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Treatment of mesenteric vein thrombosis

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Of the various causes of intestinal ischaemia, for the clinician mesenteric venous thrombosis is probably the most problematic one, because of its slower progression and less dramatic clinical picture than when the cause is arterial. It was not until 1935 it was recognized as a separate cause for mesenteric ischaemia and thereby differentiated from arterial occlusion (10, 28). Although more prolonged and symptomatically less distinct, the various clinical phases are similar, and the differential diagnosis is important to be aware of when dealing with especially elderly patients with “acute abdomen”. However, it is also well known in younger patients with risk factors such as thrombophilias, use of contraceptive pills etc.

An obvious problem with a disorder of such a low incidence, it must be made clear that existing treatment options and strategies are based on clinical judgement and experience together with pathophysiological understanding of the disease process, and randomized trials comparing various therapeutic modalities are hardly to be expected. Moreover, when the process has gone so far as to bowel necrosis, resection of the affected segment is the only solution. The primary aim of treatment must be to avoid the pathological process extend thus far, and this requires an early diagnosis before transmural gangrene, perforation and peritonitis. Once the diagnosis is established treatment must be instituted without delay.

Anticoagulant therapy

That manifest venous thromboembolism (VTE) must be treated was demonstrated by Barritt and Jordan in 1960 in their classical randomized study (6). The natural history of untreated symptomatic VTE is not well known, but their landmark randomized study in patients with clinically diagnosed VTE clearly showed that if patients do not receive anticoagulant therapy, approximately 25% will have a fatal recurrence, while another quarter of patients will experience a recurrence that is not fatal. This study together with earlier uncontrolled trials on the use of heparins, with or without vitamin K antagonists, was the basis for accepting anticoagulant therapy in the treatment of VTE.

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Treatment of mesenteric vein thrombosis has a similar aim as treating venous thrombosis in other locations, that is to stop extension of the thrombotic process and give room for the “normal” fibrinolytic activity of the organism. This means rapid heparinization, as soon as there is a diagnosis. The immediate effect can be obtained both with unfractionated heparin in therapeutic doses or with one of the low molecular weight heparins. The practical experience with the latter in this specific clinical situation is, however, limited (22) and probably many patients are treated with continuous infusion of unfractionated heparin to prolong the activated partial thromboplastin time by two to three times normal. However, there is no reason to believe that low molecular weight heparins in treatment dosages should not be as effective.

However, in a series of 121 patients with splanchnic vein thrombosis followed for 41 months recanalization was observed in 45% with anticoagulation treatment and apparently protected from recurrence, which occurred in none of the treated patients and in around 18% of those not treated with anticoagulation treatment (5). In a retrospective study of portal or mesenteric venous thrombosis recanalization occurred in 25 of 27 patients given anticoagulation but in

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non of two that did not receive anticoagulation (9). Although the rate of spontaneous recovery of venous patency is not known, these studies suggest that anticoagulant therapy increases the recanalization may be up to 80 %, and that is also in agreement with recent published consensus statements that recommend long term treatment for mesenteric vein thrombosis and even in cases with prothrombotic risk factors life long treatment with anticoagulants should be considered (25, 29). In general, patients with VTE on anticoagulant therapy with LMWH have a bleeding frequency of around 1% compared to warfarin that could be as high as 3-4% per year or higher in certain patient groups (26, 27). The definition of serious bleeding according to the International Society on Thrombosis and Haemostasis (ISTH) is: fatal outcome, bleeding in a critical organ, or a drop in haemoglobin greater than 20 g/L and requires blood transfusion (27). This problem with serious bleeding, warrants education about risk factors for bleeding both in general and especially in VTE patients. Different risk prediction models have been developed both for VTE patients and patients with atrial fibrillation and anticoagulant therapy, and are summarized in Table 1 (11, 17, 27).

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Anticoagulation with a vitamin K antagonist could be started immediately at heparinization, aiming at an INR between 2.0-3.0, but if there is a possibility that surgery could become necessary, it is better to wait and use heparin with its shorter half life and therefore less bleeding risk. It is easier to handle intra- and postoperatively

One problem with anticoagulation (or thrombolysis for that matter) is that there could be a bleeding in the bowel, when the necrotic mucosa is expelled. This possibility must not delay the anticoagulation, however, and has to be handled if and when it occurs.

The optimal duration of anticoagulant treatment is actually not known but the recurrence rate is quite substantial (16), and we recommend six months, whereafter a new decision must be taken whether or not to continue and mostly the decision is treatment on long-term basis with re-evaluation of the therapy yearly (25, 29). During this period there must have been a reasonable investigation aiming at identifying the possible cause of the mesenteric vein thrombosis, the extent of the investigation being motivated by the age and condition of the patient, comorbidities etc. In a younger patient with an identified thrombophilia for instance, indefinite anticoagulation must be considered and discussed with the patient. The longer the treatment the more delicate is the decision how to balance the beneficial antithrombotic effect against the potential risk of haemorrhagic complications.

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A non-operative approach with anticoagulation as indicated above can be successful in more than 90% of cases (8).

Thrombolysis and other endovascular treatments.

