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Solid Tumour Section

Short Communication

Inflammatory fibroid polyps

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Identity

Other names

Vanek's tumor

Note

Inflammatory fibroid polyps (IFP) are benign mesenchymal tumors which originate from the submucosa of the stomach or the small bowel. IFP occur rarely in the colon and in the esophagus.

In 1949 the Czech pathologist Josef Vanek reported on six cases of gastric lesion which he referred to as gastric submucosal granuloma with eosinophilic infiltration: "A peculiar lesion was observed consisting of more or less loose collagenous tissue with fibroblasts, lymphocytes, and eosinophilic polymorphonuclear leukocytes. The pathologic tissue thus composed appeared as a circumscribed focus in the submucosa, spreading toward the mucosa of the stomach. Macroscopically, it caused a bulging of the mucosa, and in some cases even a polypous formation." (Vanek, 1949).

At the same time the German pathologist Franz Bolck noticed these lesions, too, and referred to them as granuloblastoma of the stomach (for review see: Bolck and Katenkamp, 1982). The term inflammatory fibroid polyp was introduced four years after the initial description (Helwig and Ranier, 1953). Since then several hundred reports, mainly case series and reports on single cases, have been published which predominantly focussed on clinical and morphologic aspects. Notably, inflammatory fibroid polyps have been regarded as reactive lesions for decades. In 2008, however, the neoplastic nature of IFP became evident by the detection of activating PDGFRA mutations in these tumors (Schildhaus et al., 2008).

Classification

Note

Inflammatory fibroid polyps are mesenchymal tumors of unknown lineage.

Since some tumors tend to show considerable collagen production some authors have postulated a fibroblastic lineage. IFP are clearly distinct from gastrointestinal stromal tumors by their morphology, submucosal origin and clinical behavior although both entities share common mutational subtypes of the PDGFRA gene.

IFP are benign. So far local recurrences have been described only anecdotally.

No convincing case with invasive growth or aggressive outcome has been reported.

Classification

Benign mesenchymal tumor of the gastrointestinal tract.

Clinics and pathology

Phenotype / cell stem origin

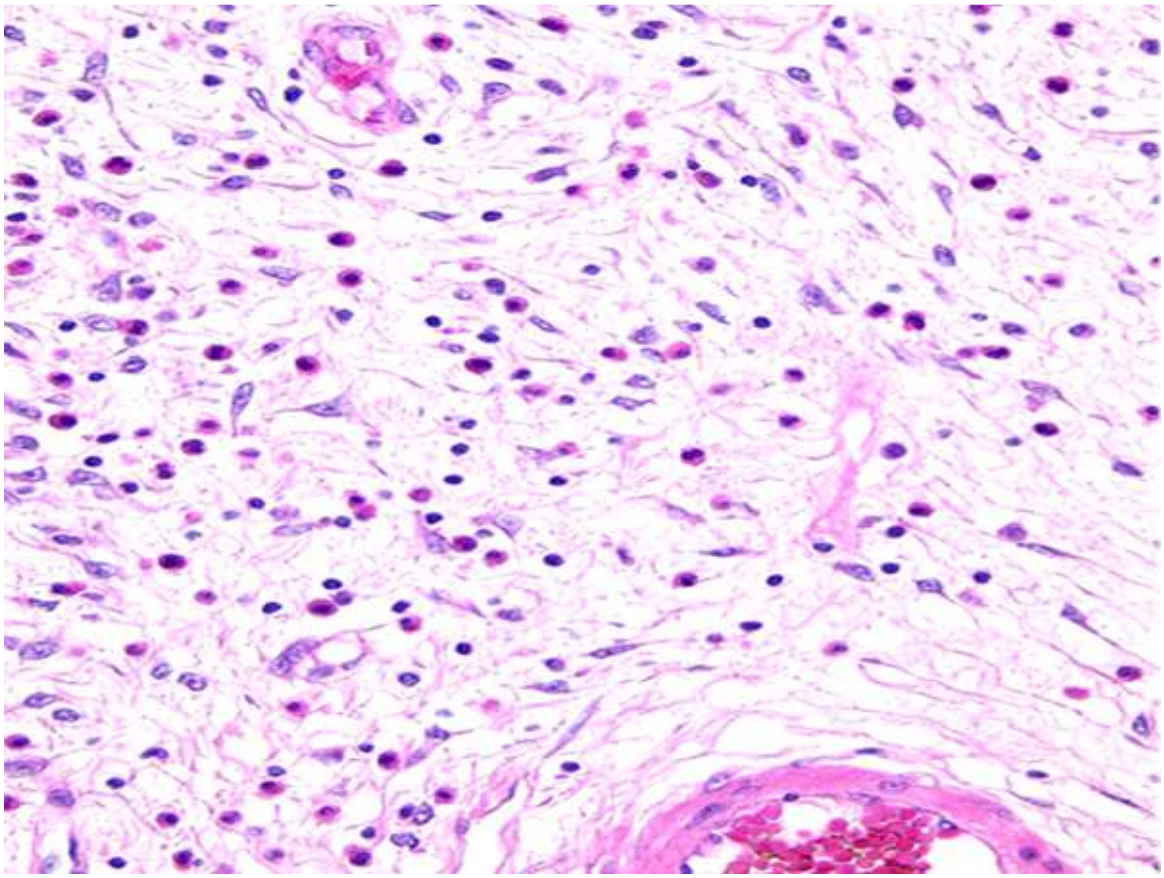
A progenitor cell of inflammatory fibroid polyps has not yet been established.

