European Review for Medical and Pharmacological Sciences 2014; 19: 375-380

Systemic granulomatosis after surgical injection of silicone oil for retinal detachment in a child affected by Fisher-Evans syndrome

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Abstract. – Silicone oil is used for complicated retinal detachment, but it can be associated with relevant side effects. We report a 6-year-old South American female admitted to our hospital with steroid-resistant Fisher-Evans syndrome. She also had developed a retinal detachment, managed with intravitreal oil injection. During treatment for Fisher-Evans syndrome, she progressively developed recurrent and refractory bronchospasm, peaks of hypereosinophilia and orbital soft-tissue swelling. Despite the persistent negativity of all microbiologic tests, she was treated empirically with antibiotics. Failure of the treatment led to the execution of a biopsy of the periocular tissue that revealed an intense polymorphous infiltrate constituted by numerous monoclonal population (FR2 monoclonality) of plasma-cells. A diagnosis of lymphoma with plasmacytoid differentiation was suspected and cytotoxic treatment was started without response. For the appearance of swelling in left parotid and latero-cervical region, an excisional biopsy was performed and a diagnosis of granulomatous reaction to ocular implant of silicone oil was made. In consideration of the clinical evolution, enucleation was considered, but parents did not consent to the procedure until the child developed cerebral lesions suspected to be silicone localizations. After enucleation, eosinophilic count normalized and the child no longer presented any new episode of fever or swelling.

CONCLUSIONS: In this patient a granulomatous reaction is present at distance from the site of oil injection. This case suggests caution in using this substance even in ocular diseases, especially in immunocompromised patients.

Key Words:
Silicon oil, Retinal detachment, Systemic granulomatosis, Fisher-Evans syndrome, Childhood.

Introduction

Silicone has been used in surgery for many years in liquid, solid or particulate form because it was been considered for a long time an inert substance. The growing evidence of a high rate of morbidity and even mortality reduced its use, at least in the liquid form, which is presently banned for cosmetic purpose[1]. Treatment of complicated retinal detachment with silicone oil is still used, although it is not free from side effects. Granulomatous foreign body reaction is the most frequent local response, but distant effects due to the silicone dissemination are described.

We report the case of a child in whom intravitreal silicone oil tamponade for retinal detachment was followed by relevant local and general side effects.

Case Presentation

A 6-year-old South American female was admitted to our hospital with Fisher-Evans syndrome diagnosed three years before in her country of origin, where she had been treated with intravenous immunoglobulin, corticosteroids, splenectomy and chemotherapy. Parents reported also a left retinal haemorrhage and subsequent retinal detachment, which had been treated with intravitreal silicone oil injection.

At our Division, the child was treated with corticosteroids, anti-CD20 monoclonal antibody (rituximab) and cyclosporine-A (Cs-A). During immunosuppressive treatment, the child developed recurrent/refractory bronchospasm and hypereosinophilia (up to 3,340 eosinophils/mm^3). Chest CT scan revealed bilateral small nodular peripheral lung opacities, enlarged mediastinal and axillary nodes. Extensive microbiologic stud-

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ies were carried out. Because the parents refused a biopsy of a representative nodule, although we excluded infective causes, she was empirically treated with intravenous antibiotics without relevant clinical improvement.

After six months the child developed progressive orbital soft-tissue swelling with eosinophilic counts ranging from 2.960/mm^3 to 11.520/mm^3. A brain MRI revealed abnormal tissue in the left orbit, extending to the eyelid and to the soft tissue of temporal region (Figure 1 a, b). Despite the persistent negativity of all microbiologic investigations, she was again treated with antibiotic therapy; the failure of this treatment induced to perform a biopsy of the peri-ocular tissue.

