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doi: 10.1136/jcp.2005.033555

Accepted 10 December 2005

Competing interests: None declared.

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Neuroendocrine tumour cells in the wall of a splenic artery aneurysm

Neuroendocrine tumours are reported from the alimentary and respiratory tracts. A case of a 57-year-old man with an unsuspected histopathological finding of neuroendocrine tumour

cells in the wall of a splenic artery aneurysm is reported.

Visceral artery aneurysms are uncommon but clinically important owing to the risk of rupture and of intra-abdominal bleeding.¹ There are several possible aetiologies, atherosclerosis being one, and often the cause is unknown or at least not stated.¹ The case of a patient with two visceral artery aneurysms and unsuspected histopathological finding is reported.

Case report

A 57-year-old man presented with a 24 h history of increasingly severe upper abdominal pain. As an infant, he was operated on for an open Botalli duct. At the age of 20 years, he was conservatively treated for a pyloric ulcer. For the previous 2 years, he had been taking drugs for depression. On admission to hospital, his abdomen was tender with general guarding. A contrast-enhanced CT scan showed a splenic artery aneurysm and a mass in the pyloric region suspected as a ruptured visceral aneurysm. Both lesions were about 7 cm in diameter. An emergency laparotomy showed free blood in the peritoneal cavity and an upper right retroperitoneal haematoma.

A ruptured aneurysm of the right gastropiploic artery was resected en bloc with a part of the antrum and colon. Histopathological examination showed atherosclerosis in the wall of the aneurysm and chronic gastritis in the antrum. An elective operation was performed 4 months later and the splenic artery aneurysm repaired by proximal and distal ligation. A representative part of the splenic artery aneurysm was resected and fixed in formalin for histopathological examination.

Blood and urine samples were obtained postoperatively for hormonal and polypeptide evaluation (table 1). Values for plasma chromogranin A and urinary 5-hydroxyindoleacetic acid were slightly increased. The increased level of serum gastrin was explained by the patient's chronic gastritis.

Further investigations, including upper gastrointestinal endoscopy, colonoscopy, contrast x ray investigation of the small intestine and MRI (Octrescan)-somatostatin receptor scintigraphy were performed and found to be normal.

A capsule endoscopy showed two polypoid tumours located in the jejunum. A third laparotomy was performed 10 months after the first operation with peroperative endoscopy of the small intestine. The polypoid tumours were benign lymphangiomas. The appendix was normal at inspection.

Figure 1 Discrete finding of some divergent cells in small groups and rows in the muscularis layer of the splenic artery aneurysm wall, suggesting tumour impression.

Figure 2 Chromogranin staining of tumour cells in the wall of a splenic artery aneurysm.

Pathological findings

The histopathological examination of the resected part of the splenic artery aneurysm showed atherosclerosis, fibrosis and chronic inflammation. Furthermore, the microscopical examination showed a discrete finding of some divergent cells in small groups and rows in the muscularis layer of the aneurysm wall, suggesting tumour impression (fig 1).

Immunohistochemical staining of the tumour cells showed positivity for cytokeratin AE1/AE3 (DakoCytomation, Glostrup, Denmark), synaptophysin (DakoCytomation) and chromogranin (Ventana Medical Systems, Arizona, USA, fig 2), supporting the diagnosis of a neuroendocrine foregut type tumour. Immunohistochemical staining of tumour cells was negative for serotonin (DakoCytomation) and therefore the cells were not classic carcinoid tumour cells.

Table 1 Biochemical tumour markers

Samples	Observed value	Reference value
s-CEA	<0.5 µg/l	<5 µg/l
s-Insulin	79.2 pmol/l	<206 pmol/l
s-C-peptide	0.5 nmol/l	0.36–1.7 nmol/l
s-Gastrin	166 pmol/l	12–53 pmol/l
p-Glucagon	40 pmol/l	<60 pmol/l
p-VIP	<5 pmol/l	<15 pmol/l
Fp-chromogranin A	7.3 nmol/l	<4 nmol/l
Fp-chromogranin B	1.5 nmol/l	<2 nmol/l
tu-5-HIAA	47 µmol/day	2–33 µmol/day

p-VIP, p-vasoactive intestinal peptide; s-CEA, s-carcinoembryonic antigen; tu-5-HIAA, total urinary 5-hydroxyindoleacetic acid.

Comments

According to a new classification by the World Health Organization, the term "neuroendocrine tumours" is recommended instead "carcinoid". Neuroendocrine tumours belong to a heterogeneous group of tumours affecting almost the entire alimentary tract as well as other organs such as the lungs and thymus.² The traditional term "carcinoid tumour" is restricted to the subtype of serotonin-producing neuroendocrine tumours. Neuroendocrine tumours are neoplasms that arise from mature endocrine cells or their stem cells. Our patient had neuroendocrine tumour cells identified in the wall of a splenic artery aneurysm. The diagnosis was based on characteristic morphological and immunohistochemical findings. This tumour type is obviously extremely rare, as a MEDLINE search did not reveal any previously published case of neuroendocrine tumour cells in the wall of an artery nor in an artery aneurysm.