However, Lasota et al. have discussed whether specialized PDGF dependent mesenchymal progenitor cells in the so-called villus clusters might represent progenitors (Lasota et al., 2009).

Etiology

Historically, IFP have been thought to represent a reactive inflammatory lesion.

It was assumed that IFP might be associated for example with helicobacter infection or type A gastritis.



Inflammatory fibroid polyp of the stomach. Histological appearance of the "classic" (gastric) type with heavy inflammatory infiltrate.

After discovery of the activating PDGFRA mutations in these tumors it became apparent that IFP represent true neoplasms which are - so far as we know today - obviously driven by activating mutations in the PDGFRA gene.

Epidemiology

Inflammatory fibroid polyps are rare lesions which affect predominantly adults. Notably, the mean age of patients with gastric tumors is significantly higher compared with IFP of the small bowel (72 years vs. 53 years) (Huss et al., 2012). IFP account for 0.1 - 3.0 % of all gastric polyps (Carmack et al., 2009).

Clinics

Inflammatory fibroid polyps arise from the submucosa and tend to form polypoid lesions. They occur predominantly in the stomach (mainly in the antrum region). Most IFP remain undiagnosed for a long time or are incidental findings at endoscopy. Larger polyps tend to erode and ulcerate superficially with local bleeding representing the most common clinical symptom. Very rarely large tumors of several centimeters size have led to obstruction of the pylorus or the upper gastric sphincter. Most inflammatory fibroid polyps, however, are small measuring only few millimeters.

IFP of the small bowel may also give rise to local bleeding. Major complications in this location, however, are intussusceptions and invaginations. At least in adolescents and adults, IFP are a frequent cause of this severe and acute disease.

Inflammatory fibroid polyps are benign and do not recur nor metastasize.

Pathology

Inflammatory fibroid polyps are mostly small lesions of only few millimeters size. We have, however, seen some tumors of up to 10 centimeters (Huss et al., 2012). IFP characteristically arise from the submucosa and grow through the lamina propria towards the surface of the mucosa where typically an ulceration is found.

IFP consist of bland spindled cells which are characteristically arranged in whorls or in an onion skin like fashion around blood vessels or mucosal glands. The matrix consists of fine fibrillar collagen but might also be collagen-rich.

The "classic" (or gastric) type which was originally described by Josef Vanek is characterized by a heavy inflammatory infiltrate which is rich in eosinophilic granulocytes. These lesions show a plenty of spindle cells but only little collagen.

We and others have shown that there is another morphological subtype ("intestinal type") which, in contrast, is paucicellular and collagen-rich.

Both cellular elements, fibroblastic spindle cells and inflammatory infiltrate, are less numerous. These tumors tend to be larger than those of the gastric type (Huss et al., 2012).
Outside of ulcerations no necroses are found. There is no considerable proliferative activity as mitoses of the spindle cell are almost never seen and Ki67 is below 1%.
Immunohistochemically, the spindle cells are mostly positive for CD34 but this feature may be absent especially in the intestinal type. PDGFRA expression is frequently found. Immunostains for KIT, DOG-1 as well as S100 and EMA are consistently negative. This may be important in the differential diagnosis of gastrointestinal stromal tumors, perineuriomas and other spindle cell lesions of the gastrointestinal tract.

Treatment

Most inflammatory fibroid polyps can be endoscopically removed. Only rarely surgery is necessary.

Prognosis

Benign tumor, no risk for an aggressive clinical behavior. Patient may, however, suffer from severe disturbances due to mucosal bleeding, local obstruction or intussusception.

Genetics

Note
Activating mutations in exon 12, 14 and 18 of PDGFRA (platelet derived growth factor alpha) are the only known genetic alterations in inflammatory fibroid polyps.

Genes involved and proteins

PDGFRA

Location
4q12
Note
In the first genetic study of inflammatory fibroid polyps 16 out of 23 lesions showed mutations in PDGFRA (Schildhaus et al., 2008). This finding could be confirmed shortly after the first description by a second independent study (Lasota et al., 2009), and meanwhile four series and one case report with molecular analyses have been published covering a total of 145 IFP (for review see: Huss et al., 2012). The frequency of mutations among the case series ranged from 21.7% to 69.6%, obviously at least partially depending on the methodology used. Additionally, the tumor cell content may contribute to differences in the frequency of mutations since many IFP contain only few lesional cells in a background of heavy inflammation or are considerably small.

Activating PDGFRA mutations occur in exons 12, 14 and 18. A genotype - phenotype correlation could be established in terms of tumor location as gastric IFP harbor significantly more frequent exon 18 mutations. Exon 12 mutations are, however, associated with small bowel lesions. So far, only
two cases with exon 14 mutations have been described, one originating from the small bowel the other from the stomach.
Mutational types vary; there are point mutations as well as duplications and complex delins mutations. One mutational hot spot in IFP includes codons 567-571 of PDGFRA (exon 12) with p.566_571delinsR representing the most frequent subtype. Another frequently found mutation is a single nucleotide substitution in exon 18 (p.D842V).

Result of the chromosomal anomaly

Hybrid Gene

Note
Not known.

Fusion Protein

Note
Not known.

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