

ARTICLES

SELECTIVE ARTERIAL EMBOLIZATION FOR CONTROL OF HAEMATURIA SECONDARY TO ADVANCED OR RECURRENT TRANSITIONAL CELL CARCINOMA OF THE BLADDER

D. Halpenny, U. Salati, W.C. Torregiani, R. Browne

Aim: Haematuria is a common symptom in patients with advanced transitional cell carcinoma of the bladder. We report our experience of selective pelvic embolization using gelfoam as an embolic agent to treat intractable haematuria in these patients.

Methods: Three male patients aged 66-79 (mean 73.6 years) with inoperable or recurrent transitional cell carcinoma of the bladder underwent selective embolization to treat haematuria over a 9 month period. Initial pathological tumour stages were T2, T3, and T3a. Gelfoam was used as the embolic agent.

Results: In all patients extensive vesical neovascularisation was identified without a single focus of active extravasation. Following embolization all patients experienced cessation of haematuria. Mean transfusion requirements were 8.6 units pre-embolization and 0.3 units post-embolization. At follow up of between 6-13 months (mean 10 months) no further episodes of bleeding had been reported. No patient experienced procedure-related complications.

Conclusion: Radiologically guided embolization is a safe and effective method for palliating haematuria in patients with transitional cell carcinoma. On the basis of our experience we would recommend gelfoam as the embolic agent of choice.

Key-words: Bladder neoplasms – Hematuria – Arteries, therapeutic blockade.

Introduction

Bladder carcinoma accounts for up to 8% of malignant disease in men and 3% in women, with transitional cell carcinoma (TCC) accounting for 90% (1). The treatment of choice for TCC of the bladder is transurethral resection or cystectomy depending on tumour stage but many patients have unresectable disease at time of diagnosis. In these patients, or in those with recurrent disease, haematuria can cause significant morbidity and can occasionally be life threatening. Conservative attempts to stop haemorrhage often fail and patients may not be suitable for more radical surgical treatment options. Percutaneous embolization techniques have proven to be effective in the treatment of pelvic haemorrhage in many clinical settings (2, 3) using different embolic materials and improved catheter technology now allows superselective catheterisation of bleeding vessels to limit side effects secondary to non-target embolization. We report our experience of superselective pelvic embolization using gelfoam as an embolic to treat intractable haematuria in three male patients with advanced or recurrent TCC of the bladder.

Materials and methods

Three male patients with intractable haematuria secondary to inoperable or recurrent TCC of the bladder underwent superselective embolization of the vesical arteries over a 9 month period. Patient demographics, tumour pathology and transfusion requirements are summarised in Table I. Two patients had received radiotherapy during their treatment, however the aetiology of haemorrhage was felt to be related to underlying tumour in all cases.

Procedures were performed by an interventional radiologist in the interventional radiology suite under fluoroscopic guidance. Prophylactic IV antibiotic (Rocephin [ceftriaxone] 1 gm, Roche Pharmaceuticals) was administered to all patients 1 hr before the procedure. Conscious sedation was maintained throughout the procedure using IV midazolam (Hypnovel, Roche Pharmaceuticals) and fentanyl (Sublimaze, Janssen-Claig). Under local anaesthesia arterial access was obtained via a right femoral artery approach and a 5-French vascular sheath was inserted. A 5-French multi endhole catheter (Omniflush, AngioDynamics) was used to obtain a nonselective pelvic

arteriogram to identify the vesical arteries. A hydrophilic polymer-coated 0.035-inch angled guidewire (Radiofocus, Terumo) was used to position a 5-French Cobra catheter (Cordis) in the contralateral internal iliac artery, and selective arteriography was performed (a microcatheter was used in 1 patient). After superselective catheterisation of the vesical artery gelatine sponge (gelfoam) slurry was introduced under fluoroscopy. This was prepared by mixing precut gelfoam brick and contrast medium through a 2-way stop cock using two 10 ml syringes. Infusion was continued until occlusion of the vesical vascular bed occurred. The procedure was then repeated in the ipsilateral internal iliac and vesical arteries using a Waltman loop manoeuvre.

