A New Hope for Patients with Severe Eosinophilic Asthma

Dr. Herbert Kwok and Dr. Julie Wang

Department of Medicine,
Queen Mary Hospital

Case 1

A 67 years old patient , non smoker, who has underlying allergic rhinitis, chronic sinusitis, nasal polyps and eosinophilic asthma since age of 20.

The baseline eosinophil level was 1.82 x 10^9/L. He has been on GINA level 5 medication for his asthma, including maintenance steroid at prednisolone 7.5mg daily.

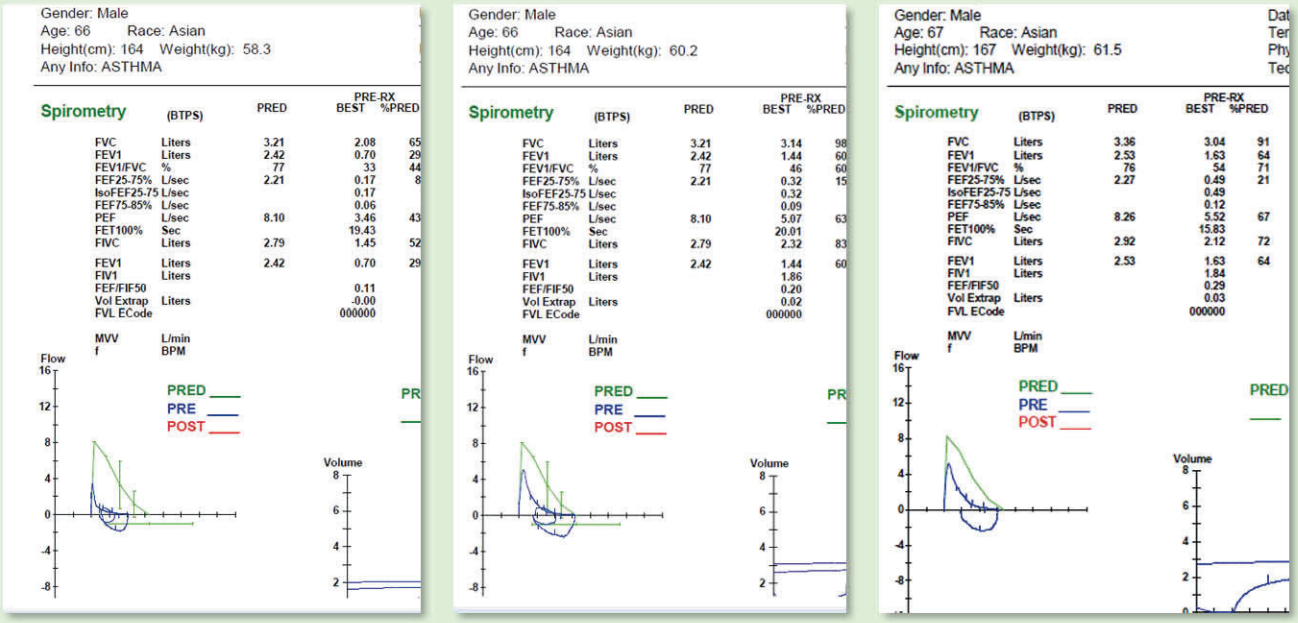
His baseline peak flow rate (PFR) is 200 L/min, asthma control test (ACT) score of 17/25. He was on domiciliary oxygen therapy.

Extensive investigations for eosinophilia including ANCA, ANA, skin prick test, IgE level, aspergillus serology, stool for ova and cyst were negative.

Despite maintenance steroid, he still had six exacerbations of asthma per year, which are triggered by cold weather or upper respiratory tract infections.

He has good drug compliance and inhaler technique all along. There are no other precipitating factors identified. His rhinitis are well controlled and there is no reflux symptom.

Option of anti-IL5 was discussed with him and mepolizumab 100 mg every 4 weeks was started since August 2018. With mepolizumab treatment, his exercise tolerance improved and his PFR improved to 350L/min. Latest ACT score is 25/25. He no longer needs domiciliary oxygen therapy after 1 dose of mepolizumab. He had no asthmatic exacerbation in-between and the steroid is tailed down to prednisolone 4 mg daily. Eosinophil level also dropped from 1.82 x 10^9/L to 0.11 x 10^9/L. Serial lung function test results also shows improvement in spirometric parameters **(Figure 1)**.



Before Mepolizumab
August 2018

After 1 does Mepolizumab
September 2018

After 5 does Mepolizumab
January 2019

Figure 1: Serial lung function test results for patient 1

During mepolizumab treatment, he experienced mild headache and muscle pain only.

Case 2

A 71 years old male ex-smoker who has underlying allergic rhinitis, uticaria, bronchiectasis, chronic obstructive pulmonary disease and asthma.

He has been on GINA level 5 medication for his asthma, including maintenance steroid at prednisolone 7.5mg daily since October 2017 as well as long term macrolide for bronchiectasis.

His baseline peak flow rate (PFR) is 190 L min, asthma control test (ACT) score of 19/25. He was on domiciliary oxygen therapy. Despite maintenance steroid, he still had repeated asthmatic exacerbations.

He has good drug compliance and inhaler technique all along. There are no other precipitating factors identified. His rhinitis are well controlled and there is no reflux symptom. Eosinophil year high level in 2018 was 1.33 x 10^9/L while IgE level was 248 IU/mL. Spirometry shows fixed airflow obstruction **(Figure 2)**.

