CASE REPORTS

Multiple coronary aneurysms in a patient with neurofibromatosis type 1: case report and intravascular ultrasound of aneurysm

J Trevelyan, M Been, R Patel

Abstract

A 54 year old woman with neurofibromatosis type 1 (NF-1) was found to have multiple coronary aneurysms. Intraoperative intravascular ultrasound (IVUS) revealed severe coronary disease proximal to the aneurysm that had not been apparent angiographically. An IVUS picture of one of the giant coronary aneurysms is also shown. The vascular manifestations of neurofibromatosis and the causes of coronary aneurysms are reviewed.

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Keywords: coronary aneurysm; neurofibromatosis; intravascular ultrasound

The vascular manifestations of neurofibromatosis were first described in 1944 by Reubi.¹ Vascular abnormalities can affect the aorta or iliac, mesenteric, renal, and cerebral arteries. There have been two previous reports of coronary aneurysms causing myocardial infarction in neurofibromatosis,^{2,3} a report of coronary ectasis and stenosis causing myocardial infarction,⁴ and a report of myocardial infarction presumed to have resulted from vasospasm.⁵ We report here the first case of multiple coronary aneurysms in association with neurofibromatosis, and present the first published IVUS picture of a giant coronary aneurysm.

Case report

A 54 year old woman presented to our hospital with a five month history of exertional chest pain. She had a past history of neurofibromatosis type 1 (NF-1), characterised by axillary freckling and multiple café au lait macules and neurofibromata, and carcinoma of the breast, treated by mastectomy. The diagnosis of NF-1 had never been genetically confirmed. An exercise test was positive at a low workload, and we proceeded to left heart catheterisation which showed inferior akinesia, severe mitral regurgitation, and two circular calcified lesions in the region of the left anterior descending coronary artery (LAD) and the distal right coronary artery near the crux. There was occlusion of the LAD, occlusion of the circumflex artery, and aneurysmal dilatation of the right coronary artery, which also filled the distal LAD through collaterals (figs 1 and 2).

Transoesophageal echocardiography showed restriction of the P2/P3 portions of the

posterior mitral valve leaflet in systole with severe mitral regurgitation, consistent with an ischaemic aetiology.

She was referred for coronary artery bypass grafting and mitral valve repair. At operation two calcified aneurysms were seen at the origin of the LAD and in the mid right coronary artery. Intraoperative intravascular ultrasound (IVUS) showed severe disease of the right coronary artery proximal to the aneurysm, which

Figure 1 Left selective coronary angiogram in the right anterior oblique projection (RAO 31°) showing occlusion of the left anterior descending coronary artery with a circular calcified lesion immediately distal to the occlusion (short arrow), and similar lesion inferiorly in the region of the right coronary artery (long arrow).

Figure 2 Right selective coronary angiogram in the right anterior oblique projection (ROA 43°) showing aneurysmal dilatation of the right coronary artery at the crux (long arrow), with no significant coronary disease apparent. The calcified lesion in the left anterior descending coronary artery region is also shown (short arrow).

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Figure 3 Intravascular ultrasound of the right coronary artery showing (A) severe coronary disease immediately before the aneurysm, and (B) aneurysmal dilatation of the right coronary artery measuring 6.5×5.5 cm at this point, increasing beyond to 8×9 cm.

had not been visible on the coronary angiogram, followed by aneurysmal dilatation, reaching 8×9 mm at its largest internal diameter (fig 3).

Discussion

NF-1 is a congenital hereditary disease with generalised neuroectodermal and mesodermal dysplasia that affects the skin, nervous system, skeleton, and vascular system. Diagnosis is based on the presence of at least two of the following seven criteria⁶:

- Six or more café au lait macules, over 5 mm in prepubertal or 15 mm in postpubertal individuals
- Freckling in the axillary or inguinal region
- Two or more neurofibromata or one plexiform neurofibroma
- Two or more Lisch nodules
- Optic glioma
- A distinctive osseous lesion, for example sphenoid dysplasia or thinning of the long bone cortex, with or without pseudarthrosis
- A first degree relative with NF-1.

Other findings that may occur include tumours of the central and peripheral nervous system and gastrointestinal system, skeletal abnormalities (scoliosis, local gigantism, subperiosteal bone cysts, short stature), intellectual, behavioural, and emotional disturbance, and

vascular abnormalities. Pheochromocytomas may be present but are infrequent.