All patients were closely monitored after embolization and were evaluated for procedure related complications. Analgesia was administered as required using a standard postprocedural pain management regimen. All patients underwent urological and radiological assessment and follow-up after the procedure (Fig. 1-3).

Results

Bilateral vesical artery embolization was performed in all patients. In all patients extensive vesical neovascularisation was identified without a single focus of active extravasation. Gelfoam was used as the sole embolic

From: Department of Radiology, Adelaide and Meath Hospitals, Tallaght, Dublin 24, Ireland.

Address for correspondence: Dr D. Halpenny, M.D., Department of Radiology, AMNCH, Tallaght, Dublin 24, Ireland.

Table I. — A summary of patient demographics, tumour type and transfusion requirements.

Patient	Age	Pathological Stage	Grade	Haemoglobin prior to embolization (g/dl)	Transfusion requirements before embolization	Number of embolization procedures
1	66	T3a	3	7.3	8 units	1
2	79	T3	2	8.1	11 units	1
3	76	T2	3	7.6	7 units	1

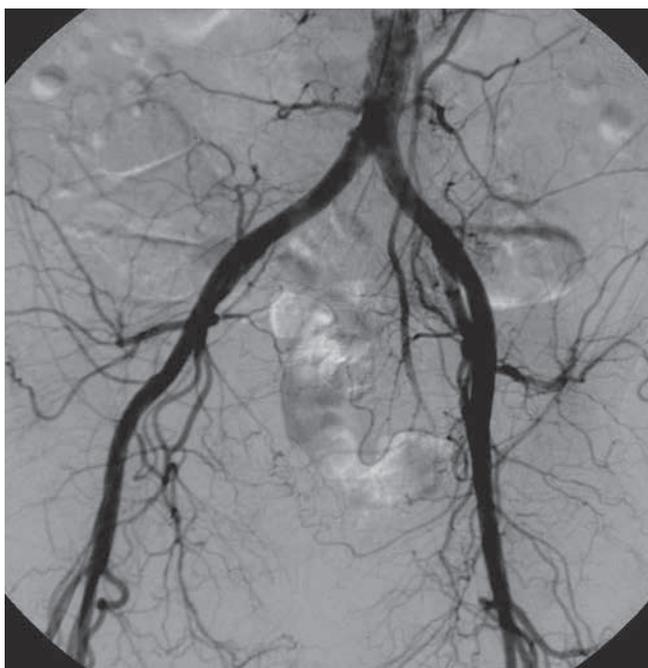


Fig. 1. — Angiography of the aorta and iliac vessels demonstrating neovascularisation involving the vesical arteries bilaterally.

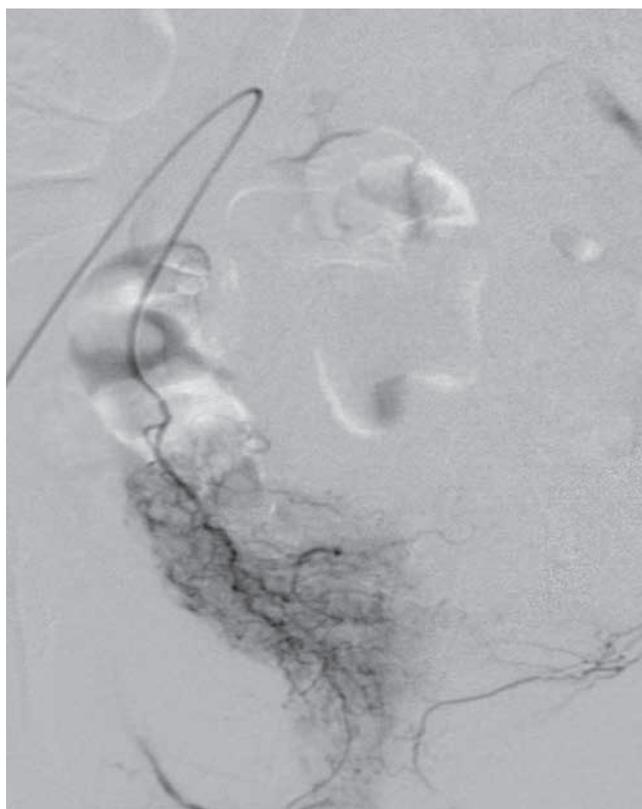


Fig. 2. — Selective catheterisation of the right vesical artery reveals the extent of underlying neovascularisation in the tumour bed.

