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Silicone allergy in ventriculoperitoneal shunts

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Abstract Reported are the cases of three hydrocephalic patients who developed a clinically heterogenous entity with an allergic rejection of their silicone ventriculoperitoneal shunts. All of the patients had an original presentation indicative of a shunt infection, but laboratory analysis revealed sterile cerebrospinal fluid in all three cases. The typical course included recurrent skin breakdowns over the shunt tract, subsequent infections and development of fungating granulomas. Treatment, with successful resolution of the symptoms, included changing the shunt material from silicone to polyurethane, with immunosuppression in one patient and removal of the shunt altogether in the other two patients. The roles of the immune system and silicone in the pathophysiology of this condition are discussed.

Key words Silicone · Rejection
Ventriculoperitoneal shunts
Allergies

Introduction

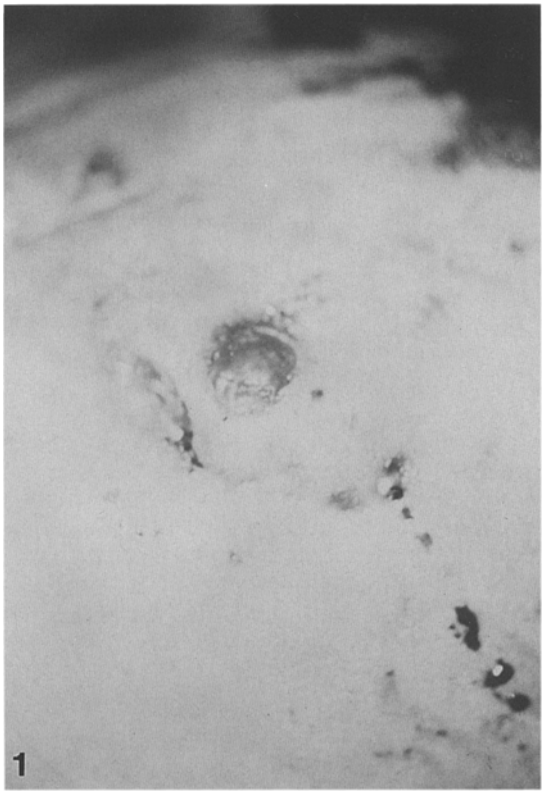
The treatment of hydrocephalus has been a major challenge to surgeons since the advent of neurological surgery in the nineteenth century. Diversion of cerebrospinal fluid using foreign materials has been tried by many but their success rate has been limited by a high failure rate. Materials such as glass wool, linen, catgut, rubber, latex, calves' arteries, silk, gold and many more have been used, but their use has been fraught with many complications [10]. However, since the clinical introduction of silicone in 1955 by Pudenz et al. [12] for shunting hydrocephalic patients, shunt rejections have not been reported as a problem. We report three patients who developed allergies to silicone resulting in multiple rejections and operations.

