

Necrotizing Sarcoid Granulomatosis: Ocular Manifestation in 3 Children of African Origin

Necrotizing sarcoid granulomatosis (NSG) is a rare systemic disease characterized by confluent sarcoid-like granulomas with necrotic areas and a variable degree of vasculitis. First described by Liebow¹ in 1973, NSG can be classified as a disease showing features of Wegener granulomatosis and sarcoidosis. The etiology and pathogenesis of NSG are so far unknown; it is considered to be unrelated to infection. Necrotiz-

ing sarcoid granulomatosis is an extremely rare disease in childhood, with only a few cases reported to date.² In this case report, we describe 3 children of African origin who were diagnosed with an ocular manifestation of NSG.

Report of Cases. Symptoms and important diagnostic results are summarized in the **Table**. Our institution does not require approval by the local ethics committees for chart review studies.

Patient 1. Patient 1 is a 9-year-old boy of half African, half Caucasian origin, who was born in Germany and grew up there. His father was born in Ghana, Africa, and is known to have sarcoidosis (Table). The oph-

thalmologic examination revealed a regular anterior segment of the eye, but chorioretinal infiltrates with retinal vascular occlusions and perivascular exudation were observed bilaterally. The histopathologic findings are shown in **Figure 1**, and the fluorescein and indocyanine green angiographic observations are documented in **Figure 2**. The child received treatment with corticosteroids (prednisolone) initially 2 mg/kg body weight for 4 weeks, which was then reduced in a stepwise fashion. Subsequently, the ocular findings improved, and the perivascular exudation disappeared after 7 months. After a follow-up of 15 months, the boy presently does not show any symptoms and is in excellent condition.

Patient 2. Patient 2 is a 10-year-old boy of African origin who was born in Germany and grew up there (Table). The ophthalmologic examination showed bilateral granulomatous panuveitis with vasculitic retinal infiltrates. Systemic treatment with prednisolone, 2 mg/kg body weight, was instituted. Complete inflammatory quiescence was obtained after a follow-up of 13 months with this therapy.

Patient 3. Patient 3 is an 11-year-old African girl who was born in Germany and grew up there (Table). The parents are from Congo, Africa. The ophthalmologic examination showed bilateral granulomatous panuveitis with mutton-fat keratic precipitates, cells in the aqueous humor, iris granulomas, posterior synechiae (**Figure 3**), vitritis, chorioretinal infiltrates, and retinal vascular exudation. She received treatment with prednisolone, initially 1 mg/kg body weight, which was subsequently tapered over 7 weeks to a dosage less than 0.1 mg/kg body weight, in combination with azathioprine (1.5 mg/kg body weight). The ocular findings improved thereafter. After 18 months, no retinal infiltrates were present. Currently, her uveitis is in complete remission.

Table. Systemic Symptoms and Results of Systemic Diagnostic Testing

Variable	Patient 1	Patient 2	Patient 3
Symptoms	Stomach aches, lethargy, fever	Nightly cough, lethargy, fever, weight loss	Lethargy, fever, weight loss
Chest radiograph	Unremarkable	Enlarged lymph nodes bilaterally	Unremarkable
Serum ACE	Negative	Negative	Elevated
Histopathologic findings in biopsy specimens	Mesenteric lymph nodes: granulomatous reaction, Langerhans cells, and caseating necrosis	Mediastinal lymph nodes: necrotizing granulomas with giant cells and vasculitis of small vessels	Omentum major: necrotizing granulomas with giant cells and vasculitis of small vessels
Mycobacterial test results in biopsy specimens: Ziehl-Neelsen stain, cultures, and PCR	Negative	Negative	Negative

Abbreviations: ACE, angiotensin-converting enzyme; PCR, polymerase chain reaction assay.