in all cases. No patient experienced procedure-related complications. Following embolization all patients experienced cessation of haematuria, obviating the need for further treatment. It took 2 days for the urine to become clear post embolization in all cases. Transfusion requirements post embolization varied from 0-1 unit packed red blood cells (mean 0.3 units), compared to a mean of 8.6 units pre-embolization. Patients were followed up to death. Mean survival post embolization was 346.3 days (68-642 days). No further episodes of bleeding were reported (Table II).

Discussion

Bladder carcinoma is the commonest neoplasm of the genitouri-

nary tract. Patients most commonly present with painless haematuria and undergo cystoscopy for diagnosis and staging. At presentation most patients will have low-grade superficial disease, which is usually treated conservatively with transurethral resection and periodic cystoscopy. Up to 45% of patients will have high-grade disease, of which 50% is muscle invasive and are typically treated with radical cystectomy (4). A significant percentage, however, are inoperable at time of diagnosis and may undergo external beam radiation or chemotherapy for palliation. Intractable haematuria can cause significant morbidity in these patients or in those with recurrent

TCC of the bladder and may in some cases be life threatening. This usually occurs as a direct result of intramural tumour invasion, though haemorrhagic cystitis may also occur post pelvic radiation. Non surgical techniques used to manage haematuria in this setting include irrigation with silver nitrate or formalin, aminocaproic acid treatment, and the application of intravesical hydrostatic pressure. However success rates using these methods are variable and may necessitate a general anaesthetic (5, 6). These patients are often not suitable for more radical surgical options such as hypogastric artery ligation, urinary diversion or cystectomy. The minimally invasive

Table II. — An outline of the embolization procedures performed including vessels embolized and embolization material used.

Patient	Embolic material	Vessel embolized	Control of haemorrhage	Complications
1	Gel foam	Anterior division of Internal Iliac artery	Permanently stopped 2 days after embolization	No
2	Gel foam	Left vesical and right anterior division of internal iliac artery	Permanently stopped 2 days after embolization	No
3	Gel foam	Right and left vesical artery	Permanently stopped 2 days after embolization	No

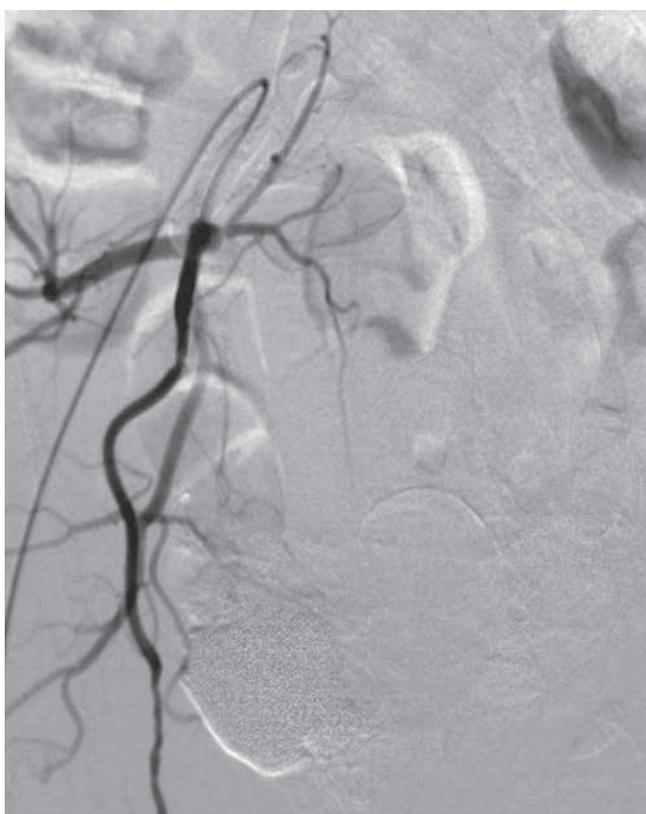


Fig. 3. — Following embolization, selective angiography demonstrates that flow to the previously identified area of neovascularisation has been ceased.

