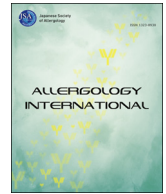




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Letter to the Editor

The relevance of obesity on asthma control in identical twins



Dear Editor

Asthma is a multifactorial disorder characterized by typical symptoms, airway inflammation, and bronchial hyperreactivity (BHR). The asthma control should be considered the goal of its management; asthma is clinically classified as controlled, partly controlled, and uncontrolled (<http://www.ginasthma.com>). The asthma control test (ACT) may be an easy way to assess the patient's perception of asthma control.¹

On the other hand, also obesity is characterized by mild inflammation.² Cross-sectional and case–control surveys reported that obesity and overweight increased the odds of asthma incidence,³ and weight loss is associated with asthma improvement in obese subjects.⁴ Consequently, there is convinced belief that a link between obesity and asthma exists.⁵ Body mass index (BMI) is considered a universal indicator of adiposity according to WHO criteria (<http://www.who.int/mediacentre/factsheets/fs311/en>). In this regard, we previously reported that BMI positively related with BHR severity in patients with asthma or allergic rhinitis.⁶ Moreover, a BMI ≥ 25 , such as overweight, is a risk factor for having impaired lung function, BHR, and bronchial inflammation in patients with allergic rhinitis.⁷ These outcomes underline the close link between adiposity and asthma. Therefore, this topic is particularly interesting for the clinician. In this regard, a recent paper addressed this issue and underlined the close association between asthma and obesity.⁸

For these reasons, we would like to present a particular case concerning two identical twins with asthma. They are males, 30 years old, and are still living with parents. They began with pre-school wheezing at 2 years. Then, they had several hospital admissions for recurrent exacerbations. Allergic rhinitis and asthma were diagnosed at 6 years. Respiratory, both nasal and bronchial, symptoms are perennial with symptom deterioration during the spring. Further, both developed oral allergic syndrome after eating apple and peach.

Typically, they ever become ill for viral respiratory infection at the same time and then typically together have asthma exacerbation. Their history is very specular also concerning allergic symptoms occurrence. In fact, living in the same familiar environment, they are exposed practically to the same triggers, including viral infections and inhaled and food allergen exposure. The only relevant difference concerns the job: one (twin A) is a harbour clerical, the other (twin B) is a taxi driver.

Recently, a reassessment of asthma and allergic rhinitis has been performed. Table 1 summarizes the principal parameters

that were evaluated. The history shows that the natural course was the same both concerning the onset age and the main triggers (infections and exercise). Further, they presented OAS initially to apple, then to peach, ever at the same time. The sensitization pattern is substantially the same, as demonstrated by the cutaneous reaction grade (measures as wheal diameter). The molecular profile of sensitization, assessed by microarray (ISAC), confirmed the skin findings. It is to note that all sensitizations correspond to true allergy toward the positive allergens. It is very singular that findings are almost superimposable. This fact is consistent with the shared genetic background as monozygote twins. The psychological profile, assessed by the HADS questionnaire, is also very similar both for anxiety and depression. They regularly assume inhaled fluticasone (250 mcg b.i.d.) since more than one year. However, the few differences affect asthma both about clinical characteristics and lung function. Twin A had controlled asthma (confirmed by a good ACT level), did never use albuterol on demand, lung function and FeNO values were normal. On the contrary, twin B had partly controlled asthma consistent with 17 ACT value; lung function measurement showed mild bronchial obstruction (i.e. impaired FEV₁, FEV₁/FVC, and FEF_{25–75}); had mild eosinophilic inflammation documented by increased FeNO levels; and reported moderate use of rescue medication on demand (2–3 times/week). It is noteworthy that the assessment of breath perception by visual analogue scale (VAS) agreed with objective lung function measurement: twin A has 8, whereas twin B has 6 (the scale ranges from 0: worst breathing to 10: optimal breathing).

