Acute disseminated intravascular coagulation following surgical resection of a myeloid sarcoma in a 57-year-old male

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Abstract

Myeloid sarcoma is a rare extramedullary tumour consisting of immature myeloid cells. It can arise at any anatomical location and often develops in the bowel. This report describes a case of severe acute disseminated intravascular coagulation (DIC) with multi-organ failure occurring in a 57-year-old man with chronic myelomonocytic leukaemia during bowel resection for newly diagnosed adenocarcinoma of the sigmoid colon. Histopathology however revealed a differentiating myeloid sarcoma encompassing a well-differentiated adenocarcinoma. This is the first documented case of acute DIC to be triggered following surgical manipulation of myeloid sarcoma.

Case Report

A 57-year-old man with newly diagnosed chronic myelomonocytic leukaemia (CMML) receiving etoposide chemotherapy presented to his Primary Medical Doctor with a two-month history of abdominal pain and altered bowel habit. Subsequent investigation with colonoscopy and computed tomography (CT) scan revealed a primary neoplasm of the sigmoid colon with tethering of the small bowel and no evidence of widely metastatic disease. The patient was clinically stable and was deemed fit to undergo surgery. His pre-operative blood film showed features consistent with stable CMML in the absence of acute leukaemic transformation or disseminated intravascular coagulation (DIC).

Two weeks following his last dose of etoposide the patient underwent an operation which demonstrated a large sigmoid mass adherent to the terminal ileum and both ureters. A high anterior resection, *en bloc* small bowel resection and loop ileostomy were performed taking 180 min. The operation progressed without complication until about 15 min before completion. It was at this point that the patient became profoundly and inexplicably hypotensive (60/40 mm Hg) with bradycardia (40 bpm) and evolution of ST depression on the two lead cardiac monitor. The patient was also noted to have copious oozing of frank blood from the incision site despite having achieved adequate intra-operative haemostasis. As part of the intra-operative resuscitation he received two 500 mL boluses of colloids and a single dose of 0.3 mg intravenous adrenaline. He was transferred as an unplanned admission directly to the intensive care unit (ICU) for further management. On arrival to the ICU, he presented in hypovolemic shock and clinical DIC (Table 1). Serial troponin I results reflected an ischaemic myocardial event, peaking at 14.68 µmol/L (reference range <0.10) on ICU day 3. A twelve lead electrocardiogram demonstrated sinus tachycardia and ST depression in leads V4-V6 with new onset right bundle branch block. Trans-thoracic echocardiogram revealed a hyperdynamic and hypovolemic left ventricle without segmental wall motion abnormality implicative of a global ischemic insult.

The patient remained intubated, ventilated and required inotropic support with a noradrenaline infusion. His profound coagulopathic state necessitated the administration of seven units of fresh frozen plasma, six units of cryoprecipitate, six units of packed red cells and four pools of platelets in the first 24 h of his ICU admission. After consultation with the patient's haematologist, he was also given 100 mcg/kg of Recombinant Activated Factor VII. By the third post-operative day, the patient was extubated but required total parenteral nutrition for a prolonged ileus and was commenced on continuous venovenous haemodiafiltration for an evolving acute kidney injury due to his initial pre-renal insult. On day 6 he had further intra-abdominal bleeding manifested by a slowly falling haemoglobin and repeat CT abdomen revealing a large abdominal collection. His coagulation profile and blood film demonstrated persisting mild DIC without evidence of an acute blast cell crisis. Given the ongoing difficulty with haemostasis, the patient was deemed too high-risk for further surgical intervention. On day 10 the patient's blood film demonstrated acute leukaemic transformation in the form of a myeloid crisis based on cytological features, which would require urgent chemotherapy to avert a rapidly fatal outcome. As it was unlikely to alter management in this setting, cytological analysis of the myeloid crisis was not undertaken. Similarly a bone marrow biopsy was not pursued at this point, and was contraindicated in the acute phase when the patient was coagulopathic. Given the patient's ongoing dialysis needs, agitation and overall debilitated state a frank discussion with family was held and a unanimous decision was made to redirect management priorities towards patient comfort. Palliative measures were given priority, and the patient subsequently died on day 13 post-operation.

Histological examination of the resected portion of the sigmoid colon found a well-differentiated adenocarcinoma extending through the muscularis propria into the subserosal fat without lymph node involvement (0/39). Adjacent to this tumour was a florid atypical myelomonocytic infiltrate consistent with a differentiating myeloid sarcoma and evidence of early transformation into acute myeloid leukaemia. The infiltrate consisted of blasts as well as a progression of more differentiated cells of both the myeloid and monocyte lineage. These cells were positive for myeloperoxidase and CD68, but were negative for CD3, CD20 and CD117 (Figures 1-4).