nature of radiologically guided embolization, combined with its efficacy, therefore make it an attractive therapeutic option in these patients.

While several case series in the literature have examined the use of embolization to control pelvic haemorrhage, there are few which specifically address haematuria secondary to TCC of the bladder or the use of gelfoam as an embolization agent in this setting. El-Assmy et al. report a

long term success rate of 57% using embolization of the anterior division of the internal iliac artery to treat 7 patients with haematuria due to bladder malignancy, with haemorrhage ceasing after a mean of 4 days post procedure (7). Jenkins et al. used a variety of embolization materials (including gelfoam, PVA, dura mater, and collagen fibres) to treat haemorrhage due to a selection of malignancies. 7 TCCs were included

in their cohort, with a temporary success rate of 86% and a long term success rate of 43%. There was, however, a 100% long term success rate in their patients in whom gelfoam was used (8). Nabi et al. treated 3 patients with TCC of the bladder using coil embolization as part of a series of patients with pelvic malignancies, but do not sub classify their results (9). Giuliani et al. also treated 3 patients with TCC, using either gelfoam or isobutyl-2-cyanoacrylate. They reported a 100% long term success rate, although 1 patient required repeat embolization (10). The largest series available evaluated 50 patients with TCC as part of a large cohort of patients with pelvic malignancies and using either gelfoam or PVA as embolic agents. While they report an overall permanent success rate of 69% they do not provide specific figures for the TCC cohort (3). All authors describe the technique of bilateral embolization to minimise the risk of haemorrhage from collaterals, while local vascular autoregulatory mechanisms result in a very low rate of tissue infarction (3, 9). Although our series is limited in number we also had a 100% cessation of haematuria with no significant side effects solely employing gelfoam as an embolic.

Gelfoam is attractive in this patient cohort as it is simple to use, rapid to deploy and does not negate further embolization if symptoms recur. It is also extremely cost effective relative to other embolics and has a low side effect profile. We feel that its success as an embolic agent stems from the inherently disorganised and proliferative vascular supply of the tumour bed within the bladder. As a result of this disorganised anatomy, it is often technically difficult to isolate a feeding artery which would benefit

from coil embolization and in our experience malignancy will quickly parasitize adjacent vessels to reconstitute its vascular supply. Because gelfoam is deployed as a liquid "slurry", it can embolize deep into the vascular bed in a manner not possible with coils. While traditionally viewed as a temporary embolization material, it is also known that gelfoam powders frequently lead to permanent occlusion due to the small size (approx 50 micrometer) of the particles and the distal level of occlusion that they achieve (11) may act as a more permanent occlusive agent, primarily because of its sclerosant properties. This would be supported by the long term cessation of haematuria that we achieved in our small cohort of patients, who had a mean follow-up period of ten months.

The most common reported complication after pelvic embolization is post-embolization syndrome (PES), with an incidence ranging from 0-65% in the series that we reviewed (3, 7, 8, 9). Other less common reported complications included distal limb emboli (2%), skin necrosis (<1%), gastric ischemia (<1%) (3) and Brown-Sequard syndrome (10). Jenkins et al. also reported 1 death from gram negative sepsis and advocate the use of prophylactic antibiotics (8). While not described in any of these series, bladder infarction is also a recognised complication of internal iliac artery embolization (12, 13). The vascular supply of the urinary bladder contains collaterals and in theory the more selective the embolization performed, the lower the risk of bladder ischemia. DeBerardinis et al. described the use of superselective embolization of the vesical artery for the treatment of haematuria, postulating that its use would result in fewer complications, including reduced rates of PES (5). We would concur with this as none of our patients experienced significant side effects