The vascular manifestations of NF-1 comprise aneurysmal and stenotic changes in large and medium vessels, including coarctation of the aorta. The most common vascular manifestation is proximal renal artery stenosis resulting in hypertension, first described by Debre *et al.*⁷ Aneurysms occur less frequently than stenoses⁸; they have been reported in association with renal artery stenosis but may occur as isolated lesions anywhere. Aneurysms of the aorta, subclavian, and vertebral arteries, carotid artery, thyrocervical trunk,⁸ and mesenteric^{9 10} and coeliac branches⁹ have all been described. Multiple intracranial aneurysms may be present.

The electron microscopic examination of the vessel wall reveals two types of vascular lesion.¹¹ Large arteries (including proximal renal arteries) may have intimal proliferation (causing stenoses), medial thinning, and fragmentation of elastic tissue (leading to aneurysm formation). These vessels may also be involved with neurofibromatous tissue. Small arteries show smooth muscle accumulation within the intima with resultant luminal narrowing. It has been postulated that vasospastic changes in the coronary arteries of patients with NF-1 reflect an abnormality of the cardiac sympathetic nerve.⁴

Coronary artery aneurysm is defined as a coronary dilatation which exceeds the diameter of normal adjacent segments or the diameter of the patient's largest coronary vessel by 1.5 times. A giant aneurysm is defined as one with an internal diameter of > 8 mm. The incidence varies from 1.5% to 5%, with male dominance and a predilection for the right coronary artery.¹² Atherosclerosis accounts for 50% of coronary aneurysms in adults. Other causes of coronary aneurysms include trauma, infective endocarditis, Kawasaki's disease, percutaneous transluminal coronary angioplasty, syphilis, fibromuscular dysplasia, and polyarteritis nodosa; their presence has also been associated with systemic lupus erythematosus, supraventricular aortic stenosis, coronary fistulae, chronic Epstein-Barr virus infection, polycystic kidney disease, Behçet's disease, and Lyme disease. Complications include thrombosis, distal embolisation, rupture, and vasospasm.

There have been two previous descriptions of coronary aneurysms in association with NF-1. Kandarpa *et al* and Daly *et al* have both described cases of NF-1 associated with coronary aneurysm and myocardial infarction.^{2 3} Fuchi *et al* described a case of NF-1 associated with coronary ectasis, vasospasm, and stenosis causing myocardial infarction.⁴ Our case is the first description of multiple coronary aneurysms in association with NF-1, and, as far as we are aware, includes the first published intravascular ultrasound picture of a giant coronary aneurysm. There was no evidence of coronary vasospasm at angiography in our case, although this was not specifically tested for by provocation. The mitral regurgitation seen was ischaemic in

Learning points

- NF-1 is a rare cause of coronary artery aneurysms, including multiple aneurysms.
- Coronary aneurysms may hide significant coronary artery stenosis.
- Intravascular ultrasound may reveal significant stenoses not visible at angiography.

origin—with restriction of the posterior mitral valve leaflet—and not directly related to NF-1. It is interesting to note that the use of intravascular ultrasound revealed severe right coronary artery disease proximal to the aneurysm, which was presumably responsible for at least some of the patient's anginal symptoms. Masking by the giant aneurysm accounted for the lack of evidence of severe disease in this area on coronary angiography. We urge that consideration be given to the use of IVUS in this setting to examine the coronary vasculature immediately adjacent to an aneurysm.

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Gas gangrene after colonoscopy

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Abstract

A case of spontaneous clostridial myonecrosis developing shortly after diagnostic colonoscopy is described. The prime underlying factor proved to be an unsuspected colonic cancer, developing in a patient with pre-existing ulcerative colitis and sclerosing cholangitis.

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Keywords: gas gangrene; colonoscopy

Gas gangrene was originally described as a complication of battlefield wounds and other penetrating injuries. Spontaneous clostridial myonecrosis can occur in patients with predisposing conditions such as diabetes, leukaemia, and other neoplasms.¹ We describe a case occurring shortly after a diagnostic colonoscopy, but the apparent causative association between the two events proved incorrect.

Case report

A 48 year old man was admitted to hospital as a day case for colonoscopy. He had a 25 year history of extensive ulcerative colitis and was also found to have primary sclerosing cholangitis. This was diagnosed by endoscopic retrograde cholangiography arranged after persistently abnormal liver function tests were noted in 1984 (fig 1). Previous regular surveillance colonoscopies had shown low grade inflammation to the caecal pole but no dysplastic features on examination of biopsy specimens;

the latest colonoscopy had been two and a half years before the present admission.

The current examination had been booked because of two attacks of abdominal pain and

Figure 1 Endoscopic retrograde cholangiography film showing typical changes of sclerosing cholangitis in the patient.

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constipation. Full blood count and erythrocyte sedimentation rate were normal when checked in the outpatient department. Colonoscopy was carried out under intravenous sedation given through a plastic cannula in the right antecubital fossa.

