Cerebrospinal fluid eosinophilia in children with ventricular shunts

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Object. Eosinophils have been reported in children with cerebrospinal fluid (CSF) shunts. The goal of this study was to describe the risk factors, relationship to infection, and clinical significance of CSF eosinophilia in a large group of shunt-treated patients.

Methods. The authors performed a retrospective review of data obtained in all patients who underwent ventricular shunt placement or revision at the James Whitcomb Riley Hospital for Children between 2000 and 2004.

Results. Eosinophils were identified during a follow-up shunt evaluation in 93 (31%) of 300 patients after initial shunt placement. Eosinophilia was statistically related to CSF extravasation (p < 0.0001), shunt infection (p = 0.031), blood in CSF (p < 0.0001), younger age at shunt insertion (p = 0.030), and the diagnosis of posthemorrhagic hydrocephalus (p < 0.0001). Patients with CSF eosinophilia had a higher risk of subsequent shunt failure (p < 0.0001).

Analysis was performed using data obtained in a cohort of patients with a total of 130 shunt infections. Cerebrospinal fluid eosinophils were identified in 118 infections (90.8%). The leukocytic and eosinophilic reactions were dependent on the infecting organism. Propionibacterium acnes had a statistically lower CSF leukocyte count but higher differential percentage of eosinophils than the other common pathogens.

Conclusions. Cerebrospinal fluid eosinophilia is a relatively common finding in children with shunts. Patients with CSF eosinophilia had an increased risk of shunt malfunction in the present series. Eosinophilia is associated with infection, CSF extravasation, and blood in the CSF. Patients with P. acnes–induced shunt infections have higher eosinophil percentages than are found in infections associated with other common organisms. Therefore, in patients with eosinophilia, extended anaerobic culture studies should be performed with particular attention paid to searching for this pathogen. (DOI: 10.3171/PED/2008/1/4/288)

KEY WORDS • cerebrospinal fluid shunt • eosinophil • hydrocephalus • infection • shunt malfunction

OSINOPHILS are granulocytes produced in the bone marrow and normally found in mucosa. They have a myriad of functions associated with hypersensitivity and inflammatory reactions. Eosinophils are not normally present in the CSF. Their presence is considered pathological and historically has been associated with allergy, intrathecal antibiotic administration, parasitic infestation, neurosyphilis, and fungal or tuberculous infection. 4,15,19,23,30,36,40

We have noted a number of ventricular shunt–treated patients with high CSF eosinophil counts that were seemingly unrelated to the traditional “causes.” In this study we describe the common factors, clinical courses, and potential causes of CSF eosinophilia in a large group of shunt-treated children.

Clinical Materials and Methods

A retrospective analysis of hospital records and laboratory results was performed for all patients < 18 years of age who had undergone a ventricular shunt procedure at the James Whitcomb Riley Hospital for Children during the study period of 2000–2004. The study began after institutional review board approval. There were a total of 1571 shunt procedures. In 300 patients a shunt was initially placed during the study period.

Cerebrospinal fluid samples were obtained as part of the clinical care. The number and timing of sample collections therefore varied among patients. Samples were acquired either at surgery, through an EVD catheter or access device, or by a shunt “tap.” The CSF data points included culture results, cell count with differential percentages, glucose, and protein levels. In patients with shunt infection, the timing of the peak number of eosinophils and WBCs was recorded in relation to the first positive CSF culture.

Abbreviations used in this paper: CSF = cerebrospinal fluid; EVD = external ventricular drainage; PMN = polymorphonuclear; RBC = red blood cell; WBC = white blood cell.
Cerebrospinal fluid eosinophilia

We defined CSF “eosinophilia” as ⩾ 1% on the CSF cell count differential. We defined an episode as the finding of eosinophils in association with a clinical event. For example, in a patient treated for shunt infection there may be multiple CSF samples demonstrating eosinophils. The “eosinophilia” in this case is related to the shunt infection. Therefore, the entire clinical course of the infection would be 1 episode. The episode ends with resolution of the clinical event: treatment of the shunt infection, shunt revision, or resolution of the patient’s symptoms.