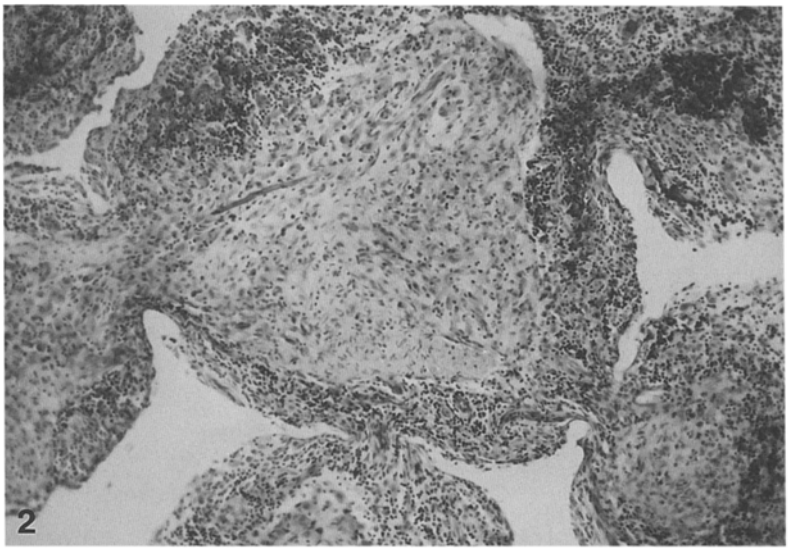
Case histories

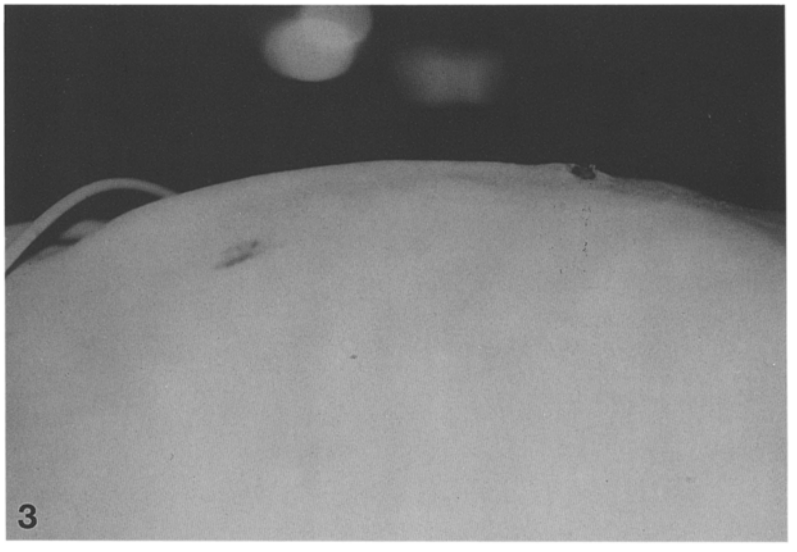
Case 1

The patient is an 8-year-old boy who was born with aqueductal stenosis and required placement of a ventriculoperitoneal (VP) shunt at 6 months of age. At 7 years of age, he required a revision after the development of a proximal shunt obstruction. He presented several weeks later with fever, malaise and a small area of breakdown over the shunt reservoir. Cerebrospinal fluid analysis revealed no evidence of infection and only a very mild pleocytosis.

The area of erosion over the reservoir enlarged, requiring a revision. Several weeks later he again developed scalp breakdown over the reservoir and shunt in areas not associated with the surgical incision or sutures (Fig. 1). The shunt eventually became infected and required revision. Two weeks later he returned with skin ulcerations over the new shunt site. At this point, he underwent replacement of the silicone shunt with a polyvinyl chloride system but rejected this unit also, with similar symptoms, within 3 months. He developed large pedunculated foreign body granulomas over the head and neck areas (Fig. 2). The patient then underwent replacement of the polyvinyl shunt with a medical grade aliphatic poly-







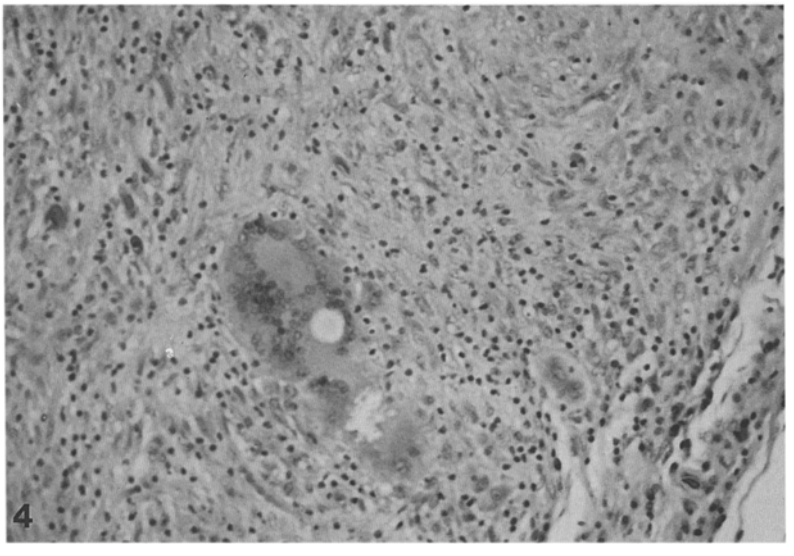


Fig. 1 Photograph showing complete erosion of the scalp over the shunt reservoir after the area had been prepared with betadine solution

