Pediatric Pulmonology 22:275–279 (1996)

Case Report

Treatment of Recurrent Hemoptysis in a Child With Cystic Fibrosis by Repeated Bronchial Artery Embolizations and Long-Term Tranexamic Acid

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Summary. The course of a 12-year-old girl with cystic fibrosis (CF) and with recurrent hemoptysis since age 8 years is described. Conservative measures failed to control her bleeding. Hemoptysis was only partially controlled by repeated bronchial arterial embolizations. However, the addition of tranexamic acid (TXA) resulted in complete cessation of bleeding. Attempts to withdraw TXA therapy resulted in recurrence of hemoptysis; this patient has, therefore, been continuously maintained on this therapy for the past 4 years. No side effects of long-term TXA treatment have been noted. **Pediatr Pulmonol. 1996; 22:275–279.** © 1996 Wiley-Liss, Inc.

Key words: Cystic fibrosis, hemoptysis, tranexamic acid, bronchial artery embolization.

INTRODUCTION

Hemoptysis in cystic fibrosis (CF) is a potentially lethal consequence[1] of chronic infection, inflammation, and bronchiectasis. Conservative treatment with antibiotics and correction of abnormal clotting factors may be successful in mild hemoptysis, but more severe or recurring bleeds require aggressive therapy with vasoconstrictors, surgical ligation or resection, or bronchial artery embolization (BAE).[2–4] Although BAE avoids the hazards of thoracotomy, it is not without risk such as inadvertent embolization of (aberrant) spinal vessels.[5,6] Furthermore, BAE is not always effective, and even when successful, hemoptysis may recur weeks to years later, necessitating repeat embolization.[3] We have observed that tranexamic acid,[7–9] an antifibrinolytic agent, is a useful adjunct to BAE in preventing recurrence of hemoptysis.

CASE REPORT

Cystic fibrosis was diagnosed when patient S.M. presented at 3 months of age with failure to thrive and pneumonia. A sweat test (by the Gibson-Cook method) showed elevated sodium (80 meq/L) and chloride (100 meq/L) concentrations. She also had pancreatic insufficiency with marked steatorrhoea and absent chymotrypsin activity in her stools. Parents were unrelated and of East Indian extraction. Tests for 12 mutations failed to detect a CF mutation in our laboratory (see Acknowledgments). S.M. had recurrent episodes of pneumonia and failure to thrive despite good compliance with standard CF therapy, including pancreatic enzymes, physiotherapy by percussion, and postural drainage. At age 3 years, severe chalasia with gastroesophageal reflux and esophagitis was diagnosed by endoscopy. Enteral feeding by a nasogastric feeding tube did not improve her nutritional status; at age 5 years, jejunostomy tube feeding was instituted followed by significant improvement in her nutritional status. The bacterial flora in her airways included *Escherichia coli* and *Staphlococcus aureus* initially. At age 5.5 years she started to have *Pseudomonas aeruginosa* in her sputum, which was replaced by *Burkholderia cepacia* at age 7.5

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Received March 25, 1996; (revision) accepted for publication June 14, 1996.

Presented in part at the Ninth Annual North American Cystic Fibrosis Conference, Dallas, Texas, October 12–15, 1995.