All patients with an initial shunt placed during the study period were identified. Any CSF sample obtained prior to insertion of the shunt was recorded. All data of subsequent procedures and CSF examinations were analyzed. Data obtained in patients with an episode of eosinophilia were compared with data acquired in those without an episode. These patients all received care and underwent all procedures at our institution.

We reviewed the cases of all patients in whom a shunt was revised during the study period. A cohort of patients with eosinophils but without evidence of shunt infection was identified and data were analyzed. A separate analysis was made of all patients treated for shunt infection. Criteria for the diagnosis of shunt infection included clinical signs of fever, abdominal pain, or shunt malfunction and a positive culture from either the CSF or shunt hardware.

Standard surgical techniques and commercially available shunt systems with synthetic silicone catheters were used. One patient had an antibiotic-impregnated catheter placed at initial shunt insertion. Our standard treatment of shunt infection is removal of all shunt hardware, placement of an EVD system, and administration of intravenous antibiotics. The antibiotic regimen is determined in consultation with pediatric infectious disease specialists. The CSF samples are cultured approximately every other day during external drainage. The standard duration of external drainage is 2 weeks following the last positive CSF culture. Intrathecal antibiotics were given in 22 patients when intravenous therapy failed to sterilize the CSF. We do not routinely administer intrathecal antibiotics during initial shunt placement. All CSF specimens drawn for infection were routinely studied with both aerobic and anaerobic cultures.

Statistical analysis was performed using SAS Version 9 software. The chi-square and Fisher exact tests analyzed associations between binary factors. Associations of ordinal factors with binary outcomes were analyzed using the Wilcoxon rank sum test. Comparisons of diagnoses between cohorts were performed using logistic regression. Spearman rank correlation coefficient was used to test pair-wise correlations between ordinal variables. Tests were conducted as two-sided at a statistical significance of 0.05. Mean data are presented ± the standard deviation.

Results

Initial Shunt Placement During the Study Period

There were 300 patients with an initial shunt placed at our institution between 2000 and 2004 (Table 1). All laboratory values and shunt procedures were studied. Cerebrospinal fluid samples were obtained when there was clinical suspicion of a shunt malfunction or infection. The mean follow-up period was 3.8 ± 2.0 years.

A total of 316 subsequent shunt surgeries were required in 138 of these patients. A CSF analysis was performed in 137 (99.3%) of the patients requiring a shunt revision. Eosinophils were identified in 73 (53.3%). A CSF analysis was performed during the follow-up visit of 121 (74.7%) of the 162 patients who did not require a shunt revision. Eosinophils were identified in 20 (16.5%). Patients with a CSF sample demonstrating eosinophils were statistically more likely to require shunt revision (p < 0.0001). The need for shunt revision was correlated with the total eosinophil number (rho = 0.370, p < 0.0001) and percentage (rho = 0.404, p < 0.0001) of the CSF differential. The need for shunt revision was not statistically correlated to the peak CSF protein level prior to initial insertion.

Statistical comparisons were made between the patients with eosinophils and the patients without this finding. Eosinophilia was statistically correlated with shunt infection (p = 0.03), use of intrathecal antibiotics (p = 0.01), and younger age at shunt insertion (p = 0.03). There was no statistical relation to a history of latex or medication allergy.

There was a strong statistical correlation between eosinophilia and the presence of CSF extravasation—either gross leakage or subcutaneous fluid accumulation at the shunt site (p < 0.0001). There were 31 (5.0%) such extravasations related to the 616 total shunt surgeries in this group. Cerebrospinal fluid eosinophils were found in 26 (83.9%) of the 31 extravasations. Ten CSF leaks were indicative of shunt infection. Cerebrospinal fluid eosinophils were demonstrated in 16 (76.2%) of the 21 patients with subcutaneous fluid accumulation without infection.