Aneurysms of visceral arteries are rare, often of unknown aetiology. In contrast to other intra-abdominal aneurysms, atherosclerosis is rarely the primary causative factor for splenic artery aneurysm, but considerable evidence exists to implicate hormonal and local haemodynamic factors in the development of these aneurysms.³ An association between carcinoid tumours and thoracoabdominal aneurysm has been reported previously.⁴

It can only be speculated whether neuroendocrine tumour cells could produce products that initiate local changes in the wall of the artery with subsequent aneurysm development. However, the most likely explanation of the finding in our patient is that the neuroendocrine tumour cells represent a micrometastasis of a still undiagnosed neuroendocrine tumour. The future strategy in this case will be reinvestigation.

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doi: 10.1136/jcp.2005.033159

Accepted 12 September 2005

Competing interests: None declared.

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SHORT REPORTS

The divergent morphological classification of variant lymphocytes in blood smears

An examination of a blood smear may be requested by physicians or initiated by laboratory staff as a diagnostic aid when a lymphoproliferative disorder or mononucleosis is suspected.¹ The classification of lymphocyte disorders is complex because there are various manifestations of these disorders.^{2,3} Three major groups can be distinguished: reactive lymphocytosis, premalignant neoplastic disorders of lymphocytes and neoplastic disorders of lymphocytes.⁴ Lymphocyte disorders may be accompanied by abnormal lymphocyte morphology; therefore it is important to recognise and report abnormal lymphocytes, such as atypical lymphocytes and lymphoblasts. The ability of individual technicians, however, to recognise abnormal lymphocytes is consistently quite poor.⁵ There are no standardised definitions regarding the morphology of the various cells, and interpretation is based on individual experience and dependent on the availability of additional clinical information. Often, transitional forms between lymphocytes and plasma cells are seen in the blood of patients with viral infections. These cells are variously known as atypical lymphocytes, lymphocytoid plasma cells or plasmacytoid lymphocytes.⁶ The so-called atypical lymphocyte is a non-neoplastic lymphocyte seen in the peripheral blood, and appears to be a non-specific response to stress from a variety of disorders.⁷ Small lymphocytes become larger in size and become capable of dividing. These atypical lymphocytes vary in morphology and surface markers.^{8,9} Hoagland developed criteria for diagnosis of infectious mononucleosis comprising $\geq 50\%$ of the white blood cell differential, with atypical lymphocytes accounting for $\geq 10\%$ of the total white blood cell count.¹⁰ The morphology of lymphoblasts is even more complicated, as morphological appearance varies from small cells with scanty cytoplasm and

coarse chromatin to large cells with an abundance of vacuolated cytoplasm and fine chromatin.¹¹

The morphological assessment of the peripheral blood smear remains a valued diagnostic tool,¹ despite the considerable interobserver variation in interpretation. New techniques such as automated recognition systems may reduce the microscopic review of blood films in the near future.¹² Nevertheless, the relevance of the morphological evaluation of abnormal lymphocytes can be questioned, considering the large variation in reported results.

In this letter we show the general inconsistency in reporting whether an abnormal lymphocyte is (non-neoplastic) reactive, neoplastic or an artefact.

Methods

From a blood smear of an orthopaedic patient (female, age 3 years) with a lymphocytosis which was normal for a child of that age, 100 white blood cells were randomly selected, microphotographed and processed in a PowerPoint presentation. This PowerPoint presentation was sent to 157 different hospital laboratories in The Netherlands and a leucocyte differential was requested. All participants were asked to differentiate the lymphocytes into normal lymphocytes, atypical lymphocytes, plasma cells, prolymphocytes or (lympho)blasts. Participants did not have any information of the patient.

All results were processed in Excel and for each laboratory and individual technician the mean differential was calculated. For each lymphocyte subtype the degree of concordance was calculated.

Results

Of the 157 laboratories, 114 responded (73%) with a total of 671 individual results. The overall mean lymphocyte count (including sub-cell types) was 56%. For 7 cells there was a concordance of $>90\%$ for normal lymphocytes (fig 1A), which means that more than 90% of the individual observers called these cells normal lymphocytes. For the other 49 lymphocytes there was no concordance in subtyping. In the majority, lymphocytes (29 cells) were classified as normal or atypical (fig 1B). One cell (fig 1C) was classified as a normal lymphocyte or a plasma cell. Nine cells were classified as normal or atypical or prolymphocyte (fig 1D) and two cells as normal or

Figure 1 Examples of the different lymphocytes. Lymphocytes classified as: (A) lymphocyte with $>90\%$ concordance; (B) normal or atypical; (C) normal or plasma cell; (D) normal, atypical or prolymphocyte; (E) normal, atypical or plasma cell; (F) normal, atypical, prolymphocyte or plasma cell; (G) normal, atypical, prolymphocyte or blast; (H) normal, atypical, prolymphocyte, plasma cell or blast.