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Inflammatory Fibroid Polyps of Gastrointestinal Tract Rarely Show Increased IgG4 Expression

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Abstract

Inflammatory Fibroid Polyp (IFP) of gastrointestinal tract is characterized by concentric perivascular fibrosis and a mixed inflammatory infiltrate rich in eosinophils and also few plasma cells. IgG4-related sclerosing diseases (IgG4-RSD) are a heterogenous group of disorders described in many organs, characterized by a significant increased of IgG4+ plasma cells in a context of storiform fibrosis, obliterative vasculitis and mixed inflammatory infiltrate containing eosinophils. The histological similarities between IFP and IgG4-RSD prompted the present study in the attempt to find a possible link between IgG4 over-expression and IFP.

The expression of IgG4 and IgG was evaluated in a series of 23 cases of IFP belonging to 23 patients. All cases were reviewed by two pathologists and the histological diagnosis confirmed. Immunohistochemistry for antibodies anti-IgG, anti-IgG4, and anti-IgA was performed on all cases and the results were evaluated by two observers.

One case of IFP out of 23 (4.3%) fulfilled the IgG4-RSD histological criteria. The case did not differ histologically from the others. The patient did not present either a raised serological level of IgG4, nor other sign of IgG4-RSD.

IgG4 increased expression can be rarely observed in IFP. Steroid therapy in cases of IFP with abundant IgG4+ plasma cells, especially in patients with multiple tumors, could be considered as an alternative to surgical treatment.

Key words: Inflammatory fibroid polyp; Gastrointestinal tract; IgG4; IgG4-related disease; Immunohistochemistry

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INTRODUCTION

Inflammatory Fibroid Polyps (IFP) of gastrointestinal tract, firstly described by Vanek[1], is characterized by concentric perivascular fibrosis and a mixed inflammatory infiltrate rich in eosinophils and also few plasma cells. IFP can present as multiple tumors, and has been recently proposed as a neoplastic process, due to the discovery of activating mutations of PDGFRA gene in up to 66% of cases[2]. Despite this genetic similarity with gastrointestinal stromal tumors, the prognosis of IFP is always benign, and metastatic progression has never been reported in the literature [3]. IgG4-related sclerosing diseases (IgG4-RSD) are a heterogenous group of disorders described in many organs, characterized by a significant increased of IgG4+ plasma cells in a context of storiform fibrosis, obliterative vasculitis and mixed inflammatory infiltrate containing eosinophils[4]. The histological similarities observed between IFP and IgG4-RSD prompted the present study. The expression of IgG4 and IgG was evaluated in a series of IFP in the attempt to find a possible link between IgG4 over-expression and the development of the tumors, analogously to what has been observed for IgG4-related tumors arisen in other anatomical sites[5].

MATERIALS AND METHODS

Twenty-three cases belonging to 23 patients were investigated. All cases were reviewed by two pathologists (LM and AMC) and the diagnosis confirmed. Clinico-pathological data of the cases are listed in Table. 1. In patients with gastric lesions, Helicobacter Pylori was absent. Immunohistochemistry was performed by using the antibodies anti-IgG (polyclonal, Ventana, Ca, USA), anti-IgG4 (clone MRQ-44, Ventana), and anti-IgA (polyclonal, Ventana). Evaluation of immunohistochemical results was performed by two different observers (SL and AMC). Criteria of evaluation for IgG4-RSD were: >50 HPF IgG4+ and IgG4+/IgG+ ratio > 40% in an average of 3 HPFs, as described elsewhere[4].

