Letters to the Editors

Malignancies in Chinese patients with immunoglobulin G4-related disease

Sirs,

Immunoglobulin G4-related disease (IgG4-RD) is a systemic and chronic fibroinflammatory disease characterised by enlargement of the affected organs along with IgG4-positive lymphoplasmacytic infiltration (1). Most patients respond well to glucocorticoids. However, the pathogenesis of IgG4-RD remains unknown. A few patients with IgG4-RD could have various types of malignancies, such as lymphoma, pancreatic cancer, and prostate cancer. Previous publications have discussed the incidence and types of malignancies in IgG4-RD patients from USA (2), Japan (3, 4) and Korea (5). The viewpoint that patients with IgG4-RD have an increased risk of malignancy, has remained controversial. Hence, we aim to analyse the incidence and category of malignancy in patients with IgG4-RD in a Chinese cohort.

We enrolled patients who were admitted at West China Hospital from January 2015 to December 2017 and met the comprehensive diagnostic criteria (1) or organ-specific diagnostic criteria for IgG4-RD. We retrospectively analysed the electronic medical notes, laboratory examinations, images, pathology data and malignancy information of identified patients. Pathological confirmation was necessary for a malignancy diagnosis. Malignancies before and after IgG4-RD diagnosis were both included in present study. The standard prevalence ratios (SPRs) were calculated by dividing the standardised cancer prevalence in observed group by corresponding cancer prevalence in China, 2011 (6).

We identified 162 patients with IgG4-RD (119, definite; 28, possible; and 15, probable). The median age at IgG4-RD diagnosis was 58.5 (47–66) years old and 129 patients (79.63%) were male. Eighty-four patients (51.85%) had multiple-organ (≥2) involvement. Organs most often affected were pancreas (43.21%), hepatobiliary tract (21.60%), lacrimal gland (16.05%), salivary gland (15.43%), and lymph nodes (14.20%). The median follow-up duration was 18.5 (6.75–37) months.

We identified 11 malignancies in 11 (6.79%) patients with IgG4-RD (Table I). Gastrointestinal cancers (n=4, 36.36%) were the most common. Eight of them had a history of malignancy, and the malignancy was diagnosed in an average of 6.4 years (1.5–20.5) before the diagnosis of IgG4-RD. Malignancy was diagnosed concurrently (interval time ≤3 months) with IgG4-RD in two patients. Only one lung squamous carcinoma was diagnosed 7.4 years after an autoimmune pancreatitis (AIP) diagnosis. Age at diagnosis was significantly higher in malignancy group than that in non-malignancy group (68 *vs.* 58, p=0.021). The SPR for malignancy was 2.70 (95% CI, 1.08–5.55). After being stratified for sex, the SPRs for malignancy were 4.47 (95% CI, 1.64-9.78) and 2.55 (95% CI, 0.26–14.36) among male and female patients, respectively.

Table I. Clinical profile of Chinese patients with IgG4-related diseases and malignancy.

Patient	Sex	Age at IgG4-RD diagnosis	Duration (from malignancy to IgG4–RD /years)	IgG4-RD organ involvement	Malignancy site	Malignancy treatment
1	F	71	13.0	AIP + sclerosing cholangitis	uterus	surgery
2	M	68	3.1	AIP + sclerosing cholangitis	rectal	surgery
3	M	70	-7.4	AIP + sclerosing cholangitis	lung	/
4	M	65	0	AIP + sclerosing cholangitis	stomach	surgery
5	F	56	4.0	lung + kidney	oesophagus	surgery
6	M	75	1.6	AIP	stomach	surgery
7	M	52	2.3	sinusitis	lymphoma	surgery + chemotherapy
8	M	73	1.5	AIP + sclerosing cholangitis	prostate	surgery
9	F	60	5.5	AIP + kidney	uterus	surgery
10	M	71	0	kidney	colon (liver metastasis)	/
11	M	49	20.5	tonsil	lymphoma	radiation

In studies on Japanese and Westerners (2-4, 7-9), the percentages of malignancy in patients with IgG4-RD varied from 6% to 16%, and the most common malignancies were different. This discrepancy was partly due to inclusion criteria bias and the difference in malignancy spectrum. Almost all studies enrolling patients with IgG4-RD who had malignancy history or experienced malignancy simultaneously showed an increased risk of malignancy (2, 5, 7, 10).

However, studies enrolling patients with IgG4-RD who developed malignancy later showed disparity. Our study showed an elevated SPR (2.70) for malignancy in IgG-RD patients. supporting that patients with IgG4-RD are at a higher risk of developing malignancy. The data about malignancy that developed after the IgG4-RD onset was limited because of the short follow-up period.

It is notable that two patients were diagnosed with malignancy and IgG4-RD simultaneously. On the one hand, it suggests that IgG4-RD may likely act as a paraneoplastic syndrome. On the other hand, it reminds physicians that IgG4-RD and malignancies could develop concurrently and routine screening tests for malignancies are necessary in patients with IgG4-RD.

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