Discussion

Myeloid sarcoma [also termed chloroma, granulocytic sarcoma and extramedullary acute myeloid leukaemia (AML)] is characterised as an extramedullary collection of immature myeloid cells, which may develop *de novo*, or on the background of acute myeloid leukaemia, myelodysplastic or myeloproliferative diseases. It is a rare neoplasm, with a reported incidence of 3.1% in myelogenous leukaemia.[1] Cases of myeloid sarcoma have been described at various stages of AML from the initial presentation, relapse and it has even been recognised to herald an impending

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blast crisis in myeloproliferative disease.[2] Myeloid sarcoma arising in synchrony with a non-haematological malignancy is very rare.[3,4]

The broad clinicopathological features of this entity was a subject of review during a workshop held in Indianapolis IN, USA by the Society for Hematopathology/European Association in November 2007.[5] While myeloid sarcoma commonly develops in the skin, bone and lymph nodes it can occur in any anatomical location including the gastrointestinal system. As a result there is considerable variability in how it presents clinically. Diagnosis is therefore dependent on clinical suspicion and should be considered in any patient with AML presenting with an extramedullary mass lesion. Indeed the manifestations of myeloid sarcoma within the bowel are usually no different to that of any other tumour. This may be in the manner of bleeding, obstruction or even intussception.[6] One of the cases examined in the Society of Hematopathology's workshop was a *de novo* colonic myeloid sarcoma in a patient who presented with abdominal pain and was preoperatively diagnosed with adenocarcinoma.[5] Intra-operatively, this was reported as a non-ulcerating mass of the transverse colon with invasion into the surrounding fat and soft tissue which was subsequently diagnosed as myeloid sarcoma.[5] These findings of locally advanced disease bear similarity to our case. However such a catastrophic event arising from tumour-induced coagulopathy has not been previously documented in myeloid sarcoma. A similar case of colonic myeloid sarcoma with a fatal outcome following resection was reported in a 60-year-old female in France however again, the process here was attributed to toxic shock and not a consumptive coagulopathy.[7]

Acute DIC complicating this patient's high anterior resection was attributed to intra-operative manipulation of the myeloid sarcoma. Acute DIC is a well-recognised systemic process characterised by activation of the coagulation system resulting in widespread thrombosis and haemorrhage. The clinical consequences of DIC vary depending on the clinical setting, but multi-organ failure due to thromboembolism and bleeding is not uncommon. Four mechanisms have been defined as giving rise to DIC including increased thrombin generation, suppression of physiological anticoagulation, impaired fibrinolysis and activation of the inflammatory pathway.[8] Sepsis, trauma, malignancy and obstetric complications are the major initiating factors for DIC. Whilst this coagulopathic process is driven by tissue factor in sepsis, it is thought that cancer procoagulant is responsible for DIC in the setting of malignancy. Cancer procoagulant is a calcium-dependent cysteine proteinase expressed by malignant cells and foetal tissue which activates factor X independently of the

Table 1. Laboratory results on admission to the intensive care unit.

	Result	Units	Reference range
Full blood picture			
Haemoglobin	65	g/L	(115-165)
White cell count	148.0	109/L	(4.0-11.0)
Platelets	67	109/L	(150-400)
Serum biochemistry			
Sodium	133	mmol/L	(134-146)
Potassium	5.3	mmol/L	(3.4-5.0)
Urea	5.7	mmol/L	(3.0-8.0)
Creatinine	201	µmol/L	(53-106)
Cardiac troponin I	2.0	µmol/L	(<0.10)
Arterial blood gas			
pH	7.05		(7.35-7.45)
pO_2	136	mm Hg	(80-95)
pCO_2	44	mm Hg	(35-45)
Bicarbonate	12	mmol/L	(22-28)
Base excess	-17	mmol/L	(-3-+3)
Lactate	7.2	mmol/L	(0.2–1.8)
Coagulation profile			
International normalised ratio (INR)	4.7		(0.9-1.1)
Activated partial thromboplastin time	96	sec	(21-33)
Fibrinogen	0.9	g/L	(2.0-4.0)

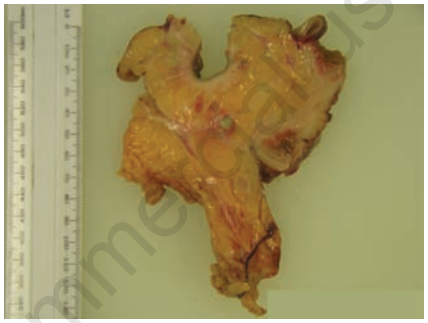


Figure 1. Macroscopic image of a portion of the resected sigmoid colon with adherent small bowel. The myeloid sarcoma is demonstrated by the tissue exhibiting a green colour due to the presence of myeloperoxidase, hence the traditional term chloroma.