Multivariate analysis showed a statistical relationship to posthemorrhagic hydrocephalus of prematurity (p = 0.038) in comparison with the other common diagnoses. Cerebrospinal fluid eosinophils were also found in 7 premature chil-

<table>
<thead>
<tr>
<th>Variable</th>
<th>No. of Cases (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>diagnosis</td>
<td></td>
</tr>
<tr>
<td>intraventricular hemorrhage of prematurity</td>
<td>62 (20.7)</td>
</tr>
<tr>
<td>myelomeningocele</td>
<td>50 (16.7)</td>
</tr>
<tr>
<td>tumor</td>
<td>56 (18.7)</td>
</tr>
<tr>
<td>aqueductal stenosis</td>
<td>28 (9.3)</td>
</tr>
<tr>
<td>idiopathic</td>
<td>34 (11.3)</td>
</tr>
<tr>
<td>Dandy–Walker syndrome</td>
<td>11 (3.7)</td>
</tr>
<tr>
<td>postinfectious</td>
<td>8 (2.7)</td>
</tr>
<tr>
<td>posttraumatic</td>
<td>3 (1.0)</td>
</tr>
<tr>
<td>hydranencephaly</td>
<td>7 (2.3)</td>
</tr>
<tr>
<td>other</td>
<td>41 (13.7)</td>
</tr>
<tr>
<td>sex</td>
<td></td>
</tr>
<tr>
<td>male</td>
<td>159 (53.0)</td>
</tr>
<tr>
<td>female</td>
<td>141 (47)</td>
</tr>
<tr>
<td>shunt infection (initial shunt)</td>
<td>25 (8.3)</td>
</tr>
<tr>
<td>patients w/ CSF eosinophilia over study period</td>
<td>93 (31)</td>
</tr>
<tr>
<td>patients w/ further shunt revisions</td>
<td>138 (46)</td>
</tr>
<tr>
<td>CSF sample acquired during study period</td>
<td>137 (99.3)</td>
</tr>
<tr>
<td>CSF eosinophils present</td>
<td>73 (53.3) of 137</td>
</tr>
<tr>
<td>CSF eosinophils absent</td>
<td>65 (47.4) of 137</td>
</tr>
<tr>
<td>patients w/ further shunt revisions</td>
<td>162 (54)</td>
</tr>
<tr>
<td>CSF sample recorded during study period</td>
<td>121 (74.7)</td>
</tr>
<tr>
<td>CSF eosinophils present</td>
<td>20 (16.5) of 121</td>
</tr>
<tr>
<td>CSF eosinophils absent</td>
<td>101 (83.5) of 121</td>
</tr>
</tbody>
</table>
dren with percutaneous ventricular taps prior to any shunt material placement.

**Cerebrospinal Fluid Eosinophilia Without Infection**

To identify a large cohort of patients with CSF eosinophilia, we reviewed data obtained in all patients who underwent a shunt procedure, including those in whom it was initially placed and any other patients in whom it was revised. A total of 1571 shunt procedures were performed during the study period. Analysis was performed of all cases involving shunt infection and all cases involving CSF eosinophilia without infection.

There were 100 patients with 107 episodes of eosinophilia with no clinical signs or cultures indicating infection. Data on these episodes are presented in Table 2. Cerebrospinal fluid samples were obtained during evaluation for shunt malfunction. Therefore, the timing of collection varied. However, sampling occurred within 1 month of a prior shunt surgery in 69.2% of patients. The mean number of days after surgery was 14.6 ± 8.7.

There were 2 factors of note in this cohort. There was CSF extravasation immediately prior to the discovery of eosinophils in 37 (34.6%) of the episodes. Cerebrospinal fluid extravasation was especially prevalent in patients with the highest percentages of eosinophils (Table 2). The workup for infection in all patients in this cohort was negative. Data in patients with positive cultures and CSF extravasation were analyzed in the shunt infection cohort.