Histological examination revealed a lesion characterized by an intense polymorphous infiltrate constituted by histiocytes with foreign-body giant cells, eosinophils and plasma-cells carrying the lambda chain (Figure 2 a1-e1). A diagnosis of lymphoma with plasmacytoid differentiation was made. Molecular studies confirmed the presence of a monoclonal population (FR2 monoclonality) and therapy with cortisone, vincristine, adriblastin, cyclophosphamide and rituximab was started. In view of the diagnosis Fisher-Evans syndrome, double-negative T-cells were evaluated, excluding an autoimmune lymphoproliferative syndrome. Extensive immunological evaluation revealed negativity of auto-antibodies panel. For clinical deterioration and radiological worsening characterized by high grade fever, increased of eosinophilic count (up to 38,230/mm^3) enlargement of the orbital mass and appearance of left parotid and latero-cervical region, excisional biopsy of an accessible lymph node was performed. Morphological, immunohistochemical and molecular findings were the same of the peri-ocular biopsy, but the presence of small clear vacuoles in the giant cells evoked the suspicion of a granulomatous reaction to silicone oil (Figure 2 a2-e2). Ultrastructural examination was performed after retrieval of a small fragment of tissue from paraffin block both from the periocular and from the lymph node. This study revealed amorphous electron-dense structures within phagocytic vacuoles, typical of silicone localiza-

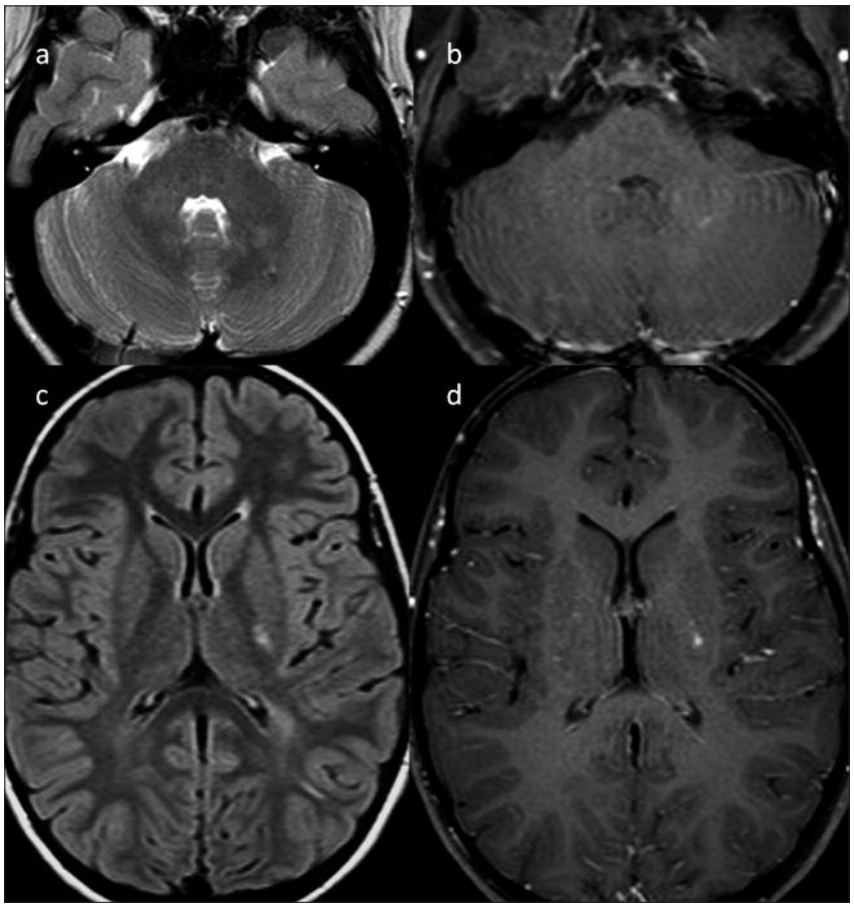

Figure 1. ***a,*** Fat-sat axial T2WI orbital MRI. ***b,*** Axial contrast-enhanced T1WI orbital MRI. ***c***, Axial T2W cerebral MRI. ***d,*** Axial contrast-enhanced T1W cerebral MRI. Abnormal tissue involves both intraconal and extraconal regions of the temporal portion of the left orbit, extending to the eyelid and to the soft tissue of the temporal region. The lesion is characterized by hyperintense signal on T2WI ***(a)*** and mild enhancement ***(b)***. The residual left microphtalmus is displaced downward. The first image shows an area of high T2 signal extending trough the right middle cerebellar peduncle, to the pons and to the right cerebellar white matter; a second lesion with the same high T2 signal is located in the controlateral cerebellar hemisphere. There is no evidence of significant mass effect ***(c)***. Contrast-enhanced image shows mild diffuse enhancement of both lesions ***(d)***.

