows muscle tissue (big arrow) of the diaphragm and granuloma (star) surrounded by adipose tissue (white arrow) close to the serosa (small arrow) of the pleura, at magnification 200x. (B) Granuloma (star) at magnification 400x. (C) Non-caseating granuloma consisting of Langerhans giant cells (big arrow) and epithelioid cells (small arrow), magnification 800x. (D) Myositis with lymphocytic infiltrate (star) of the muscle tissue, already showing destruction of the muscle cells, magnification 800x.

significantly reduced respiratory muscle strength. Interestingly, serum neopterin and sIL-2 receptor for sarcoidosis were reportedly increased in those sarcoidosis patients with respiratory muscle involvement (8), and this was also true in the current case. Therefore, respiratory muscle involvement should be specifically considered in patients with these elevated serum parameters.

Secondly, a recently published study classified sarcoidosis into different phenotypes (10). Here, one phenotype was related to the musculoskeletal-cutaneous involvement. Even though, there was no evidence for cutaneous involvement in the reported case, the musculoskeletal-cutaneous phenotype

would best fit with the current patient. However, respiratory muscle involvement related to different phenotypes should be target for further evaluation.

Thirdly, in patients with unilateral diaphragmatic dysfunction surgical diaphragm plication should not be performed too early when sarcoidosis has not been sufficiently ruled out. This is particularly true in view of the current observation that surgical diaphragm plication did not subjectively and objectively improve respiratory function. Therefore, diagnostic evaluation prior to surgical diaphragm plication should also address potential underlying sarcoidosis.

Finally, in the current case sarcoidosis was suggested by microscopic examination of diaphragm

sections revealing a lymphocytic myositis with granulomatous pleuritis containing multiple non-caseating epithelioid granulomas. This is important, since there was no clear evidence for sarcoidosis prior to surgery, even though mediastinal lymphadenopathy was evident on CT-scan. However, this was clinically suggested to be an unspecific finding. Therefore, this case report suggests that diaphragm sections for histopathological examination should be regularly taken if diaphragm plication is performed.

CONCLUSION

We hereby demonstrate for the first time a patient with right diaphragmatic elevation due to sarcoidosis. Therefore, sarcoidosis needs to be considered in any patient presenting with unilateral diaphragmatic paresis. The optimal treatment strategy needs to be established in the future.

ABBREVIATIONS

ACE: Angiotensin converting enzyme **CT:** computertomography **FEV₁/FVC** forced expiratory volume in one second / forced vital capacity **IL-2:** interleukin 2

CONFLICTS OF INTEREST: Each author declares that he or she has no commercial associations (e.g. consultancies, stock ownership, equity interest, patent/licensing arrangement etc.) that might pose a conflict of interest in connection with the submitted article.

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