The second factor was the relationship with blood in the CSF. There was no discernible relation to the peak number of RBCs in the CSF prior to shunt surgery. However, there was a statistical relationship to a finding of >100 RBCs/mm³ of CSF within 1 month of shunt insertion (p < 0.0001) and subsequent eosinophilia. There were >100 RBCs/mm³ in the CSF within 1 month of the finding of eosinophilia in 75 (70.0%) of the 107 episodes.

There was a CSF sample recorded after the episode of eosinophilia in 71 of the 107 episodes. There were no eosinophils documented in the follow-up sample in 68 cases (95.8%). Thirty-one of these samples were taken within 1 month of the eosinophilic episode. The eosinophilia had resolved in all 31 cases.

Ten patients were treated with oral steroids. All 10 patients required shunt revision within 2 months of the discovery of eosinophilia; 9 required revision within 1 month.

**Shunt Infections**

We studied 130 shunt infections. Cerebrospinal fluid was analyzed approximately every other day during external drainage. Cerebrospinal fluid eosinophils were present in 118 (90.8%) of the 130 shunt infections. The peak WBC counts and percentage of eosinophils per organism are shown in Table 3.

The timing of the peak of the WBC count and eosinophil reaction was referenced to the initial positive culture. The leukocyte differential followed a pattern of an initial influx of PMN leukocytes, followed by delayed appearance of lymphocytes, monocytes, and eosinophils. The timing of the peak of the eosinophil reaction in relation to the first positive culture is shown in Table 3.

The leukocytic reaction varied with the infecting organisms (Fig. 1 *upper*). The relative percentage of eosinophils
in the CSF cell count differential also varied (Fig. 1 lower).

The peak percentage of eosinophils was statistically significantly higher and the overall peak WBC count was lower in shunt infections caused by Propionibacterium acnes (p < 0.017). The eosinophilia resolved with successful treatment of the shunt infection in every case.

Illustrative Cases

Case 1

This 3-month-old boy had hydrocephalus resulting from an occipital encephalocele. He presented with vomiting and enlarged ventricles. Cultures of CSF demonstrated coagulase-negative Staphylococcus. The shunt was removed and an EVD system was placed on Day 0. The patient had significant CSF leakage around the external ventricular drain on Day 9 and again on Day 15. The EVD system was replaced both times. The CSF cell counts are shown in Fig. 2.

Case 2

This 8-month-old boy underwent shunt insertion for aqueductal stenosis. He presented with a fluid accumulation at the shunt site. Cultures of CSF were positive for P. acnes. His shunt was removed and an EVD system was placed. The patient improved after initiation of drainage, until Day 15 when his clinical status declined. Cultures of CSF became positive for Neisseria flavescens. Analysis showed a very high spike in the total WBCs, with low eosinophils and PMN leukocyte predominance. Antibiotics brought about a recovery, and the patient was discharged in good condition. He returned on Day 47 with fever and lethargy. Cultures of CSF were positive for coagulase-negative Staphylococcus.

The CSF leukocyte reaction varies with the infecting organism, as shown in Fig. 3. Figure 3 upper shows the eosinophil percentage and the total WBC count with vertical lines as the days of positive culture, and Fig. 3 lower shows the differential of PMN leukocytes, lymphocytes, and monocytes over the same time.