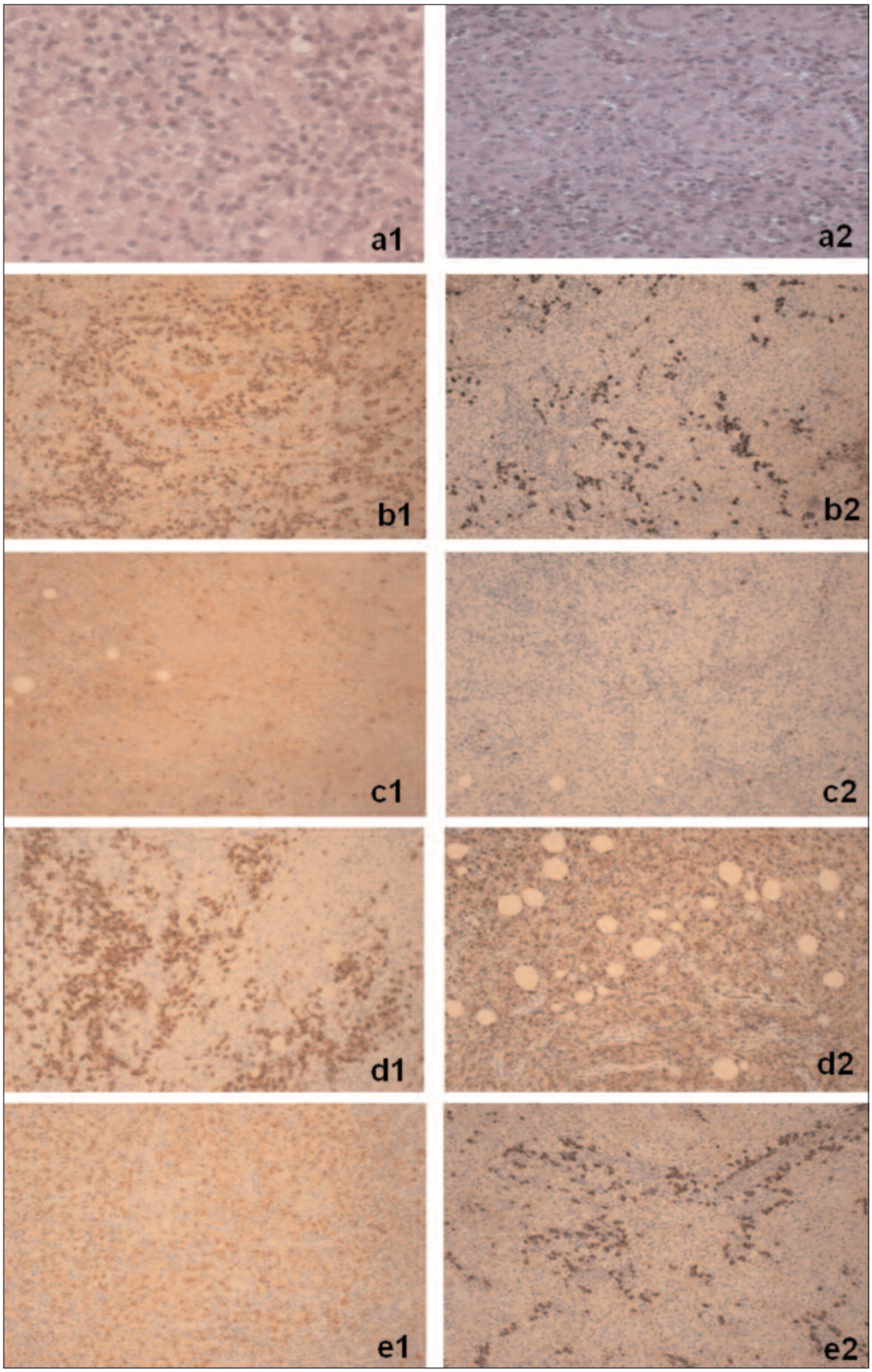

Figure 2. Similar morphological pictures are evident in periocular tissue (Figures 2.1) and in laterocervical lymph node (Figures 2.2) and consist of a granulomatous reaction with mononucleated hystiocytes, multinucleated giant cells plasmacells and eosinophyls. (***a1*** and ***a2***; E&E 40×). CD138 (***b1***, ***b2***) highlights the numerous plasmacells that express monotypic, predominantly k light chain immunoglobulin (***c1***, ***c2***: κ chain; ***d1***, ***d2***: λ chain; 10×). Images ***e1*** and ***e2*** show CD 68 stain in mononucleated and multinucleated hystiocytes (CD68 10×).

tions (Figure 3)[2]. In consideration of the clinical evolution and of the evidence of atrophy of the eyeball, enucleation was considered but parents refused the procedure.

Subsequently, a MRI performed for routinely control of lesion, showed appearance of cerebral lesions suspected to be silicone localizations (Figure 1 c, d) and led parents to agree with enucleation. Macroscopically the eye showed complete architectural disorganization. Histologically a chronic inflammatory cellular infiltrate with prevalent histiocytic and giant cells component was present, most notably in association with silicone oil vacuoles in the residual retinal tissue (Figure 4). No silicone oil vacuoles were evident in the optic nerve.

After enucleation, eosinophilic count normalized and the child no longer presented any episode of fever or swelling. Brain MRI performed 7 months after enucleation showed an important reduction in the periocular infiltrate and an almost complete resolution of cerebellar lesions. A new small lesion in the left globus pallidus was also observed.