The plausible explanation of the poor performance of twin B could probably depend on obesity: in fact, twin B had 34.4 BMI, whereas twin A was normo-weight (BMI 24.7). The possible cause of obesity should depend on anxiety-depression as the twin B is cured by a psychiatrist for this problem. Moreover, both twins do not smoke and there is no secondhand smoking as both in the office of the clerk and into cars there is smoking ban. This issue is particularly relevant as smoking is an important cause of lung function detriment.

There is impressive evidence that asthma and obesity prevalence has world-widely increased in developed countries. Dietary aspects, alcohol consumption, physical inactivity, and stress have to be considered the main lifestyle factors affecting weight gain. Indeed, the increase in affluence, typical of the western society, may result in increased availability of food and decreased physical activity associated with stress may globally contribute to promote overweight and obesity. In addition, there is evidence that obesity and overweight are associated with an increased risk of asthma.⁹ Even though the real association between obesity and asthma is still unclear.

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Table 1
Demographic, clinical, immunological, and functional parameters in the two twins.

Parameters	Twin A	Twin B
Height (cm)	173	174
Weight (Kg)	74	104
BMI	24.7	34.4
Job	Employee	Taxi driver
Wheezing onset	2 years	2 years
Allergic rhinitis	yes	yes
Post-viral asthma	yes	yes
Exercise	yes	yes
OAS	Apple, peach	Apple, peach
SPT grasses (mm)	4	4
SPT parietaria (mm)	6	8
SPT birch (mm)	7	7
SPT mites (mm)	6	7
SPT cat (mm)	3	3
ISAC Phl p 1 (ISU)	6.1	4
ISAC Bet v 1 (ISU)	37	41
ISAC Par j 2 (ISU)	18	41
ISAC Der p 2 (ISU)	32	26
ISAC Fel d 1 (ISU)	3.1	3.7
ISAC Mal d 1 (ISU)	9.9	2.1
ISAC Pru p 1 (ISU)	4.2	4.8
Asthma control grade	Controlled	Partly controlled
ACT	22	17
Breath VAS	8	6
HADS anxiety	12	11
HADS depression	11	9
FVC (% of predicted)	102	96
FEV ₁ (% of predicted)	92	79
FEV ₁ /FVC	76.5	69.9
FEF _{25–75} (% of predicted)	66	50
FeNO (ppb)	25	32
Medication	Fluticasone 250 mcg (b.i.d.) Albuterol never	Fluticasone 250 mcg (b.i.d.) Albuterol 2–3 puff/week

Both asthma and obesity derive from genetic predisposition and environmental interactions. It is evident that asthma and obesity are mutually correlated through complex mechanisms. Whereas it is likely that asthma does not influence obesity, obesity may significantly affect asthma. The link between asthma and obesity defines two main phenotypes: one with early-onset asthma (usually atopic) worsened by obesity, the second characterized by late-onset asthma (frequently non-atopic) with prevalence in females and with neutrophilic inflammation.⁹ Of course, twin B belongs to the allergic phenotype. Anyway, both phenotypes have reduced expression of glucocorticoid α receptor: this defect may explain the corticosteroid-resistance with associated higher corticosteroids dosages, more severe symptoms, and more frequent exacerbations than non-obese asthmatics.

Three main pathways of obesity-related asthma have been conceived, including: mechanical mechanisms (fewer deep

inhalation leading to sustained BHR), inflammatory events driven by adipokines (with pro-inflammatory activity, able to amplify bronchial inflammation), and lifestyle behaviours, promoting adiposity.⁹

All these considerations allow to understand the present twin model: the partly controlled asthma in twin B most likely depend on obesity, as the twins share a common genetic and environmental foundation. The stressful job and anxiety-depression of twin B could influence his lifestyle inducing weight gain.

Therefore, the present case report may suggest that BMI assessment should be routinely considered in all patients with not or partly controlled asthma.

Conflict of interest

The authors have no conflict of interest to declare.

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