

REVIEW

Angiosarcoma and Dialysis-related Arteriovenous Fistulae: A Comprehensive Review

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WHAT THIS PAPER ADDS

This review is the first comprehensive analysis of angiosarcoma cases in arteriovenous fistulae. Patient demographics, presentation, diagnostic challenges, and management of these cases have been evaluated to a level that has not been done previously. Therefore, this provides a useful platform for future cases and research to use as a reference tool for this uncommon but important pathology.

Objective/background: To conduct a comprehensive review of cases, presentation, diagnosis, and management of angiosarcoma in arteriovenous fistulae (AVF) created for haemodialysis.

Methods: Two authors independently conducted systematic searches and extraction of articles from the Embase, AMED, Health Management Information Consortium, and MEDLINE databases in keeping with the inclusion/exclusion criteria and Preferred Reporting Items for Systematic Reviews and Meta-Analyses standards.

Results: Twenty-two unique patient cases were identified; 20 of the cases were men and mean $\pm$ SD age of presentation was 54.9 ± 13.6 years. Nineteen cases were post-transplant and 18 were on antirejection agents. The most common presenting symptom was pain, with or without a mass. The initial diagnosis was most often thrombosis/infection of the AVF and the diagnostic interval to a correct diagnosis of angiosarcoma was between 2 and 40 weeks. Mean $\pm$ SD time to presentation of symptoms from fistula formation was 118.9 ± 57.5 months, while from transplant it was 96.9 ± 70.0 months. Amputation was the most common treatment modality and mean $\pm$ SD survival was 8.8 ± 3.7 months.

Conclusion: Angiosarcoma should be suspected in previously quiescent AVF that presents with pain. The presence of a rapidly enlarging mass or bleeding/bruising should be taken as alarm indicators and warrant urgent investigation in accordance with local cancer guidelines. Any surgical procedure should involve histological samples as a matter of course.

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INTRODUCTION

Arteriovenous fistulae (AVF) are the preferred method for vascular access in renal failure.¹ Favourable flow, infection, thrombosis, and cardiovascular outcome profiles compared with both arteriovenous grafts and central venous catheters have culminated in the “fistula first” initiative, an

international campaign to encourage AVF usage in patients who require or will require renal dialysis.²

Although there are guidelines on when to form AVF, there is little consensus on their management after transplant. A recent review suggested that functioning fistulae should not be ligated post-transplant in case further dialysis is required, unless complications such as steal syndrome, aneurysmal disease, or ischaemia of the associated extremity exist.³ However, these complications are dependent on blood flow and therefore cannot occur in nonfunctioning fistulae. Consequently, little evidence or guidance exists with respect to the management of the nonfunctioning fistula post-transplant. Most often with nonfunctioning

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fistulae, aesthetic and/or symptom concerns will cause patients to seek discussion with their surgeon, resulting in a form of surgical management, usually ligation or excision.

However, one risk that is relevant to both functioning and nonfunctioning fistulae is the occurrence of angiosarcoma (AS). An aggressive but rare malignancy, multiple case reports exist in the literature with regard to this phenomenon; however, apart from cursory reviews as part of these reports, no comprehensive analysis of the cases, presentation, or management exists.

MATERIALS AND METHODS

The objective was to review comprehensively the literature on the reports, presentation, diagnosis, and management of AS in AVF to date.

Data sources and search strategy

In April 2015 a predetermined search query ("angiosarcoma AND arteriovenous fistula") was used to search the Embase, AMED, Health Management Information Consortium (HMIC), and MEDLINE databases utilising the OVIDSP (EMBASE, AMED, and HMIC), and the PubMed (MEDLINE) interfaces. All databases were searched from inception. Additional articles were retrieved using hyperlinks, via references, other sources, or an internet search.

Study selection

Articles were selected for review according to the following criteria: original article or case describing or discussing AS with respect to dialysis-related AVF or grafts. Articles in other languages were retrieved and data were extracted with the aid of a native speaker. Exclusion criteria included articles not describing an AS case, not related to AVF, and articles that were only reviews or comments. Two reviewers (Y.O. and K.R.) independently assessed all retrieved articles and disagreements were resolved by consensus.

Data extraction

Data were extracted by two authors (Y.O. and K.R.) independently, using a predetermined data extraction tool. Extracted points mirrored those in Table 1.

Data were entered and tabulated in Word 2013 (Microsoft, Redmond, WA, USA) and descriptive statistical analysis performed using Excel 2013 (Microsoft). The study was planned, conducted, and reported in adherence to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) standards.

RESULTS

The search strategy returned 101 results, of which 18 were accepted and a further two added via other sources (Fig. 1). Overall, 20 were accepted for inclusion into the final review (Table 1).

Article types and levels of evidence

The majority of articles were published case reports (17/20; 85.0%) and one (5.0%) was a published case report with review. Two were not published; one was a seminar case report and one was a case presentation. All articles were assessed as being evidence level V.

Patient demographics

Two case reports concerned an identical patient; thus, 22 unique patients were identified overall. Of these the majority ($n = 20$; 90.9%) were men; mean $\pm$ SD age was 54.9 ± 13.6 years. AVF were most often reported in the right arm ($n = 11$; 50.0%) and in one case the laterality was unspecified. AVF types were most often brachiocephalic ($n = 14$; 63.6%) with other sites being radiocephalic ($n = 4$; 18.2%) or unspecified ($n = 3$; 13.6%). One (4.5%) case was in association with a polytetrafluoroethylene (PTFE) graft.

Nineteen cases (86.4%) were post-transplant and 18 (81.8%) were immunosuppressed, the discrepancy being due to one case where the transplant was removed and the patient subsequently continued on haemodialysis without immunosuppression. With regard to immunosuppressive regimen, four (18.2%) cases reported triple therapy, seven (31.8%) reported double therapy, and two (9.1%) reported monotherapy. The agents used were corticosteroids ($n = 10$; 45.5%), ciclosporin ($n = 6$; 27.3%), azathioprine ($n = 7$; 31.8%), tacrolimus ($n = 4$; 18.2%), and mycophenolate ($n = 1$; 4.5%). Two (9.1%) reports did not state what agent was used, and three (13.6%) did not state if patients were receiving immunosuppressive treatment. Transplants from deceased donors were the most commonly reported ($n = 11$; 50.0%) followed by live transplants ($n = 4$; 18.2%). Four (18.2%) reports did not report a transplant type and three (13.6%) cases did not have transplants.

Disease presentation

Pain at a previously asymptomatic AVF site was the most common initial presenting complaint ($n = 17$; 77.3%), either alone or in combination with mass/swelling ($n = 12$; 54.5%) and/or bruising and bleeding ($n = 3$; 13.6%). Three (13.6%) cases presented with only mass, one (4.5%) case with only bleeding, and one (4.5%) case was reported in an arteriovenous PTFE graft and presented with recurrent infections. Initial presenting pattern was most often with two symptoms ($n = 11$; 50.0%); only two (9.1%) presented with three symptoms.

The mean $\pm$ SD time to presentation, in those cases that reported it, from AVF formation was 118.9 ± 57.5 months, while the time from transplant was 96.9 ± 70.0 months. All reported cases were of epithelioid AS.

Diagnostic interval

Seven (31.8%) cases did not report an initial/working diagnosis. Of those that did, thrombosis ($n = 7$; 31.8%) either alone ($n = 4$; 57.1%) or with infection ($n = 3$; 42.9%) was the most often initial diagnosis made of the presenting

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