post superselective vesical artery embolization. It is not clear if the lack of ischemic side effects in our patient cohort was related to the use of superselective embolization, the use of gelfoam as an embolization agent, or a combination of both factors, however we postulate that gelfoam acts a more permanent embolization agent and therefore the lack of side effects may be due to a more distal embolization. When using microcatheters for superselective embolization with gelfoam, particular attention must be paid to ensure that the embolization material is deployed promptly once it is inserted into the catheter and that the catheter is diligently flushed following gelfoam deployment. Both of these steps reduce the risk of catheter occlusion, a potential complication which necessitates catheter exchange and a prolonged procedure time.

Conclusion

Radiologically guided embolization with gelfoam is a minimally invasive, effective and economic technique for treating haematuria in patients with inoperable or recurrent TCC. Superselective vesical artery embolization in these patients is likely to result in a reduced incidence of side effects. Although it does not influence the long term course of the disease, it provides both prompt and sustained cessation of haemorrhage. Gelfoam embolization should be considered as a primary alternative when conservative measures have failed in controlling haematuria.

References

1. Tekes A., Kamel I.R., Chan T.Y., et al.: MR imaging features of non-transitional cell carcinoma of the urinary bladder with pathologic correlation. *AJR*, 2003, 180: 779-784.
2. Margolies M.N., Ring E.J., Waltman A.C., et al.: Arteriography in the management of hemorrhage from

pelvic fractures. *N Engl J Med*, 1972, 287: 317-321.

3. Pisco J.M., Martins J.M., et al.: Internal iliac artery: embolization to control hemorrhage from pelvic neoplasms. *Radiology*, 1989, 172: 337-339.
4. Johansson S.L., Cohen S.M.: Epidemiology and etiology of bladder cancer. *Semin Surg Oncol*, 1997, 13: 291-298.
5. De Berardinis E., Vicini P., Salvatori F., et al.: Superselective embolization of bladder arteries in the treatment of intractable bladder haemorrhage. *Int J Urol*, 2005, 12: 503-505.
6. Giannakopoulos X., Grammeniatas E., Chambilomatis P., et al.: Massive haemorrhage of inoperable bladder carcinomas: treatment by intravesical formalin solution. *Int Urol Nephrol*. 1997, 29: 33-38.
7. El-Assmy A., Mohsen T.: Internal iliac artery embolization for the control of severe bladder hemorrhage secondary to carcinoma: long-term follow-up. *Scient World J*, 2007, 17, 7: 1567-1574.
8. Jenkins C.N., Mclvor J.: Survival after embolization of the internal iliac arteries in ten patients with severe haematuria due to recurrent pelvic carcinoma. *Clin Radiol*, 1996, 51: 865-868.
9. Nabi G., Sheikh N., Greene D., et al.: Therapeutic transcatheter arterial embolization in the management of intractable haemorrhage from pelvic urological malignancies: preliminary experience and long-term follow-up. *BJU Int*, 2003, 92: 245-247.
10. Giuliani L., Carmignani G., Belgrano E., et al.: Gelatin foam and isobutyl-2-cyanoacrylate in the treatment of life-threatening bladder haemorrhage by selective transcatheter embolization of the internal iliac arteries. *Br J Urol*, 1979, 51: 125-128.
11. Kaufman J.A.: Vascular interventions. In: Kaufman J.A., Lee M.J. (eds.). *Vascular and interventional radiology: the requisites*, 2004, 1st edn. Mosby, Philadelphia, pp 83-118.
12. Hietala S.O.: Urinary bladder necrosis following selective embolization of the internal iliac artery. *Acta Radiol Diagn (Stockh)*, 1978, 19: 316-320.
13. Braf Z.F., Koontz W.W. Jr.: Gangrene of bladder. Complication of hypogastric artery embolization. *Urology*, 1977, 9: 670-671.