Discussion

Eosinophils are a source of numerous growth factors and cytokines and are associated with angiogenesis, inflammation, connective tissue disease, vasculitis, atopic dermatitis, tissue repair, fibrosis, drug hypersensitivity reactions, and

<table>
<thead>
<tr>
<th>Organism</th>
<th>No. of Cases (%)</th>
<th>No. w/ CSF Eosinophilia (%)</th>
<th>Mean Peak WBC Count/mm³ of CSF</th>
<th>Mean Peak Eosinophil of WBC Count (%)</th>
<th>Peripheral Eosinophilia (%)</th>
<th>Days From Positive Culture to Peak Eosinophilia</th>
</tr>
</thead>
<tbody>
<tr>
<td>coagulase-negative Staphylococci</td>
<td>47 (36.1)</td>
<td>40 (85.1)</td>
<td>933.8 ± 2396.0</td>
<td>26.9 ± 22.8</td>
<td>8 (17.0)</td>
<td>11.3 ± 7.5</td>
</tr>
<tr>
<td>S. aureus</td>
<td>28 (21.5)</td>
<td>27 (96.4)</td>
<td>1821.3 ± 4143.5</td>
<td>14.6 ± 16.4</td>
<td>11 (39.3)</td>
<td>13.4 ± 8.3</td>
</tr>
<tr>
<td>P. acnes</td>
<td>14 (10.8)</td>
<td>14 (100)</td>
<td>452.4 ± 584.8</td>
<td>43.3 ± 30.9</td>
<td>3 (21.4)</td>
<td>9.4 ± 9.3</td>
</tr>
<tr>
<td>Streptococci sp.</td>
<td>9 (6.9)</td>
<td>9 (100)</td>
<td>1513.3 ± 2195.5</td>
<td>12.0 ± 20.3</td>
<td>3 (33.3)</td>
<td>11.9 ± 9.4</td>
</tr>
<tr>
<td>E. coli</td>
<td>7 (5.4)</td>
<td>5 (71.4)</td>
<td>2785.0 ± 5978.3</td>
<td>9.6 ± 8.4</td>
<td>2 (28.6)</td>
<td>8.4 ± 6.5</td>
</tr>
<tr>
<td>P. aeruginosa</td>
<td>6 (4.6)</td>
<td>4 (66.7)</td>
<td>1835 ± 3118.7</td>
<td>14.0 ± 12.8</td>
<td>2 (33.3)</td>
<td>8.8 ± 5.6</td>
</tr>
<tr>
<td>Klebsiella sp.</td>
<td>4 (3.1)</td>
<td>4 (100)</td>
<td>3407.8 ± 5437.1</td>
<td>25.3 ± 27.4</td>
<td>4 (100)</td>
<td>32.5 ± 19.2</td>
</tr>
<tr>
<td>Candida sp.</td>
<td>3 (2.3)</td>
<td>3 (100)</td>
<td>123.0 ± 77.9</td>
<td>24.0 ± 35.5</td>
<td>0 (0.0)</td>
<td>14.3 ± 4.7</td>
</tr>
<tr>
<td>Enterobacter sp.</td>
<td>3 (2.3)</td>
<td>3 (100)</td>
<td>430.7 ± 599.2</td>
<td>17.3 ± 6.4</td>
<td>2 (66.7)</td>
<td>2.0 ± 3.5</td>
</tr>
<tr>
<td>Corynebacterium sp.</td>
<td>2 (1.5)</td>
<td>2 (100)</td>
<td>1547 ± 711.3</td>
<td>32.5 ± 14.8</td>
<td>1 (50)</td>
<td>11.0 ± 1.4</td>
</tr>
<tr>
<td>Serratia marcescens</td>
<td>2 (1.5)</td>
<td>2 (100)</td>
<td>117772 ± 160128.6</td>
<td>3.5 ± 3.5</td>
<td>0 (0.0)</td>
<td>8.0 ± 2.8</td>
</tr>
</tbody>
</table>

* Defined as < 5% eosinophils in complete blood count differential.
† There was 1 peritoneal infection in which a definitive organism could not be cultured, and single shunt infection each with Stenotrophomonas maltophilia, Haemophilus influenzae, Neisseria flavescens, and Acinetobacter baumannii.

Table 3: Data obtained in 130 cases involving shunt infections

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Fig. 1. Bar graphs of peak WBC count (upper) and eosinophil percentage (lower) for the most common infecting organisms.

