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Prognostic factors for PM/DM-ILD. A dilemma of treatment intensity?

Polymyositis (PM) and dermatomyositis (DM) are idiopathic inflammatory myopathies of unknown causes. In PM/DM, interstitial lung disease (ILD) is one of the extramuscular manifestations and the principal cause of death. To improve the prognosis of PM/DM-ILD, it is important to optimize disease management based on the prognostic factors for improving clinical outcome. Thus we retrospectively assessed clinical data, treatments, and clinical outcomes in patients with PM/DM-ILD to identify predictive prognostic factors for PM/DM-ILD, through the use of the multicenter database, in which patients of six hospitals associated with Yokohama City University are registered.

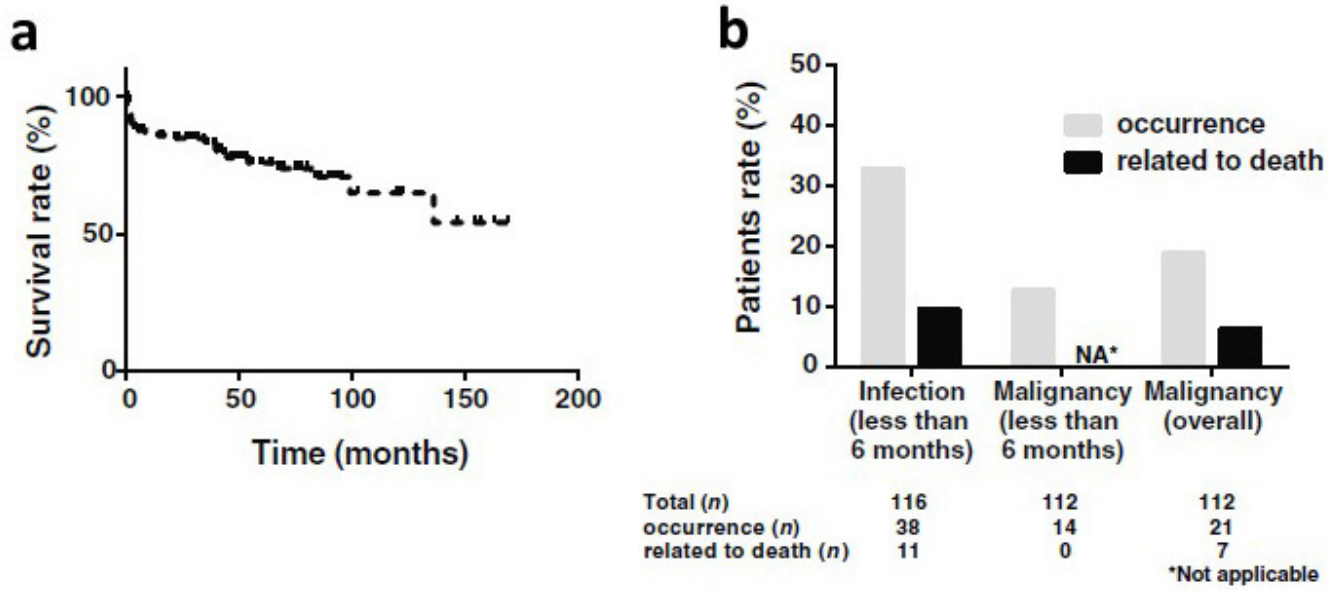

Fig. 1. Survival curves for patients with PM/DM-ILD over the observation time. (a) The survival curve for the patients with PM/DM-ILD. (b) Frequency of infections and malignancies (gray columns) or deaths from infection and malignancy (black columns) in patients with PM/DM-ILD up to 6 months after initiating treatment and within three years before and after diagnosis of PM/DM in the overall observation period.

One hundred sixteen patients with PM/DM-ILD were enrolled in the study. During the observation period, 28 (24.1%) died at 26.3 ± 34.9 months from diagnosis (Fig. 1a). ILD was directly related to early death in 12 (85.7%) of 14 patients who died within 6 months after the diagnosis. We compared baseline clinical features between the survivors and the short-term non-survivors, who died within 6 months from the diagnosis of PM/DM-ILD, and conducted multivariate analysis using the binomial logistic regression. Accordingly, we found that severe ILD lesion of upper lung fields above the aortic arch in high-resolution computed tomography images (OR 8.01, $p = 0.016$) and low arterial partial pressure of CO_2 level (<34.5 mmHg, OR 6.85, $p = 0.038$) were independently associated with early death. Both of the risk factors were related to the progression of ILD, especially the extension of ILD lesions into the upper lung fields at the baseline.