Fig. 2 Low magnification of granuloma: granulomatous inflammation with epithelioid and chronic inflammatory cells. HE, ×13

Fig. 3 Swollen and necrotic shunt tract over the chest with an area of ulceration along the tract

Fig. 4 Photomicrograph showing a multinucleated foreign body giant cell with what may be silica crystals inside the cell. HE, ×25

urethane shunt. He was also treated with high-dose immunosuppresion with cyclosporine for several days and high-dose prednisone, which was tapered to a low-dose maintenance level for almost a year. His clinical condition improved immediately and he has been symptom-free for 4 years.

Case 2

The second patient was diagnosed as having Soto syndrome (seizure disorder, megaloencephaly and gigantic features of the hands and feet), and at 2 years of age experienced an abrupt increase in head circumference. A CT scan demonstrated ventriculomegaly, which was treated with a VP shunt. Seven months later, he presented with fever, irritability and mild obtundation. A shunt tap revealed no organisms, normal glucose and protein and a mild lymphocytic pleocytosis. After a short stay in hospital he was discharged symptom-free.

In subsequent months he was readmitted with similar symptoms and during one of those admissions he was found to have a skin breakdown over the reservoir and shunt tubing. A shunt tap showed an infection with gram-positive cocci, and the shunt was therefore externalized. After appropriate treatment the boy underwent a revision but returned 1 month later with a shunt tract that was necrotic and an exposed shunt tubing (Fig. 3). Histological examination of the shunt tract demonstrated chronic inflammatory tissue, giant cells, foreign body granulomas and many polymorphonucleocytes (Fig. 4). The patient was also noted to have an erythematous rash under the hospital's silicone identity badge at his wrist. The shunt was replaced with a polyurethane shunt but he continued to experience skin breakdowns. He subsequently developed shunt infections and a brain abscess. A lumboperitoneal shunt was placed but again, skin ulcerations over the shunt occurred, necessitating removal. The shunt was removed and a custom-designed Teflon-coated polyurethane VP shunt was placed. Three weeks later the patient returned with the shunt extruding from the neck. Our patient himself externalized the shunt where it had eroded through the skin. A ventriculostomy was placed and later removed. The patient has remained symptom-free for 18 months.

Case 3

The patient is a 15-year-old girl born with hydrocephalus and mild mental retardation. She had undergone two shunt revisions for obstructions since the original operation at 1 year of age. She presented with symptoms of shunt infection but was found to have a sterile CSF. Several days later she developed a skin breakdown over the shunt's reservoir and tract over the scalp area. The shunt was removed and another one was placed on the contralateral side, but she developed similar erosions over the shunt on that side. She eventually developed infections requiring multiple shunt revisions. During one of the externalizations, the area around the ventriculostomy exit site was found to be necrotic. Once again an attempt was made to see whether she could tolerate closure of the ventriculostomy, and she did well for 72 h, when it became dislodged accidentally. Although she was experiencing mild headaches, the shunt was not replaced and she has now been symptom-free for 1 year.

Discussion

Silicones (polysiloxanes) comprise a group of inorganic compounds that have been in use for nearly 40 years. F. S. Kipping developed the basic principles of silicone chemistry during the late 1800s. In 1945, Dow Corning Corp. began large-industrial-scale production of silicone. Pudenz, in 1955, developed the first successful shunt made of silicone for the treatment of hydrocephalus. Soon thereafter, polysiloxanes became the material of choice for all the shunting of hydrocephalus.