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The number of circulating eosinophils is tightly regulated but may rise in certain conditions. Cerebrospinal fluid eosinophils have historically been associated with neurosyphilis, fungal infections, tuberculous meningitis, malignancy, and parasite infections. Bosch and Oehmichen have examined 10,000 qualitative CSF cytological preparations and found eosinophilia in 1%. Eosinophils were present mainly in inflammatory reactions, vascular disease, and tumors. Of note, there were only 8 patients with hydrocephalus and 6 with shunts in the series. Given the overall rarity of eosinophils, their presence was considered pathological.

During the follow-up period, we identified CSF eosinophilia in 93 (31%) of the 300 patients who underwent placement of an initial shunt. We performed statistical analysis in this group, comparing the patients with eosinophils and those without. Patients in whom shunts were placed for intraventricular hemorrhage of prematurity had a higher rate of eosinophilia than those with other major diagnoses (p = 0.038). Other statistical associations included younger age at shunt insertion (p = 0.030), CSF extravasation (p < 0.0001), infection (p = 0.031), use of intrathecal antibiotics (p = 0.010), and blood in the CSF (p < 0.0001). Patients with eosinophilia had a higher incidence of shunt revision (p < 0.0001).

Eosinophilia was absent on subsequent CSF analysis in 95.8% of samples in patients without infection and in all cases of successful treatment of shunt infection. Given the variability of the timing of CSF analysis, we cannot accurately assess the duration of eosinophilia. However, our data agree with previously published works indicating that CSF eosinophilia is a transient finding.

Cerebrospinal Fluid Eosinophilia Without Infection

Previous reports indicate that noninfectious CSF eosinophilia may be caused by an allergic reaction to the shunt material. Niggemann et al. demonstrated an elevated immunoglobulin E level specific to latex in the CSF in a patient with 84% eosinophils. They suggested that latex allergy was responsible for the eosinophilia. Jimenez et al. reported 3 on patients with allergic reactions to shunt material in whom the clinical course was marked by recurrent skin breakdowns and granuloma formation. In our series, there were no patients with an escalating clinical response or recurrent granuloma formation suggestive of allergy. We found no statistical relationship between CSF eosinophils and a history of latex or medication allergy, although 4 of 5 patients with the highest percentages of eosinophils had latex allergies. The eosinophilia was transient, despite the fact that the same shunt material was reimplanted at revision surgery.

We found 2 strong correlations with noninfectious eosin-
Cerebrospinal fluid eosinophilia

Eosinophilia in both the initial shunt group in the cohort analysis. There was a statistical relationship between eosinophilia and CSF leakage or fluid accumulation under the skin (p < 0.0001), especially in patients with the highest percentages of eosinophils. The cause of this is unknown. The timing of eosinophilia in relation to CSF extravasation is a point of consideration. One possibility is that eosinophils contribute to shunt malfunction, which, in turn, causes extravasation around a blocked catheter. A second possibility is that eosinophilia is a reaction to the extravasation. In Case 1, the patient underwent CSF sampling both before and after leakage through the skin. There was a small eosinophlic reaction to his initial shunt infection. However, there were pronounced rises of eosinophils after CSF leakage. This suggests that the eosinophilia is more a reaction than a cause. We speculate that eosinophilia occurs when CSF leaves the immunologically privileged area of the ventricular system and comes into contact with the skin. Inflammatory cells may be introduced in patients where CSF "washes" in and out of a dural opening. It remains to be seen if shunt insertion techniques that require a larger bur hole or dural opening are associated with a higher risk of eosinophilia.

The second correlation is with blood in the CSF. Although there was no direct relationship between the total numbers of RBCs prior to shunt insertion, there was a correlation between eosinophilia and a CSF sample obtained within 1 month of shunt insertion, in which we observed > 100 RBCs/mm³ (p < 0.0001). The cause of this relationship is unknown. As with extravasation, hemorrhage into the CSF potentially exposes this immunologically privileged space to inflammatory cells.