Table 1
Clinico-Pathological Data f 23 Cases f IFP

Case	Gender/	Size	Anatomic	Histologic pattern	Eosinophils	Plasmacells	Lymphocytes	Fibroblastic	Storiform pattern	Other features
N#	Age	(mm)	Site	Sec.Kim et al.(8)	Proliferation					
1	F/76	10	stomach	fibrovascular	numerous	moderate	moderate	marked	yes+focal perivasc. fibrosis	
2	M/75	3	stomach	nodular	numerous	moderate	moderate	marked	no	
3	F/64	23	stomach	fibrovascular	numerous	moderate	moderate	marked	yes+perivascular fibrosis	
4	F/57	7	stomach	fibrovascular	numerous	moderate	moderate°	marked	yes	
5	M/64	16	ileum	sclerotic	numerous	few	few	marked	no	
6	M/67	35	ileum	sclerotic	moderate	moderate	moderate	mild	no	
7	F/46	23	stomach	sclerotic	numerous	moderate	moderate°	marked	yes+focal perivase. fibrosis	
8	F/83	20	stomach	fibrovascular	numerous	moderate	moderate°	marked	yes+perivasc. fibrosis	
9	F/53	10	stomach	fibrovascular	numerous	moderate	moderate°	marked	yes+focal perivasc. fibr	
10	M/45	7	stomach	fibrovascular	numerous	few	few	marked	yes	
11	M/52	27	ileum	edematous	moderate	numerous	numerous	moderate	mild+perivascular fibrosis	ulceration
12	F/47	23	ileum	fibrovascular	numerous	few	few	marked	yes+focal perivasc. fibrosis	
13	F/68	8	stomach	sclerotic	numerous	moderate	few	mild	no	ulceration
14	F/58	25	large bowel	edematous	numerous	moderate	moderate°	marked	no	ulceration
15	F/72	30	ileum	edematous	numerous	few	few	marked	no	ulceration
16	F/81	23	ileum	fibrovascular	rare	rare	rare	marked	yes	floret cells
17	M/74	8	stomach	nodular	unmerous	numerous	numerous	marked	mild+perivascular fibrosis	
18	F/40	20	large bowel	fibrovascular	numerous	numerous	numerous	marked	yes+perivasc. flbrosis	
19	M/73	15	stomach	fibrovascular	numerous	numerous	numerous	marked	yes+perivase. fibrosis	
20	F/44	5	stomach	fibrovascular	numerous	moderate	moderate	marked	yes	
21*	F/72	30	stomach	fibrovascular	numerous	moderate	moderate	marked	yes+perivase. fibrosis	floret cells
22	F/83	20	stomach	edematous	numerous	moderate	moderate°	moderate	yes+perivase. fibrosis	
23	F/65	15	stomach	edematous	numerous	moderate	moderate°	marked	no	

Note. °with lymphoid follicles, *case fulfilling criteria sec.Cheuk and Chan(5).

RESULTS

One case of IFP out of 23 (4.3%) fulfilled the IgG4-RSD histological criteria. Two other cases showed a slightly increased number of IgG4+ plasma cells. Most cases displayed rare IgG4+ plasma cells, usually in a background of few IgG+ plasma cells. In the case with increased IgG4+ plasma cells, both IgG+ and IgG4+ plasma cells were concentrated in the stroma of the polyp, whereas very few IgA+ plasma cells were observed (Figure 1). From the histological point of view, the cases with significant or slightly increased number of IgG4+ plasma cells did not differ from the others. The patient presenting IFP with significantly increased IgG4 expression did not show elevated serological level of IgG4, nor other signs of IgG4-RSD.

DISCUSSION

Few cases of inflammatory conditions and tumors, characterized by significant number of IgG4+ plasma cells, have been reported in GI tract, raising the possibility

of an IgG4-RSD. Two cases reported in the esophagus, presented as esophagitis with stricture. In one patient a raised IgG4 serum level was also found; none of the patients presented other signs of IgG4-RSD[6-7]. Gastric involvement has been reported as thickening and multinodularity of mucosa[8], or multiple polyps [9]; in both cases the patients presented also autoimmune pancreatitis (AIP). Few other cases presenting as pseudotumors were described showing high number of IGg4+ plasma cells, but none of the patients had elevated serum level of IgG4 nor other IgG4-RSD[10-13]. Two cases of gastric ulcer were reported, one of the patients presenting a raised serum level of IgG4, but no other IgG4-related manifestations[14-15]. An IgG4-related pseudotumor has been described in major duodenal papilla[16], and in the ileal conduit after surgery for urinary bladder cancer[17], again not associated to other IgG4-RSD. A solitary jejunal ulcer has been described as an IgG4-RSD, in a patient presenting also a raised serum level of IgG4[18]. Involvement of colon by IgG4+ plasma cells has been reported in a polyposis of a patient suffering from AIP[19]; two other cases of colonic IgG-4 fibrosclerosing nodular lesions appeared not related to other IgG4-RSD[12]. Recently, a significant increase of IgG4 positive plasma cells has also been observed in the colonic polyp of a patient with Cronkhite-Canada syndrome[20].