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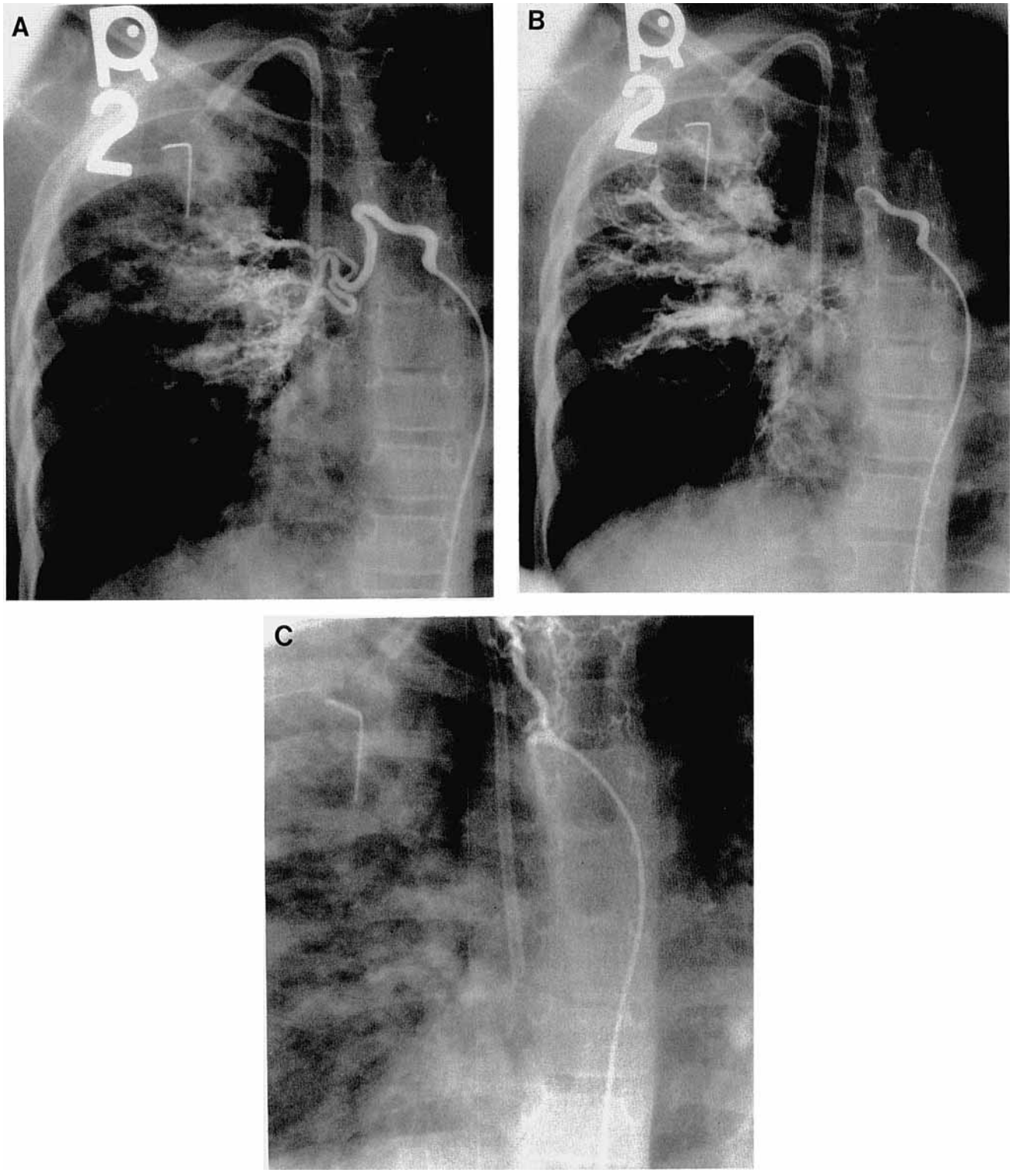

Fig. 1. S.M. at age 8.3 years: Selective broncho-arteriogram. A,B: Pre-BAE studies showing the early and late phases after contrast injection. They show enlarged arteries and extensive collateral flow into the area of chronic lung disease in the right upper lobe. C: Post-embolization angiogram showing occlusion of bronchial artery and filling of para-spinal arteries.