The colonoscope was passed to the hepatic flexure, but the right side of the colon could not be seen adequately. Multiple biopsy specimens were taken from the large bowel mucosa for dysplasia screening. As there was quite a lot of blood in the proximal transverse colon and a caecal lesion could not be excluded on this incomplete examination, a barium enema was arranged to evaluate the proximal large bowel.

Two days after the colonoscopy the patient was readmitted to hospital with pain and swelling in the right arm for the previous 12 hours. He was feverish and unwell. The right upper arm was markedly swollen, with mottling of the skin and some blister formation at the elbow. The initial differential diagnosis was of a cellulitis or axillary vein thrombosis. The latter was excluded by a Doppler ultrasound scan, while a plain x ray revealed gas in the tissue planes (fig 2). *Clostridium septicum* was isolated from multiple blood cultures.

An urgent surgical debridement of the upper arm was performed and repeated four times during the next week. High dose intravenous penicillin was given, together with intravenous metronidazole and ofloxacin.

Ten days after his admission the patient had a large rectal bleed followed by increasing abdominal pain and distension. A plain abdominal film showed dilated small bowel loops suggestive of obstruction. At laparotomy, a perforated caecal carcinoma was found. The liver showed macronodular cirrhotic changes. A right hemicolectomy was performed, but the

patient developed disseminated intravascular coagulopathy and hepatorenal failure, leading to death eight days after the abdominal surgery.

Discussion

This patient's admission with gas gangrene two days after colonoscopy caused understandable concern to the gastroenterology unit, particularly as the indwelling cannula for the intravenous sedation had been placed close to the site of the later development of myonecrosis. As matters evolved, it became evident that the condition was likely to be secondary to the underlying colorectal cancer. Spontaneous myonecrosis caused by *Clostridium septicum* is associated with colonic cancer in about one third of cases.² The organism probably gains access to the blood stream through mucosal defects in the large bowel caused by an ulcerating tumour, and may be particularly likely to infect normal areas of muscle, as it is more aerotolerant than *C perfringens*.³ Release of exotoxins results in haemolysis, vascular injury, cytolysis, and inhibition of neutrophil function, leading to massive tissue necrosis. Treatment involves aggressive surgical debridement or amputation in cases of limb involvement, together with systemic antibiotic treatment. When available, hyperbaric oxygen may help by inhibiting clostridial growth and toxin production, but there are no controlled studies of the clinical value of such treatment.⁴ Even with aggressive therapy, the prognosis of spontaneous myonecrosis is poor, with a mortality of 60–100%.

In this case, the underlying cancer developed on a background of long term extensive ulcerative colitis and primary sclerosing cholangitis. Ulcerative colitis is a well recognised antecedent of colorectal cancer. Since the description of a close relation between colonic neoplasia and mucosal dysplastic changes in ulcerative colitis,⁵ and the wide availability of colonoscopy in general hospitals, it has become conventional to undertake regular surveillance endoscopy in patients with colitis thought to be at particular risk of cancer development. Although some series have claimed that colonoscopic surveillance reduces the cancer mortality,^{6–8} a critical analysis of the data available implies that such programmes may be largely ineffective in the detection of tumours at an early and curable stage, while involving significant utilisation of resources for a very limited reward.^{9–10} Nevertheless, 92% of endoscopy units in the United Kingdom still perform surveillance colonoscopy for ulcerative colitis, in the perhaps optimistic expectation of reducing cancer deaths.¹¹ The chance of developing colonic dysplasia or neoplasia appears to be particularly increased if a colitic patient also has primary sclerosing cholangitis.^{12–13} As a result, close endoscopic surveillance with multiple biopsy sampling—probably at yearly intervals—has been advised in such cases to try to reduce the mortality from colorectal tumours.^{14–15} In our patient, domestic circumstances made him a rather poor complier with follow up, and the interval between colonoscopies was arguably longer than ideal.

Figure 2 Plain x ray of the right arm, showing gas in the tissue planes (arrows).

At necropsy examination, the patient had established liver cirrhosis related to his primary sclerosing cholangitis. Circulatory changes in the liver allowing easier access of colonic organisms to the systemic vasculature may have been an additional risk factor for gas gangrene development; myonecrosis caused by a gas forming coliform has been described in a case of decompensated liver disease and spontaneous bacterial peritonitis.¹⁶

Although apparently precipitated by the endoscopic procedure, this case of spontaneous clostridial myonecrosis was almost certainly an example of the known association between that condition and bowel cancer. Patients with long term ulcerative colitis and primary sclerosing cholangitis may require careful surveillance for tumour development, but this report describes a unique presentation of the problem.

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