Daum O., Grossmann P., Vanecek T., Sima R., Mukensnabl P., Michal M. (2006): Diagnostic morphological features of PDGFRA-mutated gastrointestinal stromal tumors: Molecular genetic and histological analysis of 60 cases of gastric GISTs. Ann. Diagn. Pathol. In Press

Summary

In this study, 60 gastrointestinal stromal tumors (GISTs) of the stomach were analyzed to elucidate the possible relation of their morphology to mutation status of *KIT* and *PDGFRA* genes. The patients included 27 men and 33 women with a mean age of 63,8 years (range 12 to 92). Only one tumor occurred before the age of 21 years. *KIT* mutations were detected in 31 cases (51,7%), *PDGFRA* mutations in 22 cases (36,7%), and seven cases (11,7%) were *KIT* and *PDGFRA* wild type. When the mutation status was correlated with histological features of the tumors, epithelioid or mixed epithelioid/spindle cell pattern and mast cell infiltration were found as the most reliable signs of *PDGFRA* mutation. Neoplastic rhabdoid cells and multinucleated giant cells, also previously reported as features of *PDGFRA* mutated GISTs, seemed to be less specific but still helpful markers in our study. Finally, tumor infiltrating lymphocytes and myxoid stroma do not seem to be valuable histological signs.

Daum O., Klecka J., Ferda J., Treska V., Vanecek T., Sima R., Mukensnabl P., Michal M. (2005): Gastrointestinal stromal tumor of the pancreas: case report with documentation of KIT gene mutation. Virchows Arch. 446, 470-472

Summary

Gastrointestinal stromal tumor (GIST) is the most common mesenchymal tumor of the gut. Although it was occasionally described in some extragastrointestinal sites, such as gallblader, urinary bladder, omentum and mesentery, there are no reports on its occurence in the pancreas

until the end of 2003. This report describes a gastrointestinal stromal tumor of the pancreatic head in a 70-year-old woman treated by Whipple´s hemipancreatoduodenectomy. The tumor was well demarcated, rubbery, white, with central cystic changes. Its greatest diameter was 5 cm. Histologically, it was composed predominantly of spindle cells with occasional perinuclear vacuoles. Skeinoid fibers were readily discernible. Perivascular hyalinization, myxoid changes, necrotic foci and cystic degeneration occured in central parts of the tumor. Mitotic index was 2 mitoses/50 HPF. The lesion showed immunocytochemical reactivity for vimentin, KIT protein, smooth muscle actin and muscle specific actin. Molecular genetic evaluation revealed deletion of 6 base pairs in exon 11 of c-kit. Finally, the tumor was diagnosed as GIST of the head of the pancreas. To the best of our knowledge, there have been no other properly documented cases of pancreatic GIST reported in the world literature.

Daum O., Vaněček T., Šíma R., Michal M. (2006): Gastrointestinální stromální tumor: současný pohled. Klinická onkologie 19, 203-211

Summary

Gastrointestinal stromal tumor is the most frequent mesenchymal tumor of the alimentary tract, currently being defined as a tumor composed of spindle and/or epithelioid cells presumably differentiating towards interstitial cells of Cajal. The majority of these tumors are KIT – immunoreactive and almost all carry mutated c-kit or *PDGFRA* gene encoding two transmembrane class III tyrosinkinases. The most frequent location of gastrointestinal stromal tumor is stomach followed by other sites of gastrointestinal tract. Occasional sites of occurrence are mesenterium, omentum, retroperitoneum, gallbladder, urinary bladder, pancreas and vagina. Light microscopic examination of slides stained with haematoxylin and eosin is highly reliable in most cases. Useful ancillary diagnostic techniques are immunohistochemical investigation with antibodies against KIT protein

(CD117) and detection of mutations of either c-kit or *PDGFRA* genes. Nevertheless, negative results do not exclude histologically proven diagnosis. All gastrointestinal stromal tumors should be regarded as potentially malignant with risk of aggressive behavior being determined on the basis of mitotic count and the largest diameter of the tumor. Mutational status of the neoplasm serves as a predictor of therapeutic response to imatinib mesylate.

Daum O., Hes O., Vanecek T., Benes Z., Sima R., Zamecnik M., Mukensnabl P., Hadravska S., Curik R., Michal M.(2003): Vanek´s tumor (inflammatory fibroid polyp). Report of 18 cases and comparison with three cases of original Vanek´s series. Ann. Diagn. Pathol. 7, 337-347

Summary

Eighteen cases of Vanek's tumors are presented. The patients included nine men and nine women between the ages of 45 and 93 years (mean age 66,2 years). Nine cases were clinically diagnosed as polyps of the gastric antrum, five cases as polyps of the stomach (not otherwise specified), one polyp was located in the ileum and the three remaining ones in the small intestine (not otherwise specified). The thirteen polyps with the available information of their size measured from 0,4 to 5 cm in the greatest diameter (mean 2,2 cm). Immunohistochemically, the affections were positive for vimentin (18/18) and CD34 (15/18). All the cases negative for CD34 also lacked concentric onion-skin-like formations of the spindle cells around glands and vessels. The different immunophenotype and the absence of concentric formations could be explained by the existence of two different lesions commonly designated as Vanek's tumor (inflammatory fibroid polyp) or by the hypothesis of various evolutional stages. In the differential diagnosis it is important to distinguish namely eosinophilic gastroenteritis, gastrointestinal stromal tumor, inflammatory pseudotumor, hemangioendothelioma and hemangiopericytoma. In contrast to gastrointestinal stromal

tumors, genetically no substitution, deletion or insertion occurred in c-kit exon 11 in all analyzed samples. Likewise, no deletion or insertion in part of c-kit exon 9 was observed.

Daum O., Vanecek T., Sima R., Curik R., Zamecnik M., Yamanaka S., Mukensnabl P., Benes Z., Michal M. (2004): Reactive nodular fibrous pseudotumors of the gastrointestinal tract: report of 8 cases. Int. J. Surg. Pathol. 12, 365-374

Summary

Eight cases of reactive nodular fibrous pseudotumor of the gastrointestinal tract are presented. The patients included six men and two women between the ages of 1 and 68 years (mean age 41.5 years). Five of the investigated lesions were located in the large bowel. Of these, two originated in the sigmoid colon, one in the cecum, one in the appendix and one in the large bowel not otherwise specified. The remaining three tumors involved the small intestine. The tumors´ size reached from 3 to 10 cm in the greatest diameter (mean 6,2 cm). Histologically, they were composed of stellate or spindle cells resembling fibroblasts arranged haphazardly or in intersecting fascicles, embedded in a collagen-rich stroma with sparse intralesional mononuclear cells frequently arranged in lymphoid aggregates. Immunohistochemically, the affections were positive for vimentin (7/7), smooth muscle actin (8/8), muscle specific actin (5/7), cytokeratins AE1/AE3 (6/7) and CAM 5.2 (1/7), and antigen CD68 (1/7). No case (0/8) reacted positively with antibodies to CD117 (c-kit). Genetically, no substitution, deletion or insertion occurred in exon 11 in all analyzed samples. Likewise, no deletion or insertions in part of exon 9 were observed. Ultrastructurally, the tumor cells revealed features typical of myofibroblasts. According to the morphologic, immunohistochemical and ultrastructural features mentioned above, especially to the positivity of low-molecular weight cytokeratins,

we propose this lesion to be related to a proliferation of multipotential subserosal cells rather than ordinary myofibroblasts or fibroblasts.