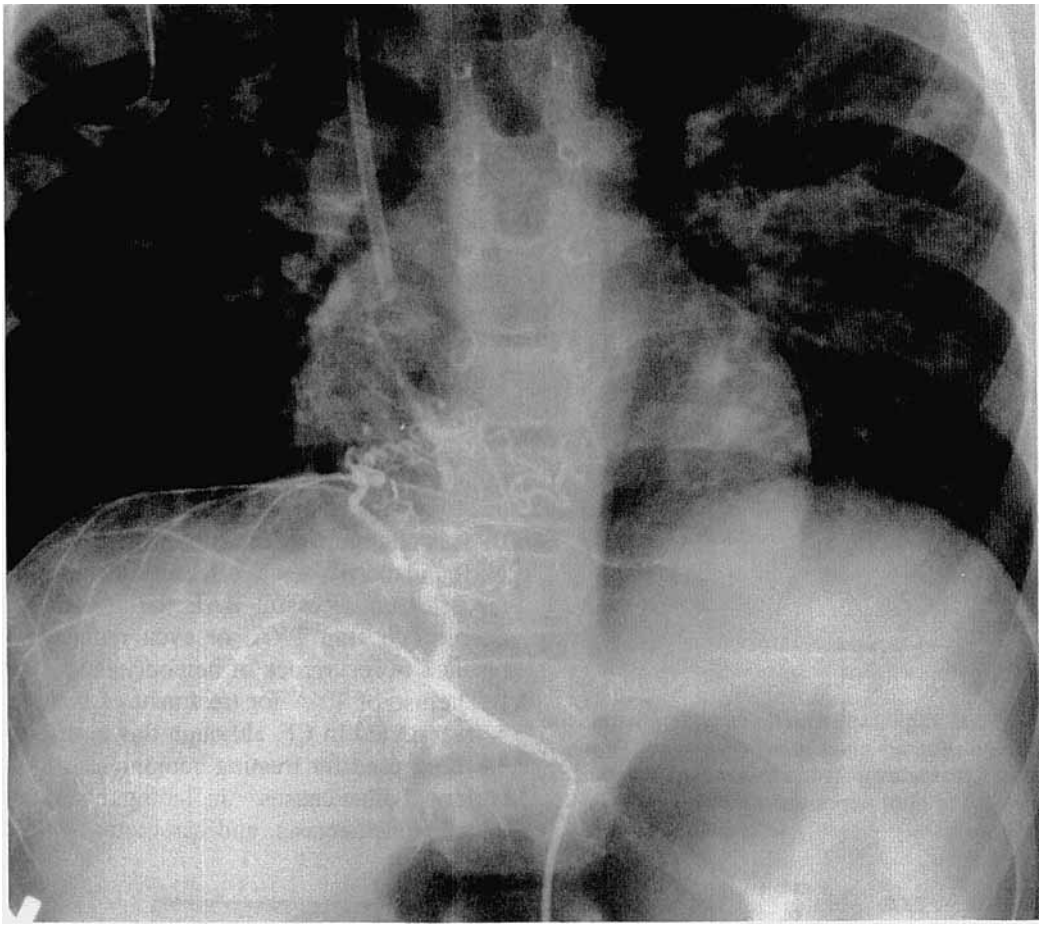

Fig. 2. S.M. at age 8.3 years. Selective inferior phrenic artery injection showing collateral blood supply into the lower right lung.

years. At age 8, she developed allergic bronchopulmonary aspergillosis.

S.M. started to have mild episodes of hemoptysis at age 3.5 years with each pulmonary exacerbation. These episodes responded promptly to antibiotic treatment. However, at age 8.3 years hemoptysis worsened, causing expectoration of up to 30 ml of fresh blood three to four times daily. Her blood hemoglobin dropped from 12.7 g/dl to 11.2 g/dl in 1 week. Angiography revealed enlarged arteries to the right lung, arising from two bronchial arteries and a right inferior phrenic artery (Fig. 1A,B). The larger bronchial artery was selectively embolized with initial arrest of bleeding (Fig. 1C).

One week later, severe bleeding recurred, necessitating a second BAE of the same bronchial artery. The phrenic artery could not be embolized because of collateral branches to the diaphragm, adrenal gland, and mediastinum (Fig. 2). Following BAE, bleeding continued, although it was diminished. Tranexamic acid (TXA; Cyklokapron, Pharmacia) was then started, initially with an intravenous dose of 60 mg/kg/day divided into four doses. Bleeding stopped within 1 day. Subsequently, TXA therapy was changed to oral TXA 500 mg q.i.d. (90 mg/kg/day). Because of concerns over the long-term use of TXA, the dose was tapered beginning in May 1992, and TXA was stopped in August 1992. One month later hemoptysis recurred, resulting in 20–30 ml of bloody expectorate a day. This necessitated a third BAE (Fig. 3), again with only partial resolution of bleeding. Oral TXA was restarted and bleeding stopped again. Since this time, two attempts to reduce TXA below 500 mg t.i.d. (60 mg/kg/day) have resulted in further bleeding. The patient has, therefore, been maintained on this dose up to the present time. Her severe pulmonary disease has remained relatively stable on continued aggressive CF therapy. She has