Discussions

Silicones are a family of polymers that consist of an inorganic silicone-oxygen backbone (R-Si-O-Si-O-Si-O-R) with organic side groups attached to the silicone atoms. Polydimethylsiloxane, the silicone for medical use, can be in form of rubbers, gel or oil[3]. The use of silicone was first described in ocular (1962)[4] and in breast surgery (1963)[5]. In spite of the initial believe that it is biologically inert, numerous complications, even serious ones, have been increasingly reported. Complications may be both local, with an inflammatory granulomatous reaction to vacuoles of silicone in involved tissue, and systemic, with more important effects, namely pulmonary and neurologic. Pulmonary pathology can be manifest as embolism, congestive pulmonary disease, pneumonitis, diffuse alveolar damage or alveolar haemorrhage[6,7]. The exact mechanism of pulmonary pathology remains to be defined, but several factors have been implicated, such us large volume injections, particle migration, high pressure infiltration, and intravascular injection[8]. In cases with neurologic complications, microinfarctions from microparticles of silicone have been documented[9]. Cardiac, hepatic, and gastrointestinal involvement has also been reported[10]. Other important systemic complications include lymphadenopathy, granulomatous hepatitis, arthritis and connective tissue disease[11-13]. Silicone embolism syndrome (SES) is a well recognized systemic syndrome with multiple pulmonary involvements that occurs in patient treated with liquid silicone injection for cosmetic purpose[1].