It is well known that different types of inflammatory lesions in the gastrointestinal tract, such as Inflammatory Bowel Disease, can present increased, but not significant, number of IgG4+ plasma cells[21]. Based on the most recent consensus, a diagnosis of IgG4-RSD should comprehend histopathological criteria, elevated serum l*Note*.evel of IgG4, involvement of other organs, and response to steroid therapy[5].

The finding of a clinically relevant mass with abundant IgG4+ plasmacellular infiltrate has been proposed as the minimum criterion to make a diagnosis of IgG4-related GI disease[22]. The observation of a significant number of IgG4 positive plasma cells fulfilling the criteria for IgG4-RSD in only one case of our series of 23 IFP's, suggests that an IgG4-related pathogenesis for this lesion is unlikely. Nevertheless, rare cases showing a high content of IgG4 positive plasma cells can be encountered. In such cases, steroid therapy could be reasonably offered[22], thus avoiding surgical treatment. Interestingly, an ampullary pseudotumor resulted cured after steroid therapy for AIP[23], whereas cases of IFP in patients suffering from Helicobacter Pylori infection were reduced in volume by treating the patients with eradication therapy[24-25].

In conclusion, the histological entity currently called IFP is not only characterized by genetic mutations, as observed in a large percentage of cases[2], but few cases could be also related to infections or immunological processes, suggesting different therapeutic approaches. More cases should be studied to detect the real incidence and significance of IgG4 expression in IFP.

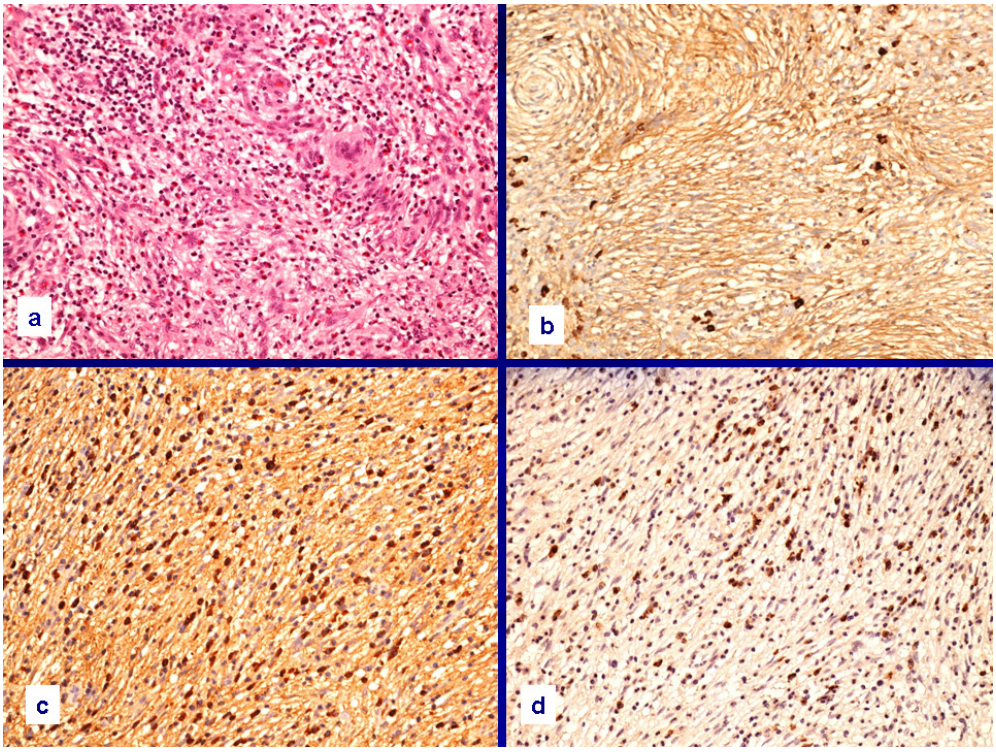

Figure 1
A Case of IFP of the Stomach (a), Showing Few IgA+ Plasma Cells (b), and a High Number of IgG+ (c) and IgG4+ Plasma Cells (d)

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