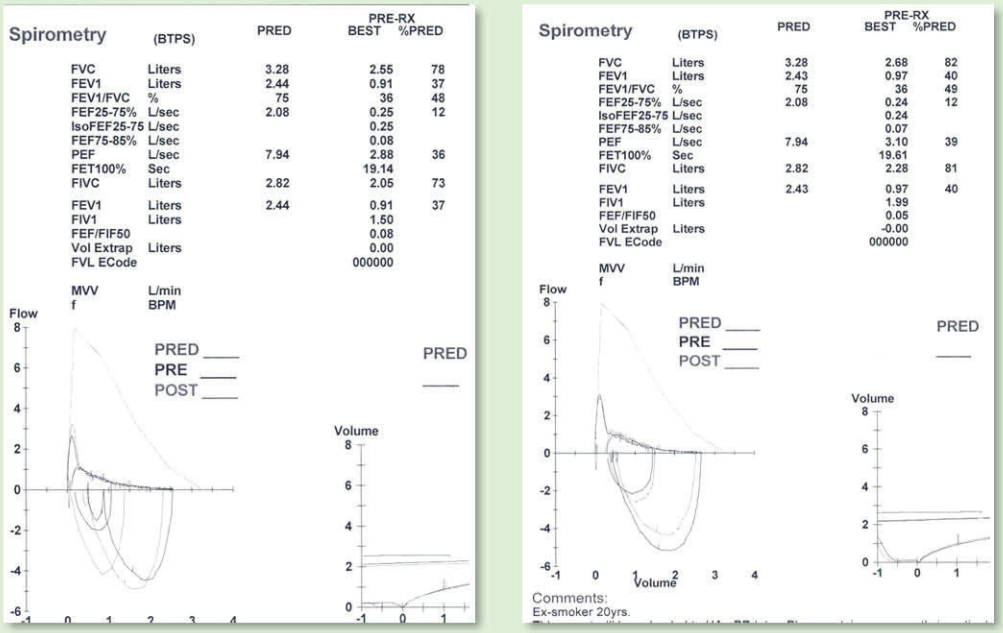


Figure 2: Lung function test result for patient 2

Option of anti-IL5 was discussed was discussed with him and mepolizumab 100 mg every 4 weeks was started. With mepolizumab treatment, his exercise tolerance improved with ACT score 24/25. He had no asthmatic exacerbation in-between and the steroid is tailed down to prednisolone 2.5 mg daily. During mepolizumab treatment, he experienced mild headache muscle pain and transient urticaria on 5th day after third dose of mepolizumab.

Discussion

According to ERS/ATS definition, severe asthma is defined as asthma which requires treatment with high dose inhaled corticosteroids plus a second controller (and/or systemic corticosteroids) to prevent it from becoming uncontrolled or which remains 'uncontrolled' despite this therapy. The prevalence of severe asthma is 5-10%[1]. Many patients remain symptomatic despite standard of care medications.

Eosinophilic asthma is defined as airway eosinophilia with T2 inflammatory reactions. The diagnosis is established by sputum eosinophilia and measurement of T2 cytokine mRNA in sputum. Eosinophil level between 200 and 300/microL or fraction of exhaled nitric oxide (FENO) levels above 20 ppb support an underlying active Type 2 immune process. According to latest GINA recommendation, add-on anti-IL5 or anti-IL5R for severe eosinophilic asthma can be considered.

IL-5 is responsible for recruitment, maturation, activation and survival. Mepolizumab is a humanised mAb that targets IL-5. Mepolizumab Inhibits bioactivity of with nanomolar potency. It also blocks binding of IL-5 to the alpha chain of the IL-5 receptor complex expressed on the eosinophil cell surface and inhibits IL-5 signalling and reduces production and survival of eosinophils.

DREAM study is a multicentre, double-blind, placebo-controlled trial that include patients with a history of recurrent severe asthma exacerbations and had signs of eosinophilic inflammation. Patients were randomly assigned to receive intravenous mepolizumab at dose of 75 mg, 250 mg, 750 mg or placebo. Mepolizumab was shown to significantly reduce exacerbations when compared with placebo, by up to 48%[2].

MENSA study is a randomized, double-blind, double-dummy study that recruit patients with recurrent asthma exacerbations and evidence of eosinophilic inflammation despite high doses of inhaled glucocorticoids. Patients were assigned to receive mepolizumab as either a 75-mg intravenous dose or a 100-mg subcutaneous dose, or placebo. Mepolizumab was shown to significantly reduce asthma exacerbations by 47% and 53% in intravenous and subcutaneous group respectively[3].

SIRIUS study showed that mepolizumab has significant glucocorticoid-sparing effect. The likelihood of a reduction in the glucocorticoid-dose stratum was 2.39 times greater in the mepolizumab group than in the placebo group. The median percentage reduction from baseline in the glucocorticoid dose was 50% in the mepolizumab group, as compared with no reduction in the placebo group. Mepolizumab also reduced exacerbations and improved control of asthma symptoms. Patients in the mepolizumab group had a relative reduction of 32% in the annualized rate of exacerbations and a reduction of 0.52 points with respect to asthma symptoms on the Asthma Control Questionnaire 5[4].

Conclusion

Severe asthma is a common problem encountered by respiratory physicians. In the past, medications are limited, require adherence, and long term systemic corticosteroid can have serious side effects. The development of biologics is going to bring new hope to patients with severe eosinophilic asthma.

References:

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