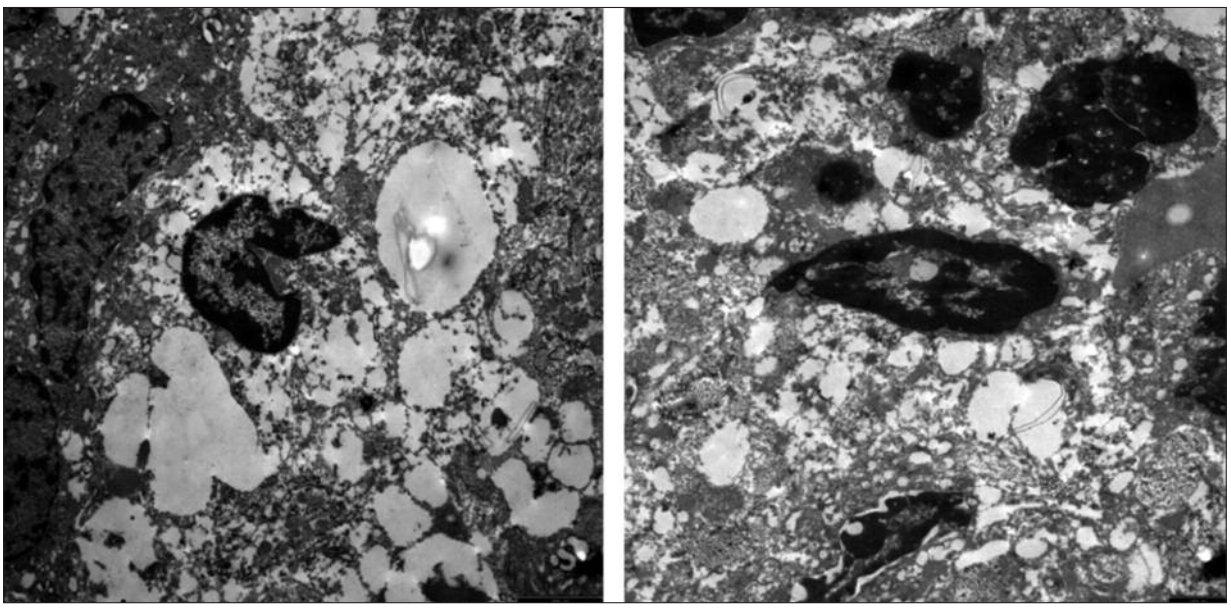

Figure 3. Electron microscopy: macrophages with multiple vacuoles contain silicone that appear as amorphous electron dense structures.