Thrombolysis is an option, when it is considered important to rapidly get rid of the thrombotic burden. Thrombolysis can be given as a systemic treatment or preferably – to keep the doses down and minimize the bleeding risk – as an intrathrombotic treatment using a transhepatic portography to place the catheter in the thrombus (4). Thrombolysis has also been given locally into the superior mesenteric artery to increase the concentration in the actual anatomic segment (2). Thrombolysis has moreover been used in combination with various percutaneous thrombectomy devices (12, 24, 31). Therefore the clinical observation must be very rigorous with a liberal indication for exploration not to miss a bowel gangrene. Some authors advocate start of thrombolysis within 24 hours to be successful (13). Direct aspiration thrombectomy without thrombolysis has also been reported successful (21).

Surgery

The decision to perform surgery should be based on clinical grounds, that is patients developing peritonitis, localized or general. Then immediate exploration is indicated. The aim with surgery – if laparotomy is considered necessary– is two-fold. First, it is possible to make a venous thrombectomy through the superior mesenteric vein using a Fogarty catheter-technique in combination with manually squeezing or milking out thrombotic material, which usually is localized very distally in small veins. The mesenteric vein is easiest reached, where it goes parallel and right to the artery at the lower margin of the pancreas, the transverse colon being lifted superiorly. Successful venous thrombectomy has been reported infrequently (7, 14, 15, 20, 23). Second, a decision must be taken if a bowel resection is necessary and although there have been various methods to evaluate the bowel viability (studies with fluorescein, Doppler ultrasonography), it often comes to clinical judgement by the experienced surgeon. The aim of the resection is to conserve as much bowel as possible. Contrary to the case in arterial ischaemia, the border between ischaemia and vivid bowel can be more diffuse and difficult to define. No vein thrombosis should be allowed at the resection margins. When in doubt about radicality it is probably wise to exteriorize the bowel ends and perform an anastomosis later. Primary anastomosis should also be avoided in case of peritoneal contamination because of perforation. Usually the middle segment of the small intestine is involved, colon very rarely. At conclusion of the operation a decision should be taken whether or not to perform a second look – that is an explorative laparotomy after around 24 hours (18). If this has been decided, there must not be discussion afterwards if a wait and see attitude should be followed instead. Changing the decision on the second look must be strongly motivated as a negative explorative laparotomy is a minor operation, if necessary a completion resection must be made. To wait for symptoms of peritonitis to occur could be

what puts the patient into a serious state with a high mortality. Laparoscopic second look has reported to be successful (30).

A further indication for surgery and bowel resection is mucosal bleeding of a magnitude, which cannot be handled conservatively.

Non-specific measures

- pain must be dealt with adequately and often the patients have pain out of proportion to their initial abdominal findings. This must not be misinterpreted as simulation or exaggeration from the patient's side.
- nasogastric tube to empty as much bowel contents as possible, thereby decreasing the mechanical pressure on the already circulatory compromised bowel wall, also contributing to diminish bowel movements.
- broad-spectrum antibiotics are probably reasonable, also if it does not come to perforation or peritonitis.
- fluid, electrolyte and acid base balance must be adequately taken care of. During the course intravascular fluid is lost resulting in hypovolemia and eventually shock. Dextran should be considered to improve microcirculation in addition to volume expansion.
- arterial spasm is a common finding at laparotomy and intraarterial papaverin should be considered, the aim being to optimize the circulatory condition of the bowel. Vasopressors are contraindicated in treatment of shock.

Outcome

Acute mesenteric venous thrombosis is a very serious clinical condition with mortality reported up to as high as 50% (19). There is a tendency that mortality has decreased in recent patient series (14, 20, 23). Of special importance for the still high mortality is the age of the patient, comorbidities or coexisting conditions such as malignancy and the existence of a delay in diagnosis and thereby treatment. Obesity is an independent risk factor for fatal mesenteric vein thrombosis (3). The most prevalent associated conditions are inflammatory bowel disease, recent abdominal surgery, liver cirrhosis, and abdominal malignancy. The delay in diagnosis is still frequent despite modern diagnostic tools and methods. Being aware of the possibility is of utmost importance to a rapid and correct diagnosis and thereby adequate therapy. Admission to a surgical ward seems associated with a decrease in mortality (2). One reason could be more dramatic symptoms and therefore greater diagnostic and therapeutic activity. One contributing factor to mortality is synchronous pulmonary embolism (2, 3). Of patients surviving there is usually a prolonged and complicated course with a number of problems causing long stay in intensive care unit and thereafter in the ordinary ward (23). In cases of extensive bowel gangrene with need for resection the long term consequences of a short bowel syndrome are added, although this is not as common as when the cause is arterial ischaemia. In the series from the Mayo Clinic short bowel syndrome was reported in 23% (23). A short bowel syndrome significantly increases both 30-day and 5-year mortality (1).

Table 1. Risk factors for bleeding in conjunction with anticoagulant therapy.

- Age > 65 years
- High level of anticoagulation, i.e. INR > 5.0
- History of prior serious bleeding
- Renal disease (clearance < 30 mL/min)
- Liver disease
- Ethanol abuse
- Reduced platelet count
- Malignancy
- Hypertension (uncontrolled)
- Stroke
- Anaemia
- Excessive fall risk

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