

# Treating AVMs with rapamycine and bleomycine: about 3 cases

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## KEYWORDS

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## ABSTRACT

Arteriovenous malformations (AVMs) are complex vascular anomalies characterized by direct connections between dysplastic arteries and dilated veins. They often present during puberty or adulthood, most frequently in the head and neck, and may cause complications such as pain, ulceration, bleeding, or high-output cardiac failure. Conventional management with embolization and surgery can be hazardous, while novel biologics are not always accessible. We report three cases of AVMs treated with a combined regimen of systemic rapamycin and perilesional bleomycin injections. The first patient, a 12-year-old girl with a breast AVM, achieved sustained stability after two years of treatment and seven years of follow-up. The second, a 31-year-old woman with a labial AVM, showed complete and durable regression after three years of therapy and six years of follow-up. The third, a 29-year-old woman with a cheek AVM, experienced significant clinical and hemodynamic improvement following two years of combined treatment, after pregnancies had initially limited therapeutic options. These cases highlight the efficacy and tolerability of rapamycin plus bleomycin in controlling AVMs, avoiding disfiguring or high-risk surgery. The findings suggest that this combination may represent a valuable therapeutic option in settings where embolization or advanced biologics are unavailable.

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## 1. Introduction

Arteriovenous malformation AVM is a vascular malformation due to direct communication between dysplastic arteries and enlarged veins, connecting through fistulas creating a nidus. AVMs can be congenital, discovered at puberty and others seem acquired in adulthood. Superficial AVMs usually appear as warm angiomatous blumps with pulsations, thrill and bruit at auscultation. Head and neck is most common location. Ultrasonography with color Doppler UCD is the best diagnosis tool showing low resistance high velocity arterial flow, CT angiography CTA, magnetic resonance angiography MRA and arteriography, describe the nidus and

the involved vessels. Complications can be observed such as pain, ulceration, bleeding, and cardiac failure with a fatal evolution. Resorting to (partial excision, ligation, or endovascular occlusion of the feeding artery) aggravate AVMs. Embolization with various agents followed by wide surgical resection and reconstruction is recommended to manage AVMs. New biotherapies with anti-angiogenic properties like trametinib were recently used in difficult cases. As embolization techniques and biologics are not always available we used rapamycin and bleomycin in three cases, here reported.

## 2. Case Report

### Case 1

A young girl, 12 years old presented a red hot blump on her left breast with discreet pulsations. UCD was normal. Cutaneous biopsy suspected an AVM. The lesion was at Schobinger stage 1, indicating simple monitoring. At the age of 18, a marked increase in local heat, size and pulsatility was noted.

As embolization and biologics were not available, patient received during 2 years rapamycin 1.5 mg/d and bleomycin perilesional injections (1mg/ml) every 2 months. At the end the lesion had improved and remained stable after a follow up of 7 years.

### Case 2

A woman, 31 years old presented a swollen right labial commissure and upper lip. The lesion was warm with pulsations. Facial CTA was performed to evaluate facial blood vessels and retained a right labio commissural AVM. Treatment with rapamycin and bleomycin sclerotherapy was ini-

tiated but stopped after a month due to planned pregnancy. This aggravated the lesion but no hemorrhagic event was observed. After delivery artificial feeding allowed treatment to be resumed and continued for 3 years. A complete and sustained regression was observed with a follow up of 6 years.

### Case 3

A woman 29 years old presented with a warm, violaceous, pulsatile cutaneous mass on the left cheek, overlying the zygomatic bone. A Doppler ultrasound examination revealed an arteriovenous malformation (AVM) with dilated draining veins. MRA demonstrated serpiginous vessels. Due to two successive pregnancies over a four-year period, the lesion was managed conservatively with clinical and imaging surveillance. Subsequently, treatment with rapamycin at a dose of 2 mg/day was initiated, but no clinical improvement was observed. A third

pregnancy necessitated discontinuation of the treatment. During this period, the AVM flow increased from 180 mL/min to 300 mL/min. After delivery, rapamycin was reintroduced, in combination with monthly perilesional radial injections of bleomycin. This combined treatment during 2 years led to marked clinical improvement, with Doppler showing a non-significant residual flow of 30 mL/min.

### 3. Discussion

Management of arteriovenous malformations (AVMs) is challenging. The hemorrhagic risk makes surgical intervention hazardous and requires highly experienced multidisciplinary teams. AVMs typically do not undergo spontaneous regression over the course of a patient's life. Spontaneous regression has only been observed in very elderly patients, likely due to senescence-related vascular changes. In women, management is further complicated by reproductive factors. Hormonal activity, the use of contraceptives, and pregnancy can exacerbate AVMs. Breastfeeding must be discontinued during antiangiogenic therapy. Certain AVMs located in surgically inaccessible or high-risk areas necessitate

conservative approaches, including close surveillance and compression garments. However, recent advances have enabled targeted embolization via superselective microcatheterization, which preserves the vascular supply to adjacent vital structures. In our patients, growth, puberty, pregnancy, and breastfeeding were all aggravating factors that also interfered with treatment. The combination of systemic rapamycin with perilesional (non-endoluminal) bleomycin injections allowed for effective control of the lesions. Although the treatment duration was relatively long, disfiguring or mutilating surgery was avoided in all three cases.

### 4. Conclusion

The combined treatment with rapamycin and perilesional bleomycin injections constitutes an effective and well-tolerated therapeutic approach, albeit with a slow onset of action. It remains a va-

luable option for patients in whom surgical excision is difficult due to the facial location of the lesion and the risk of significant, cosmetically unacceptable scarring.