Eosinophils are known to migrate to areas rich in fibroblasts and enhance tissue remodeling through release of numerous cytokines. Eosinophils interact with endothelial cells and enhance angiogenesis through growth factors. All these conditions are present during the healing after surgery. There is also the potential for hemorrhage or CSF contact with the skin during shunt surgery. In this series, 69.2% of episodes of noninfectious eosinophilia occurred within 1 month (mean 14.6 ± 8.7 days) of shunt surgery. Patients with CSF eosinophilia had a higher incidence of shunt malfunction (p < 0.0001) in the group in which shunt placement was the initial surgery. A relation between eosinophilia and shunt malfunction has been noted by other authors as well. Sterile shunt malfunctions may occur as the tubing clings with a foreign body, choroid plexus, ependymal cells, or brain tissue. Gower et al. performed electron microscopy on 20 distal catheters from patients with shunt malfunction. They discovered cellular clumps with proteinaceous debris on the inner surface of the catheter tubes. Kossovsky and Snow examined 25 catheters with intraluminal tissue. They found evidence of an active inflammatory process in 8 specimens. Three catheters had giant cells and eosinophils that were "suggestive of a hypersensitivity reaction." Our experience with shunt malfunction in patients with eosinophilia is similar in that inflammatory debris block the catheter or the valve. In the present study this was not simply a matter of elevated CSF protein at the time of insertion as malfunction rates were unrelated to peak protein levels. Eosinophils are known to propagate many inflammatory responses through secretion of chemicals involved in upregulating adhesion systems and cellular trafficking. Perhaps the large eosinophilic response in some patients promotes the attraction and adhesion of cells, contributing to shunt blockage. The number of shunt revisions in this series was correlated with the total number (r² = 0.370, p < 0.0001) and percentage (r = 0.404, p < 0.0001) of eosinophils in this series.

Glucocorticoids inhibit the production and survival of eosinophils by suppressing the transcription of inflammatory mediators such as interleukin-3, -4, and -5, as well granulocyte monocyte colony-stimulating factor and other chemokines. Vinchon et al. reported a case of treating CSF eosinophilia with steroids. The patient had a reduction in CSF eosinophil counts and prolonged shunt survival when treated with methylprednisolone. We treated 10 patients with steroids, and each required a shunt revision within 2 months. Nine required shunt revision within 1 month. Further evaluation of the efficacy of steroids is needed. Our anecdotal experience is that steroids reduce the CSF leukocyte and eosinophil counts but may not prevent shunt failure.

Cerebrospinal Fluid Eosinophilia Related to Shunt Infection

Eosinophilia was related to shunt infection (p = 0.031) in the patients with initial shunt placement. Our infection rate for the initial shunts was 8.3%. This rate is comparable with that in other published series.

We performed a cohort analysis of data obtained in all patients treated for shunt infection throughout the study period. A total of 130 shunt infections were studied (Table 3). Eosinophils were found in 118 (90.8%). The eosinophils occurred at an average of 11.9 ± 9.2 days after the first positive culture. Eosinophils may be simply part of the natural leukocyte progression from the initial influx of PMN leukocytes to a delayed rise in lymphocytes, monocytes, and eosinophils.

Intraventricular administration of vancomycin and gentamycin was statistically correlated with CSF eosinophilia (p = 0.01). This correlation has been noted by other authors as well. Intrathecal antibiotics were administered in 22 of the 130 cases of shunt infections in this series.

Eosinophils related to infection have been reported in other studies. Vinchon et al. published a series of 22 patients with CSF eosinophilia in shunt infection. They noted that higher levels of eosinophils were associated with lower levels of PMN leukocytes. As in our series, eosinophils normalized with treatment of infection and did not return after the shunt was replaced.

