

**Tuberculid reactions:  
A multi-institution cohort study  
from 2 academic medical centers  
in the United States**

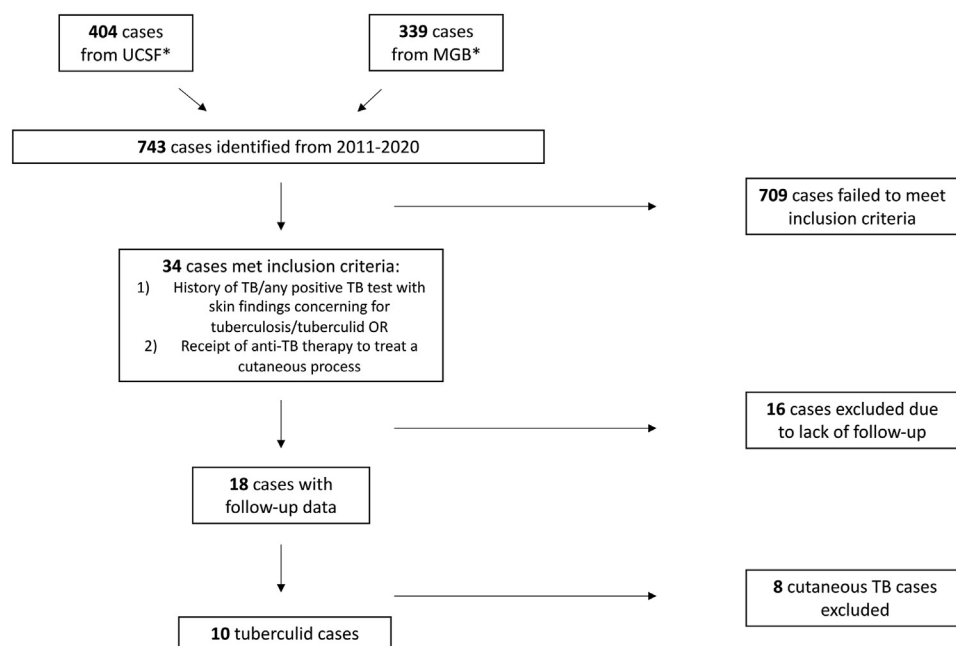


*To the Editor:* Tuberculids are cutaneous hypersensitivity reactions to tuberculosis (TB) elsewhere in the body. Clinical response to TB treatment is diagnostic in the appropriate clinical setting.<sup>1,2</sup> Literature surrounding the disease course and response to treatment in US populations is limited. We sought to characterize tuberculid reactions across 2 US academic medical centers.

Patients diagnosed with tuberculids from January 2011 to May 2020 at Mass General Brigham and University of California San Francisco Health were identified via institution-specific electronic medical records system using terms related to cutaneous TB/tuberculid (Appendix 1, available via Mendeley at <https://data.mendeley.com/datasets/m7rgh7c27g/1>) yielding 743 cases (Fig 1). Cases were screened for history of (1) TB/any positive TB test associated

with skin findings concerning for tuberculid and (2) empiric treatment for tuberculid, resulting in 24 records. Fourteen cases were excluded because of incomplete treatment data, resulting in 10 patients.

Of the 10 patients, 3 patients (30%) were Asian, 2 (20%) were Black, 2 (20%) were White, 1 (10%) was American Indian/Alaska Native, and 2 (20%) were of unspecified race. Ages ranged from 21 years to 77 years, and 60% of the patients were female. One patient had end-stage renal disease, and 1 patient was receiving immunosuppressive therapy. Seven patients had erythema induratum, 1 had papulonecrotic tuberculid, 1 had erythema nodosum, and 1 had granulomatous vasculitis. All 10 patients had extremity involvement, and 2 patients also had truncal involvement. One patient with truncal lesions also had head/neck involvement (Table I). Three patients (30%) had systemic symptoms, 1 of whom (10%) had pulmonary symptoms. Morphologies included subcutaneous nodules and erythema as well as livedoid changes. Two patients



\*using search terms related to tuberculid reactions/cutaneous TB (appendix)

**Fig 1.** Determination of study population. Data obtained from electronic health records of 2 hospital systems: University of California, San Francisco (UCSF) and Massachusetts General/Brigham and Women’s Hospital (MGB).

**Table 1.** Clinical presentation, diagnosis, and response to treatment

Patient	Age (y)	Sex	Race	Subtype	Distribution	PPD	IGRA	AFB smear	Response to treatment
1	55	Female	Asian	Erythema induratum	Extremities	Positive	Positive	Negative	Partial
2	59	Female	American Indian/ Alaskan Native	Erythema induratum	Extremities	Positive	Positive	Negative	Partial
3	21	Female	Black/African American	Erythema nodosum	Extremities	Negative	Positive	Negative	Partial
4	44	Female	Other	Erythema induratum	Extremities	Positive	Positive	Negative	Partial
5	77	Male	Asian	Granulomatous vasculitis	Trunk, Extremities	Negative	Negative	Negative	No response
6	47	Female	Asian	Erythema induratum	Extremities	Positive	Unknown	Negative	Full
7	49	Male	Unknown	Erythema induratum	Extremities	Unknown	Indeterminate	Negative	Full
8	27	Female	White/Caucasian	Erythema induratum	Extremities	Unknown	Positive	Negative	Full
9	54	Male	White/Caucasian	Erythema induratum	Extremities	Unknown	Positive	Negative	Partial
10	36	Male	Black or African American	Papulonecrotic tuberculid	Head and neck, trunk, extremities	Positive	Unknown	Positive	Partial

AFB, Acid-fast bacillus; IGRA, Interferon Gamma Release Assay; PPD, purified protein derivative test.

(20%) had ulcerations. After 10 weeks of antimicrobial therapy, 3 patients (30%) had complete resolution of skin lesions, 4 (40%) partial resolution, and 1 (10%) no response. Two (20%) patients for whom follow-up data were available by 15 weeks showed partial response. Of 9 patients with full/partial response, that is, “responders,” 1 received rifampin monotherapy and 8, a multidrug treatment regimen indicated for the treatment of active TB. Eight responders had skin biopsies showing lobular septal, granulomatous, or other panniculitis, granulomatous vasculitis, and other granulomatous patterns. Five of 9 responders had skin tissue cultures (all negative). Interferon Gamma Release Assay was available and positive in 6 of 7 (85.7%) and indeterminate in 1. Purified protein derivative (PPD) skin test was positive in 5 of 6 (83.3%), and both purified protein derivative and Interferon Gamma Release Assay were positive in 3 of 3 cases where both were available (100%). Eight responders had a skin acid-fast bacillus smear; only 1 was positive. The lone nonresponder received multidrug therapy for a granulomatous vasculitis with pan-negative TB testing history.

Although limited by its small sample size and incomplete data, this United States-based study suggests skin lesions concerning for tuberculid tend to improve with anti-TB therapy in patients with and without positive TB testing. However, complete resolution of skin lesions was seen in only a minority of patients, raising several questions including (1) the role of antibiotics in creating a nonspecific antiinflammatory effect, (2) incomplete eradication of organisms in some cases, and (3) long-term immune altering effects from infectious triggers that persist beyond initial presentation.

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#### **Conflicts of interest**

Dr Haemel reports serving as a consultant to CSL Behring and Guidepoint.

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