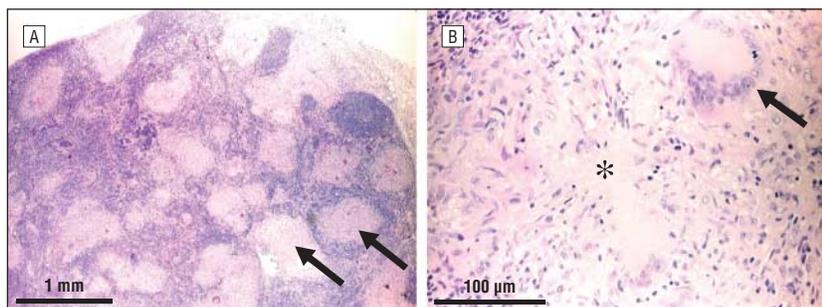


Figure 1. Lymph node biopsy of patient 1 showing multiple granulomas. A, Hematoxylin-eosin (HE) stain; arrows indicate granulomas. B, HE stain in more detail, with 1 granuloma with necrosis (asterisk) and a Langerhans giant cell (arrow).

Comment. Only a few reports have described involvement of the eyes in necrotizing sarcoid granulomatosis.^{3,4} Posterior segment manifestations have rarely been documented. Our case series describes the chorio-retinal involvement in detail, including the findings from fluorescein and indocyanine green studies.

Granulomatous inflammation and caseating or noncaseating necrosis plus vasculitis seen on biopsy of enlarged lymph nodes identified on computed tomography and magnetic resonance imaging scans are not disease specific but meet the criteria for the diagnosis of extrapulmonary NSG.^{1,2} Regarding the finding of partially caseating necrosis in the setting of a pediatric patient, tuberculosis represented the most likely diagnosis in the differential, but all biopsy specimens were negative for bacteria, fungi, and acid-fast bacilli (typical and atypical mycobacteria) on histologic stains, cultures, and polymerase chain reaction assay. Histopathologically, caseating or noncaseating necrosis was atypical for sarcoidosis, and serum angiotensin-converting enzyme levels were negative in 2 of the 3 children. Nevertheless, increased angiotensin-converting enzyme levels are not a specific marker for sarcoidosis. Other causes for necrotizing granulomata were also excluded, including Wegener granulomatosis, microscopic polyangiitis, Churg-Strauss syndrome, Crohn disease, infectious diseases (varicella zoster, leishmaniasis, and aspergillosis), Hodgkin lymphoma, and postsurgical granulomata.

It may be assumed that NSG might be a subtype of sarcoidosis. However, none of our patients had pulmonary findings consistent with sarcoidosis. The main characteristic that distinguishes sarcoidosis from NSG is necrosis in the center of the granulomas. This necrosis may arise from granulomatous vasculitis with progressive vessel occlusion. The retinal findings described for our patients reflect this histopathologic characteristic. The hypofluorescent spots that were seen in our patients in the indocyanine green studies are typical of granulomatous infiltrations in the choroid. In addition, mutton-fat keratic precipitates and the

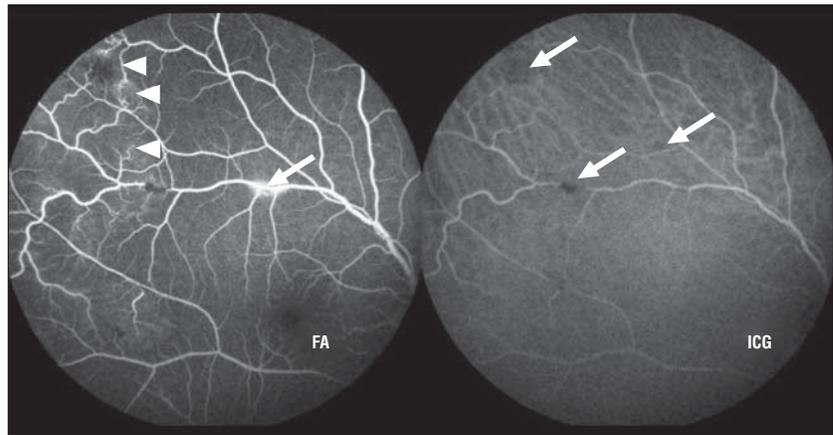


Figure 2. Fluorescein and indocyanine green (ICG) angiographic observation in patient 1 from the right eye, both at 5.09 minutes. Fluorescein angiogram (FA) shows retinal vascular occlusions and shunt formation in the fundus periphery (arrowheads) with retinal leakage (arrow). By ICG angiography, hypofluorescent spots can be observed in the choroid (arrows), likely from inflammatory infiltration.