Abbreviations	
BAE	Bronchial artery embolization
CF	Cystic fibrosis
TXA	Tranexamic acid

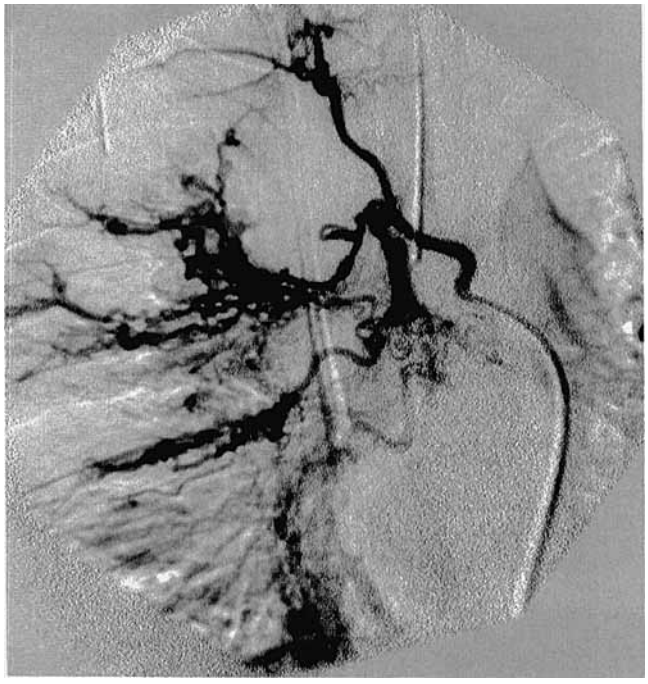

Fig. 3. S.M. at 9.1 years. Digital substraction angiogram from the selective broncho-arteriogram of the same vessel as in Figure 1, but approximately 1 year later. Note the re-opening of extensive collateral vessels to the right upper and mid-lung.

had no evidence of toxicity attributable to TXA. Her pulmonary function test results are shown in Figure 4, and her total Shwachman score at age 12 years was 40.

DISCUSSION

The clinical course of this child with CF is noteworthy for the early onset of hemoptysis, which usually affects older CF patients. It has been estimated that about 7% of adult CF patients develop significant hemoptysis, which is usually self-limiting.[10] This patient developed severe bronchiectasis as a result of recurrent pulmonary infections, aggravated by gastroeosophageal reflux and aspergillosis. Her hemoptysis was not well controlled by the usual conservative treatment and required BAE, which had to be repeated twice. Recurrence of hemoptysis after BAE is common, requiring repeated BAE.[11] In this child we found that TXA was effective in controlling the bleeding after unsuccessful BAE for the past 3 years. Two attempts to stop TXA, or even reduce the dose, have resulted in recurrence of hemoptysis.

The use of TXA for treatment of hemoptysis has not been reported in CF, although this antifibrinolytic agent has been used for treating hemoptysis in adults due to a variety of other causes,[7,9] including tuberculosis, aspergilloma, bronchiectasis, and carcinoma, with a daily dose