Several characteristics have made silicone the material of choice for bioproducts. It is one of the most inert materials available for use in medicine today. It has been found to possess minimal biological reactivity and toxicity when it is implanted. Its chemical properties have been characterized by no chemical toxicity or abrasive properties. These elastomers have high flexibility [1] and chemical stability [4]. Their high level of heat resistance [15] makes them ideal for heat sterilization, since their physical properties do not change at high temperatures. Silica rock (made of silicon and oxygen), is heated allowing silicon to escape, which is then treated with methylchloride and allowed to condense to form long chains of silicon oxygen with two methyl groups on each molecule. This forms the backbone of most medical-grade silicones: the dimethylpolysiloxane group (Fig. 5).

These polymers are manufactured in many shapes and forms, with marked variation in their elastic properties. Silicones are poor conductors of electricity and do not form any dynamic interactive properties of major importance. Generally, there is no immunological reactivity to their presence and they do not act as haptens to combine with other proteins to produce an antigen–antibody reaction [6]. In order to modify the surface of these polymers, they undergo a process of surface modification called plasma treatment. Briefly, this process involves the placement of the polymer in a reaction chamber containing specific gases that are excited with a high-frequency field causing them to ionize. The gas plasma that is produced causes modifications on the surface of the polymer, which affect only the outermost 10–1000 Å. This process increases the bondability, biocompatibility, wettability and hydrophobicity of the polymer. It also allows for printing with ink on the surface of the polymer. Aro-

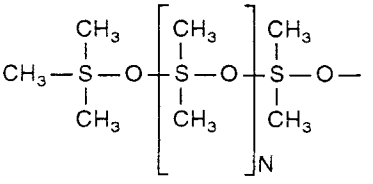


Fig. 5 The dimethyl/polysiloxane group, which forms the backbone of most medical-grade silicone

matic and aliphatic polyurethanes form families of elastomeric materials that are used for production of a number of biomedical products (i.v. tubing, indwelling catheters, dialysis devices, etc.). Aliphatic polyurethanes are excellent materials for this type of product, because of their high biocompatibility, low toxicity and greater tensile strength. The shunt that we used on our first patient was of the aliphatic group.

Silicone reactions

Although chemically inert, silicones are not necessarily biologically inert. There have been a number of reports, mostly in the plastic surgery literature, implicating silicone as the causative agent in a number of reactions. The body's reaction to silicone can be classified into three major categories: (1) local reaction and granuloma formation, (2) silicone migration and (3) human adjuvant disease. In all cases following the implantation of silicone there is the development of a chronic type of reaction to the implant, which includes the formation of a fibrous tissue pseudocapsule with minimal inflammatory reaction. This constitutes the very familiar shunt tract. Another form of reaction that has been recognized is the formation of granulomas, termed "siliconomas" by Winer and Sternberg [16]. These are focal collections of macrophages, histiocytes, epithelioid cells, giant cells, lymphocytes and plasma cells. The granulomatous reaction constitutes a cellular response to irritating, persistent and poorly soluble substances. The silicone elastomer (as found in VP shunts) produce a foreign body giant cell reaction with lymphoid hyperplasia and chronic inflammation. These siliconomas have been found in the subcutaneous and soft tissues of patients who have received injections of the liquids and gels. They have also been produced in laboratory animals following injection of the gels [13].

Another way in which silicone can affect an implant patient is with the phenomenon of migration. Clinically, several patterns have been identified: lymphatic, hematogenous, and local. Lymphatic migration has been most commonly reported in the axillary nodes of patients with breast implants. The silicone "bleeds" and migrates out of the implants, to be found later in the regional lymph nodes [5]. Lymph node migration has also been reported with the use of finger joint prostheses [2, 7]. Hematogeneous migration has been reported to occur to almost every organ, including brain, liver, spleen, kidneys, adrenals, lungs and bone marrow [3]. This phenomenon is most commonly seen in patients with a cardiac valve prosthesis, those undergoing cardiopulmonary bypass and those who frequently undergo hemodialysis [9]. Local migration has been implanted and a local granulomatous reaction has taken place.