The leukocytic reaction in the CSF was related to the infecting organism (Fig. 1). Gram-negative organisms often have a more fulminating clinical course than other pathogens. Escherichia coli, Pseudomonas species, and Klebsiella species caused a very high WBC reaction but had relatively few eosinophils. In contrast, the more indolent P. acnes and coagulase-negative Staphylococci caused a lower overall WBC reaction, but a higher relative percentage of eosinophils. Case 2 involved a patient with 3 shunt infections with different organisms. Figure 3 shows the CSF reaction in relation to the infecting organism. There was a high percentage of eosinophils during the P. acnes infection, an extremely low level with Neisseria flavescens, and a moderate reaction with coagulase-negative Staphylococci.
Wiersbitzky et al. noted a higher percentage of eosinophils in patients with Staphylococcus epidermidis shunt infections than in patient with other organisms. There were no infections caused by P. acnes in their series. Our findings showed relatively high numbers of eosinophils with coagulase-negative Staphylococci, but there were even higher levels withP. acnes. There was a statistically significantly (p < 0.017) higher peak percentage of eosinophils and lower total WBC count with P. acnes compared with the other common infecting organisms (Fig. 1).

Propionibacterium acnes is a gram-positive, anaerobic diphtheroid that is part of the normal skin flora and may infect a shunt. The clinical course of shunt infection may also be more indolent and symptoms may appear in a more delayed fashion than is seen with other organisms. The diagnosis is challenging as CSF gram negative showed relatively high numbers of eosinophils with coagulase-negative Staphylococci, but there were even higher levels with P. acnes. There was a statistically significantly (p < 0.017) higher peak percentage of eosinophils and lower total WBC count with P. acnes compared with the other common infecting organisms (Fig. 1).

Propionibacterium acnes is a gram-positive, anaerobic diphtheroid that is part of the normal skin flora and may infect a shunt. The clinical course of shunt infection may also be more indolent and symptoms may appear in a more delayed fashion than is seen with other organisms. The diagnosis is challenging as CSF gram stains are often negative, and the WBC reaction may be low. Also, this organism may be present in thioglycolate broth tubes as a contaminant. Propionibacterium acnes does not reliably grow in aerobic cultures and requires a significant-ly longer incubation time than many of the more common shunt pathogens.

Limitations of the Study

There are limitations to this study. The data were derived from a retrospective analysis of samples collected during a clinical event. The number and timing of CSF analyses varied widely among patients. Our conclusions must be considered in light of this significant limitation. It is possible that we are underestimating the number of patients with eosinophils and exploring only those patients with exaggerated or symptomomatic conditions. We acknowledge this limitation, but we believe that it is unlikely that a prospective study with scheduled, standardized CSF analysis will ever be performed, as shunt access introduces a small but definite risk of infection.

There was a discrepancy in the number of cases of eosinophilia identified among the 300 patients with initial shunt placement and the patients with the 1271 shunt revisions over the study period. A possible explanation for this is that the patients with shunts placed at our hospital probably had all their subsequent evaluations and CSF samples performed by our service. Some of the patients with shunt infections or the need for revisions were transferred from outside facilities, and their CSF study results were not always available.

Conclusions

Cerebrospinal fluid eosinophilia is a relatively common, transient occurrence in children with shunts. This finding may be present without the traditional “causes,” as there were no cases of parasitic infection, syphilis, or true allergic reaction to shunt material in our series. There was a statistical relationship between eosinophilia and the presence of blood in the CSF. There was also a strong relationship with CSF extravasations (leakage or accumulation under the skin). Patients with eosinophilia had a higher rate of subsequent shunt revision. In a limited number of patients, steroids reduced the eosinophil and WBC count but did not prevent the need for subsequent shunt surgery.

Eosinophils were present in 90.8% of shunt infections and may be part of the natural progression of CSF leukocytosis. The eosinophilic reaction was dependent on the infecting organism. In particular, P. acnes showed a significantly elevated eosinophil percentage. We therefore recommend extended anaerobic culture studies particularly searching for this organism in patients with CSF eosinophilia.

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