

PEDIATRIC CASE OF SEVERE GPA WITH LARGE VESSEL INVOLVEMENT

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BACKGROUND

Granulomatosis with polyangiitis (GPA) is an **ANCA-associated necrotizing vasculitis** that affects **small- to medium-sized vessels**. The clinical picture is variable and is caused by granulomatous inflammation, most commonly of the respiratory tract and the kidneys. The pathogenesis is driven by the presence of anti-neutrophilic cytoplasmic antibodies (ANCA) targeted against proteinase 3 (PR3) in neutrophils. Large vessel involvement (LVI) is extremely rare in GPA patients and, has – to our knowledge – not yet been reported in pediatric patients.

CASE REPORT

Presentation

A 16-year-old female, with no family history of rheumatic diseases, presented with

- Recurring colds, partly with bloody nasal discharge
- Red eyes
- Coughing for 5 months

Clinical findings

- **Polyarthrititis** (ankle and finger joints)
- Keratoconjunctivitis bilateral
- Raynaud's phenomenon and erythematous palmar papules
- Weight lost of 5 kg in 5 month, night sweats, fever 38.7°C

Diagnostic findings

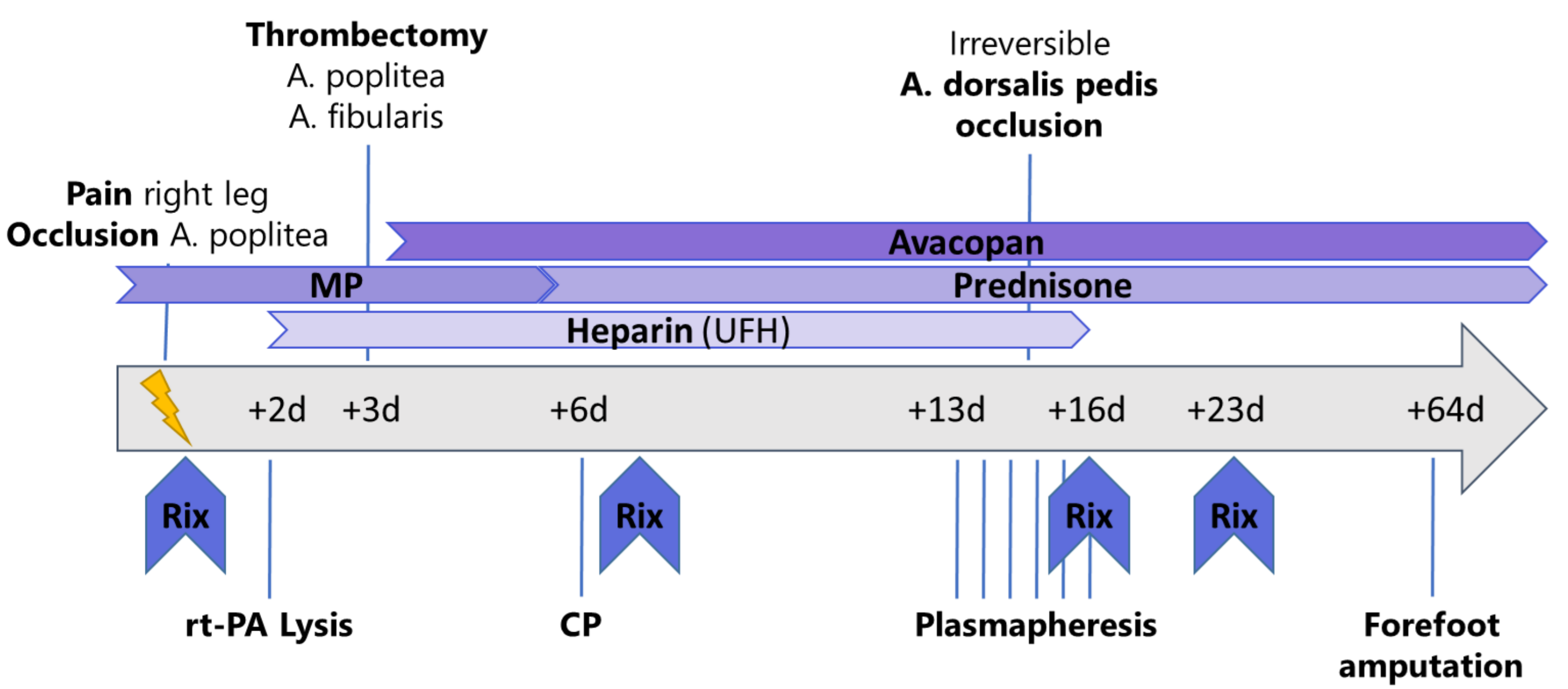
- **Cutaneous papules** (granulomas on histology)
- **Pulmonary infiltrates** on X-ray and chest CT (Fig. 1); with necrotizing inflammation without granuloma or vasculitis on histology
- **Pauci-immune glomerulonephritis** (on histology) with arterial hypertension (160/100 mmHg)
- positive ANCA and **anti-PR-3 antibodies** (Tabl.)