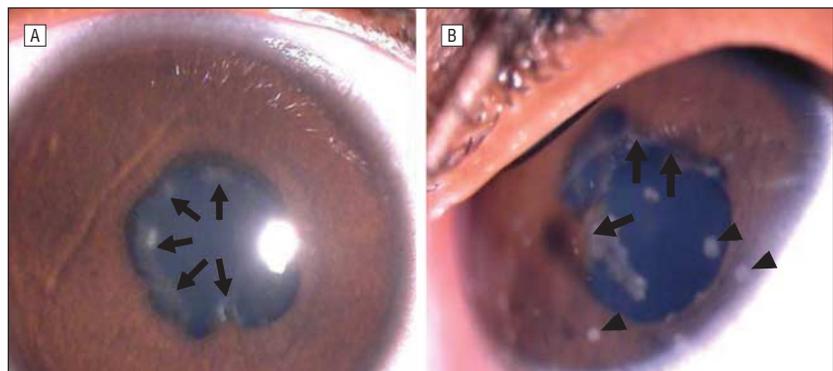


Figure 3. Anterior segment photography in patient 3 showing posterior synechiae (arrowheads) and mutton-fat keratic precipitates (arrows) of the right (A) and left (B) eyes.

granuloma formation in the iris support the granulomatous character of the eye manifestation. Furthermore, the fluorescein features show the frank perivascular exudation that is typical for sarcoidosis and the retinal occlusion that may occur in patients with granulomatous uveitis. Taken together, these findings support the hypothesis that NSG may be a variant of sarcoidosis and not a clinical entity of its own.

Interestingly, all of our patients were of African origin. Presently, no data are available showing a higher incidence of NSG in Africans. Indeed, only 1 case report of NSG in an African patient has been published. One of our patients had a familial predisposition to sarcoidosis; his father has this disease. To our knowledge, so far only 1 instance of NSG has been described in which a positive family history of sarcoidosis was present.⁵

Necrotizing sarcoid granulomatosis is reported to respond very well to immunosuppressive treatment with corticosteroids. In patients 1 and 2, we observed a timely response to systemic administration of corticosteroids. Patient 3 had to be treated with azathioprine in addition to corticosteroids to achieve remission. All 3 patients went into remission, and the clinical and angiographic findings improved. However, it is important to follow up these patients because relapses have been reported after treatment was discontinued.

Claudia Schumacher, MD
 Anne Lohr, MD
 Marion Kaup, MD
 Peter Walter, MD
 Johannes Roth, MD
 Alberto Perez-Bouza, MD
 Norbert Wagner, MD
 Arnd Heiligenhaus, MD

Author Affiliations: Department of Ophthalmology, St Franziskus Hospital, Muenster (Drs Schumacher and Heiligenhaus); Departments of Pediatrics (Drs Lohr and Wagner), Ophthalmology (Drs Kaup and Walter), and Pathology (Dr Perez-Bouza), University Hospital RWTH Aachen, Aachen; and Department of Pediatric Rheumatology, Institute of Immunology, University of Muenster, Muenster (Dr Roth), Germany.

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Correspondence: Arnd Heiligenhaus, MD, Department of Ophthalmology, St Franziskus Hospital, Uveitis-Center and Ophtha Lab, Hohenzollernring 74, 48145 Muenster, Germany (arnd.heiligenhaus@uveitis-zentrum.de).

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Correction

Error in Author Affiliations. In the Epidemiology article titled “Use of Eye Care Services Among Diabetic Patients in Urban Indonesia” by Adriono et al, published in the July 2011 issue of the *Archives* (2011;129[7]:930-935), an error occurred in the author affiliations. The affiliations for Drs Adriono and Octavianus should have been Department of Ophthalmology, Faculty of Medicine, Universitas Indonesia—Cipto Mangunkusumo Hospital, Jakarta, Indonesia. This article was corrected online.