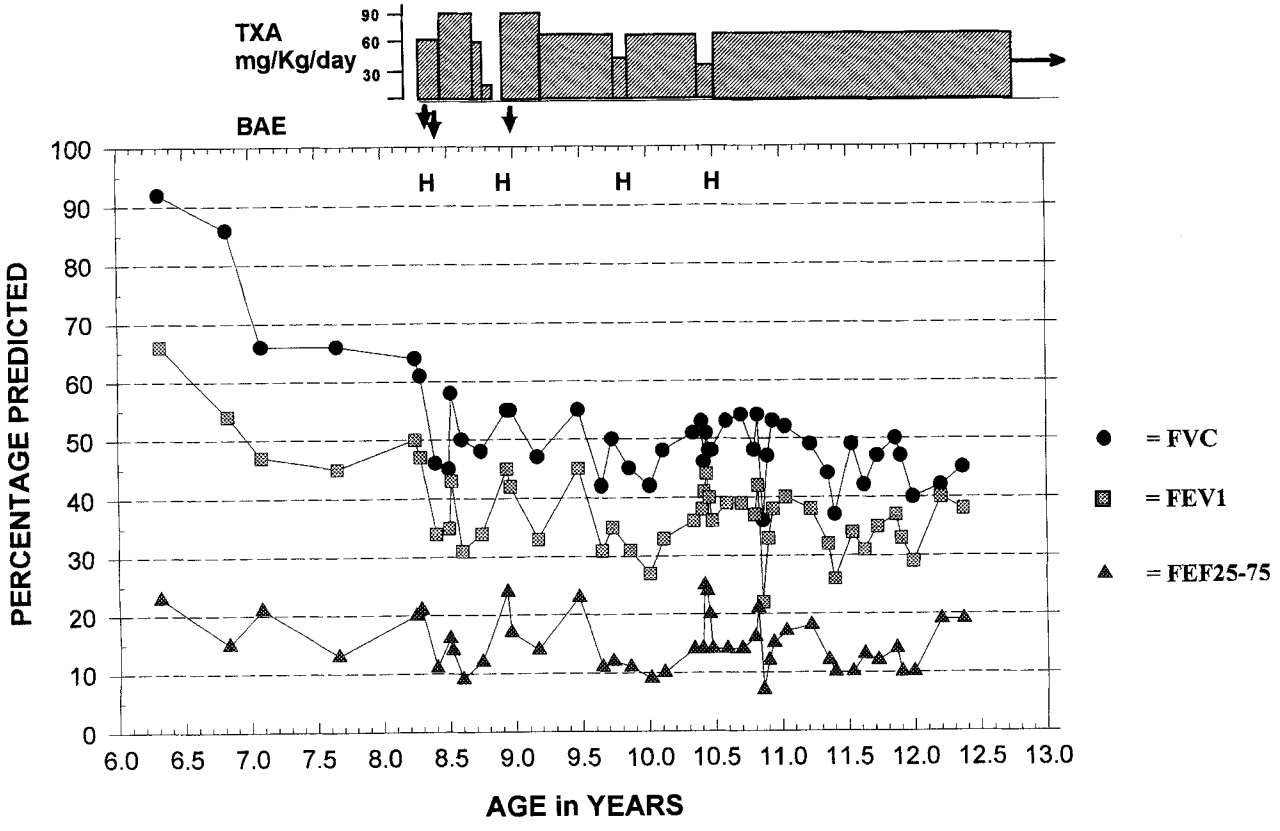

Fig. 4. Pulmonary function tests of S.M. from age 6.5 to 12.5 years. Occurrence of hemoptyses (H), treatment using BAE (↓), and TXA dosage are indicated.

of 0.75–2.25 g TXA. TXA has also been used in the neonatal period for treatment of giant hemangiomas at doses of up to 45 mg/kg/day with no side effect attributable to TXA. The main side effects of TXA therapy are gastrointestinal irritation with nausea, vomiting, and diarrhea. Retinal changes have been observed in experimental animals but have not been observed in human subjects and have not occurred in our patient. Our experience suggests that TXA may be a useful and well-tolerated medication for the treatment of intractable hemoptysis in CF. Further clinical trials are needed to confirm efficacy and safety, and to define the place of TXA in controlling hemoptysis in CF.

ACKNOWLEDGMENT

We acknowledge the performance of the polymerase chain reaction tests by Dr. S. Langlois for the common CF mutations: ΔF508. ΔI507, G551D, R553X, G542X, R560T, S549N, S549I, S549R, W1282X, 621 + 1G-T, and N1303K2.

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