Treatment

- i.v. Methylprednisolone (MP) single 3-day-pulse and subsequent oral prednisone for 6 months
- Rituximab (RIX), 4x dosages (375 mg/m²)
- Avacopan (C5aR antagonist for complement inhibition; 1 year)
- i.v. Cyclophosphamide (CP), single dose (500 mg)
- Plasmapheresis, 6x
- Cotrimoxazole PCP-prophylaxis since 11 months

Clinical course

- Rapid and sustained response of small vessel vasculitis features (pulmonary infiltrates ↓, proteinuria ↓ and renal function ↑)
- Reversible occlusion of A. poplitea but **irreversible occlusion of A. dorsalis pedis**, resulting in **forefoot amputation** (Fig. 2)



Laboratory and Imaging

Parameter	Laboratory Findings
ESR	90 mm/h [<20 mm/h]
Leukocytes	21.3 G/l [4.0-12.7 G/l]
Thrombocytes	650 G/l [160-400 G/l]
Creatinine	2.1 mg/dl [<1.0 mg/dl]
GOT (AST)	23 U/l [10-35 U/l]
CK	41 U/l [<240 U/l]
LDH	434 mg/l [135-220 mg/l]
Ferritin	5.755 µg/l [15-150 µg/l]
Fibrinogen	>700 mg/dl [160-400mg/l]
D-Dimers	26 [$< 0,73$ mg/l FEU]
Urine Status	Microhematuria, Proteinuria (Albumin 393 mg/g Crea)
c-ANCA	1:320
anti-PR3 antibodies	>200 IU/ml [0-10 IU/ml]

Table: Laboratory findings [normal range]

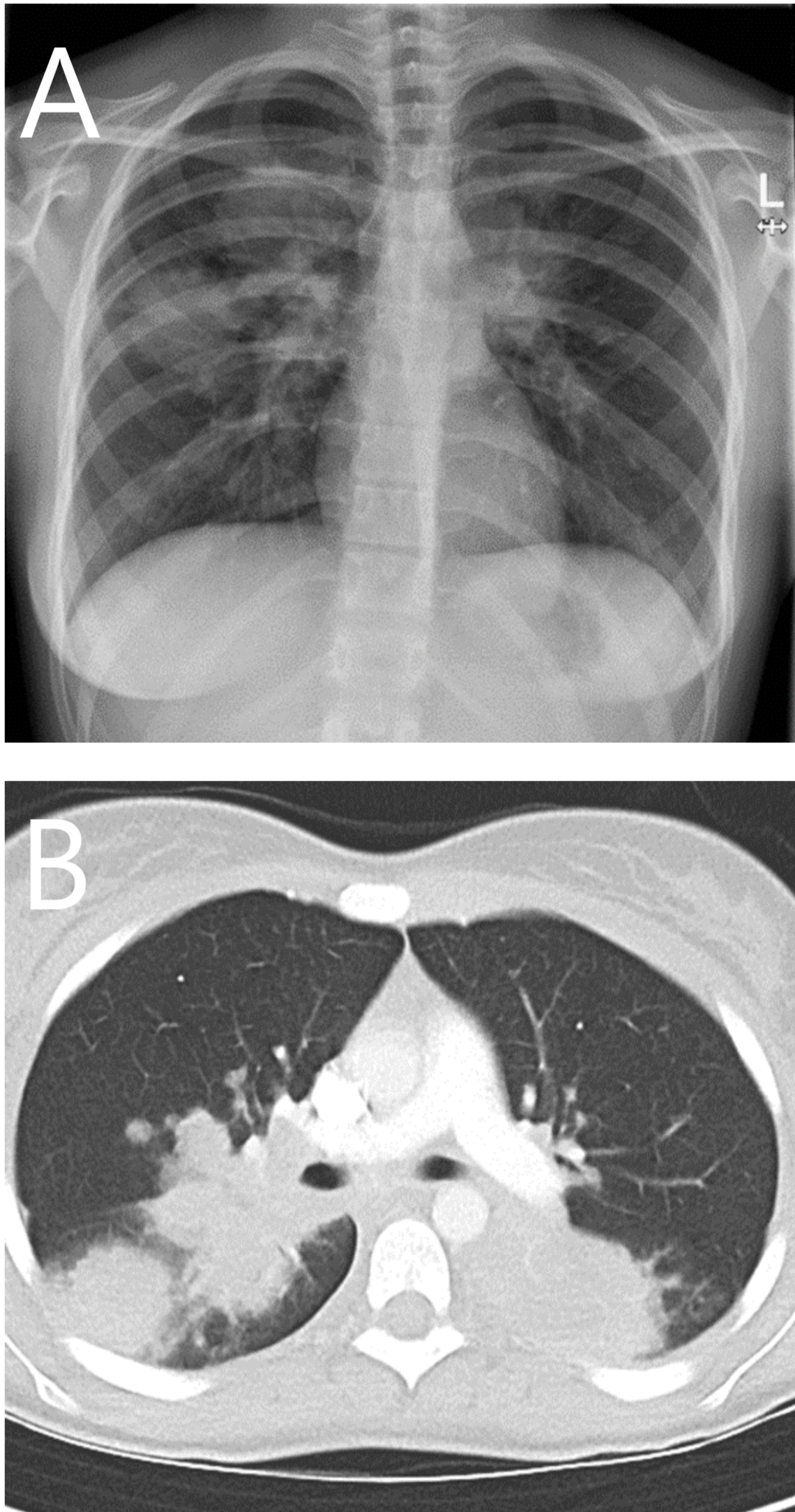


Fig. 1: Chest X-ray (A): infiltrates and lymphadenopathy; Lung CT scan (B): multi-local consolidations