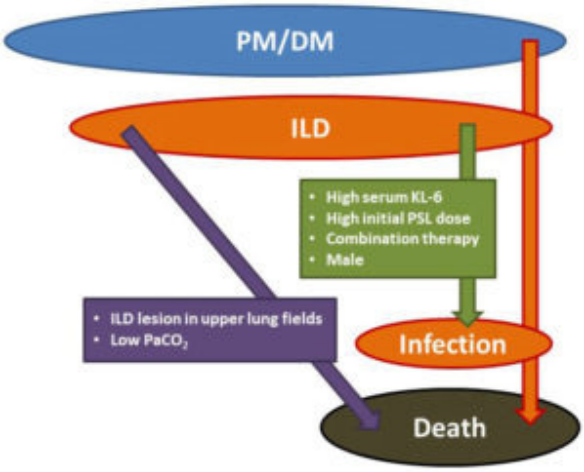

Fig. 2. Schematic representation of the predictive prognostic factors for PM/DM-ILD.

Complicated infection was another critical prognostic factor especially for survival in the early phase (Fig. 1b). By multivariate analysis using the binomial logistic regression, the serious infection was identified as an independent factor for early death after starting treatment in PM/DM-ILD (OR 6.49, $p = 0.012$). Therefore, our analysis also focused on serious infectious events within 6 months from starting treatment in PM/DM-ILD. Bacterial infection was the most frequent among causative pathogens. A total of 34 bacterial infection events consisted of 16 pneumonia, 9 urinary tract infections, 4 catheter-related bloodstream infections, 3 cellulitides, one lung abscess, and one femoral intramuscular abscess. Fungal infection was found in 15 including 9 *Pneumocystis* pneumonia, which was prevalent in patients not receiving prophylactic therapy. Multiple infections were found in 13 patients, including 10 short-term non-survivors. The respiratory infection, which was the most common focus, was found in 13 patients, including 10 short-term non-survivors. Moreover, early death was associated with multiple infections including the respiratory infection, which was directly involved in the lethal events. Multivariate analysis using the binomial logistic regression identified high serum KL-6 level (≥670 U/mL, OR 3.68, $p = 0.027$), initial glucocorticoid dose (prednisolone (PSL) dose ≥0.55 mg/kg/day, OR 4.18, $p = 0.013$), combination therapy with a calcineurin inhibitor and intravenous cyclophosphamide (IVCY) (OR 5.51, $p < 0.001$) and male (OR 3.38, $p = 0.024$) as independent risk factors for serious infections.

Taken together, our data shows the ILD progression at baseline is the most critical factor for survival and that infection is an additive prognostic factor under the potent immunosuppressive treatment (Fig. 2). We should reconsider the appropriate therapeutic regimen for PM/DM-ILD because the clinical outcome was favorable in the regimen using 0.5 mg/kg/day of PSL with a calcineurin inhibitor as compared with more potent therapy using 1.0 mg/kg/day of PSL or IVCY. As the choice of either regimen has not been controlled in this study, unintended bias could be introduced. Thus we need to analyze this issue in a prospective study in the future. At any case, what we can do in the management of PM/DM-ILD patients receiving intensive

immunosuppressive therapies at this moment is to be careful enough to control infection by prophylaxis based on screening, and by early detection using monitoring and subsequent treatment.

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Publication

The predictive prognostic factors for polymyositis/dermatomyositis-associated interstitial lung disease.
Sugiyama Y, Yoshimi R, Tamura M, Takeno M, Kunishita Y, Kishimoto D, Yoshioka Y, Kobayashi K, Takase-Minegishi K, Watanabe T, Hamada N, Nagai H, Tsuchida N, Soejima Y, Nakano H, Kamiyama R, Uehara T, Kirino Y, Sekiguchi A, Ihata A, Ohno S, Nagaoka S, Nakajima H.
Arthritis Res Ther. 2018 Jan 11