A third and more serious reaction has recently been described [14]. Human adjuvant disease or autoimmune disease can occur following implantation of paraffin or silicone polymers. It usually takes several years, and the patients typically develop signs and symptoms that are suggestive of an autoimmune process. Symptoms include arthritis, arthralgia, and local and regional lymphadenopathy. There have been reports of patients developing connective tissue disease according to the criteria of the American Rheumatologic Association. These include systemic lupus erythematosus, Sjøgren syndrome, Hashimoto thyroiditis [8], scleroderma and primary biliary cirrhosis [11]. Commonly found are elevations of serum globulins, erythrocyte sedimentation rate and a positive rheumatoid factor. All of these cases have been found to occur in women who have undergone injection or implantation of silicone for breast augmentation.

Upon exposure to a foreign antigen, humans react immunologically by mounting either a cell-mediated or a humoral-mediated response. The cell-mediated response is activated by macrophages and lymphoid cells and is associated with the phenomenon of delayed hypersensitivity. In contrast, the humoral response is associated with immediate hypersensitivity and is mediated by the production of antibodies. The mechanism by which silicone implants elicit an immune response is not entirely clear. The silica that is added to the medical grade polysiloxane to increase its viscosity is known to have biological irritability and antigenic potential. However, the silica is tightly bound by fillers used in the production of medical silicone. One hypothesis states that with biodegradation of the implants, the filler that binds the silica erodes and thus exposes the antigen to the immune system. Another possibility is that the conversion of silicone to silica by the macrophages exposes the antigen with the subsequent immune rection [6]. Yet another possibility is that the silicone microparticles present in the elastomers or in the gels may act as hapten-like substances to then combine with other molecules to form an antigenic complex [16].

The cases presented in this report clearly do not reflect a single entity. However, they appear to constitute several points along the spectrum of clinical allergic reactions. The clinical presentation ranged from the more severe rejection presenting with fungating granulomas and skin breakdown to the less, albeit, important recurrent skin breakdowns over the shunt area. The exact mechanism remains unclear. It may be due to a number of factors, the most important of which is the patient's own cellular and humoral response as it relates to the genomic control of expression of their transplantation antigens (HLA). We do not believe that they represent the simple localized reaction that has been reported by many and that includes the development of a fibroconnective capsule with infiltration of macrophages and lymphocytes. Whether it represents a very mild form of human adjuvant disease or

a very severe local reaction is not clear. Nevertheless, these cases represent important clinical entities, which so far have not been reported. Fortunately, two of the patients were able to tolerate the permanent removal of the shunt with subsequent and complete resolution of their symptoms. The third, and most severely affected, patient was succesfully treated with immunosuppression and the placement of a polyurethane shunt.

Conclusions

Several important points have emerged from our experience. Foremost, there appears to be a condition in which hydrocephalic patients reject their shunts. We do not think that this is the result of suture-related rejection, since the suture lines were not involved with the skin erosions and the breakdowns occurred elsewhere. The original presentation of these patients was nonspecific and closely resembled a shunt infection. However, infections occurred in all patients following persistent breakdowns. Once this condition develops, it presents a significant and formidable challenge to the clinician. We have described our approach to this problem, which includes changing the shunt material for aliphatic polyurethane along with long-term immunosuppression. Our two prior cases were successfully treated with shunt removal, although this is quite unlikely to be successful in many other patients. In order to fully and better define this entity, we propose that any child suspected of having a shunt rejection undergoes the following tests: erythrocyte sedimentation rate, complement (C_3 and C_4) levels, immunoglobulin levels (IgG, IgA, IgE and IgM), FANA (fluorescent antinuclear antibodies) and if positive, ENA (extractable nuclear antibodies), ribonucleoprotein, rheumatoid factor, tissue biopsy and even HLA typing. Reporting these cases and their tests results should allow for better characterization and definition of this uncommon yet very important problem.

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