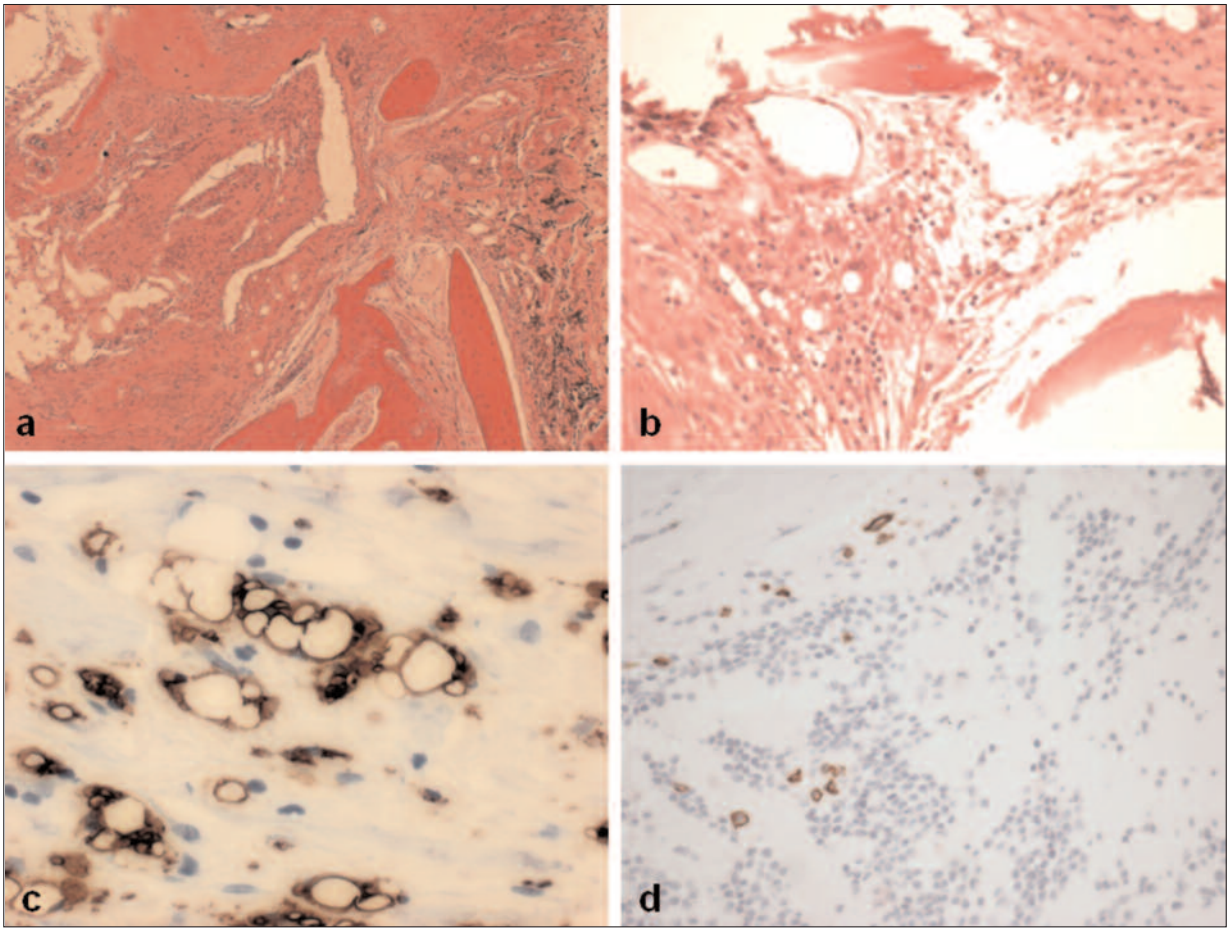

Figure 4. Enucleated eye show complete architectural disorganization with total retinal detachment, chronic inflammatory response and bone formation (***a, b,*** E&E 10×). The inflammatory infiltrate contains numerous macrophages with phagocytosed silicone oil (***c,*** CD68 10×) and rare plasmacells (***d,*** CD138 10×).

Complications of silicone oil injection in ocular pathology were first described by Cibis[14] in 1965 who reported a case of aseptic endophtalmitis and two cases of uveitis. Parmely et al[15] in 1986 first described a foreign body giant cells lesion in a human eye treated with intravitreal silicone oil injection and enucleated 20 months later. Afterwards, other authors described local intra or extraocular complications. Biswas et al[16], in a review of eight cases, showed the presence of silicone oil vacuoles in various tissue of all eyes in association with chronic inflammatory infiltrate. No association was found with patient age, reason for intraocular tamponade, persistence of silicone oil inside the eye or postoperative course. Only the presence of silicone in the optic nerve correlated with an increase of intraocular pressure. Episcleral spillage of silicone oil, with granulomatous reaction in periorbital tissue was described by Srinivasan et al[17] and by Cooke et al[18]. No description of distant granulomatous reactions to intravitreal silicone oil tamponade has been found in literature except intracranial silicone oil migration, most likely through the optic nerve[19,20].

Silicone oil has been considered to be immunologically inert for a long time, but a growing number of reports demonstrate otherwise[21,22]. First of all, even a foreign body reaction is anyway an immunological response; moreover, some patients have been found to have specific antipolymer IgG selectively binding to silicone particles[23].

In our case, the presence of a clonal plasma cell population appears to be strictly correlated with the stimulus of the silicone oil outside the ocular globe. The presence of a monoclonal plasma cell proliferation reactive to an exogenous stimulus in a child is unique, especially considering that monoclonal proliferation of plasma cells

is not found in the pediatric age. This case is, furthermore, the first in which a granulomatous reaction is present at a distance from the ocular region. This finding could probably be related to the immunocompromised status of the child. Migration through the optic nerve was not evidenced in the child. Although we did not have a formal histological prove of the presence of silicone oil in the lung or in the brain, it is more than reasonable to consider them as due to systemic silicone oil dissemination.

Conclusions

This case suggest caution with the use of silicone even in ocular pathology in pediatric immunocompromised population.

Informed Consent

Written informed consent was obtained from the patient for publication of this Case report and any accompanying images. A copy of the written consent is available for review by the Editor-in-Chief of this journal.

Conflict of Interest

The Authors declare that there are no conflicts of interest.

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