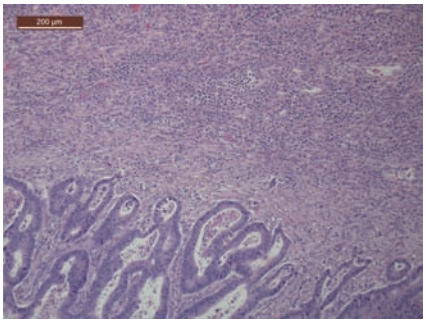


Figure 3. Microscopic image demonstrating the differentiating myeloid sarcoma at a higher magnification.

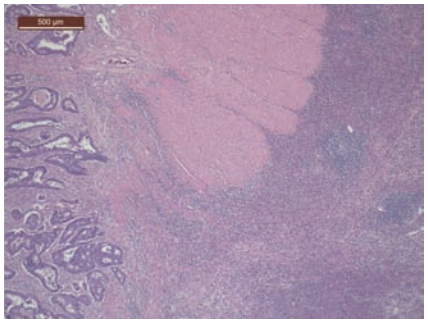


Figure 2. Microscopic image of the resected sigmoid colon illustrating the adenocarcinoma (left) with an adjacent infiltrate of immature myeloid cells consistent with myeloid sarcoma (right).

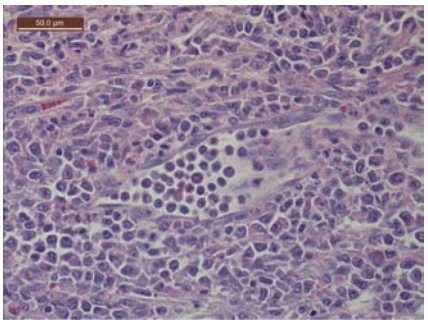


Figure 4. Higher magnification microscopic image illustrating immature myeloid infiltration of a blood vessel.

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tissue factor – factor VIIa complex.[9,10] Cancer procoagulant along with increased expression of annexin II receptor has been implicated in the development of DIC in acute promyelocytic leukaemia (APML). The presence of annexin II receptor on the surface of leukaemic promyelocytes has been shown to stimulate the production of t-PA-dependent plasmin more efficiently.[11] This may further account for the haemorrhagic complications typically seen in APML.

The presentation in this case report is not dissimilar to previous accounts of colonic myeloid sarcoma.[3-5] The complicated post-operative course due to acute DIC however raises two main issues. Firstly, the coagulopathy that was triggered by direct surgical manipulation of this tumour has not been previously reported. Acute DIC is known to be mediated by cancer procoagulant in the setting of malignancy, and the role of annexin II receptor has been highlighted in APML. It is conceivable that a peripheral promyelocytic blast crisis in this case may have accounted for the DIC that ensued. However this was not clearly demonstrated on cytology, and furthermore the clinical onset of DIC preceded that of myeloid crisis by ten days. Resection of the tumor and systemic spread of promyelocytic cells could also be hypothesized as the mechanism for this phenomenon, but again such a finding was not demonstrated on analysis of the peripheral blood. Further studies are therefore needed to understand the mechanisms causing DIC in myeloid sarcoma, which in this case was severe and very difficult to control. The second issue pertains to diagnosis and management in view of the complications that were observed. While clinical suspicion is important, the detection of myeloid sarcoma ultimately requires tissue for a formal diagnosis. To complicate matters, myeloid sarcoma occurring in the *shadow* of a more sinister malignancy may evade detection until surgical resection is undertaken. This case clearly demonstrates that making a pre-operative diagnosis is very difficult in the context of another, more obvious malignancy.

Finally, this begs the question as to whether management might have been modified if the diagnosis of myeloid sarcoma (and the prospect of a haemorrhagic complication) had been established in advance of surgery. The impending transformation into acute leukaemia in this patient may suggest a role for pre-operative chemotherapy, but there is no evidence that this would necessarily avert intra-operative DIC. Furthermore, this is the only known report of DIC from surgical resection of myeloid sarcoma and probably represents a very rare outcome. Although there are no firm grounds to anticipate similar complications occurring in similar circumstances, such a possibility is at least worthy of consideration in any patient with a myelogenous leukaemia who is undergoing surgery for an extramedullary tumour.

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