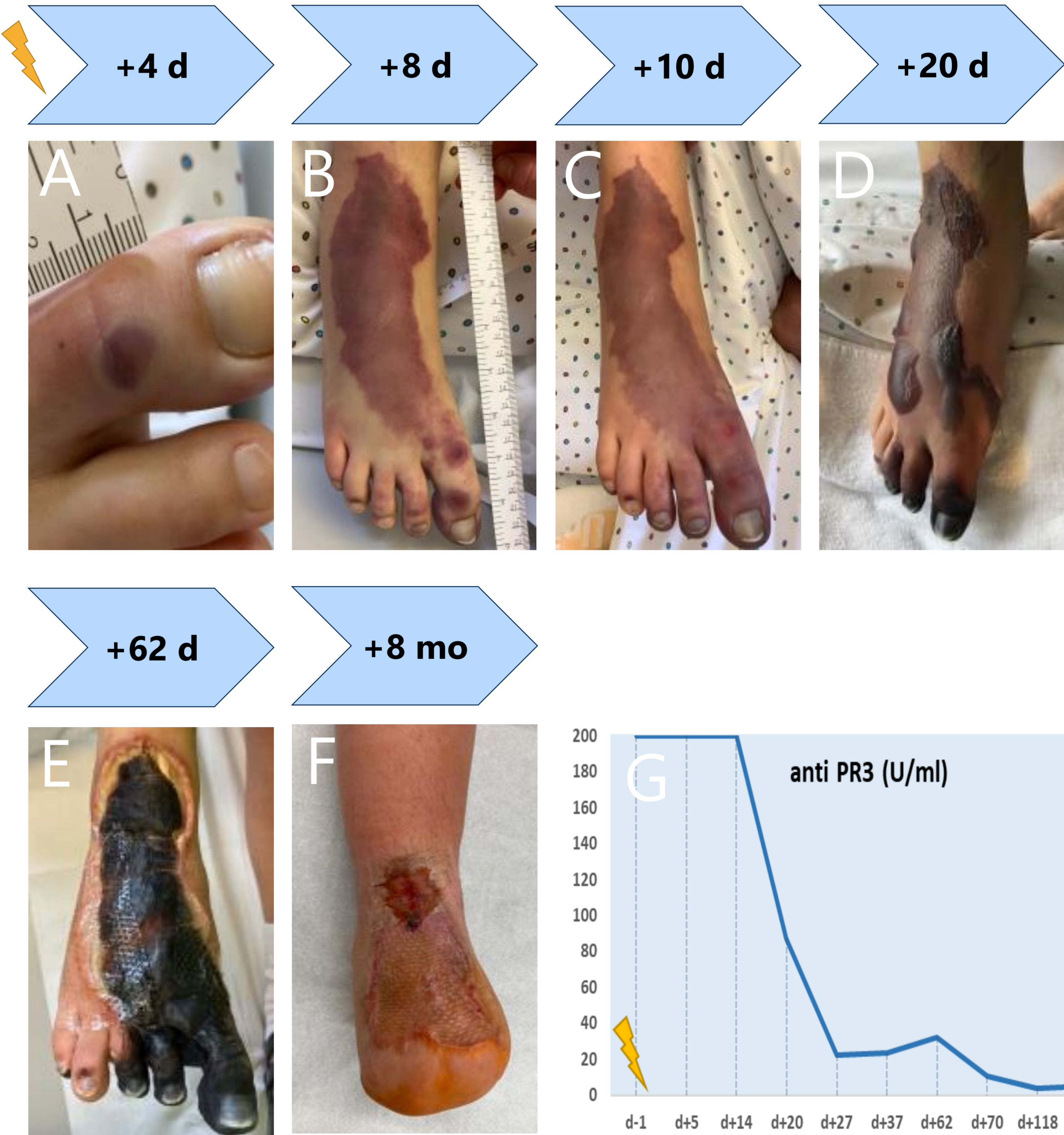


Fig. 2: Clinical course (A-E): occlusion of A. dorsalis pedis; (F) S.p. forefoot amputation; anti-PR3 levels (G)

CONCLUSION & OUTLOOK

- Large vessel involvement (LVI) in GPA has to be considered
- Risk factors for LVI and prognostic factors are still unclear
- Avacopan therapy planned for a minimum of 1 year
- Rituximab therapy planned for a minimum of 2 years