Epidural hibernoma as a complication of corticosteroid treatment

Case report

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Centripetal fat deposition is a well-recognized consequence of excessive use of corticosteroids, either endogenous or exogenous. Recently, several patients receiving large doses of corticosteroids have suffered compressive myelopathies due to excessive epidural fat collections, labeled "epidural lipomatosis." Two of these have been children, and a third child is reported here. This child was receiving chronic steroids for juvenile rheumatoid arthritis when he presented with such a myelopathy, which was confirmed by metrizamide computerized tomography myelography as well as by surgical exploration. Histological examination revealed that the epidural tissue was a brown-fat tumor or "hibernoma." An epidural hibernoma has not been described previously. The histological and endocrine features of fat in Cushing's syndrome are discussed, and the literature concerning hibernoma and epidural lipomatosis is reviewed.

KEY WORDS: hibernoma • epidural lipomatosis • corticosteroid • Cushing's syndrome • children

Corticosteroids are prescribed in the chronic treatment of transplant recipients, asthmatic patients, and rheumatological disorders. The side effects of excessive use, either endogenous or exogenous, of these drugs are well known and include centripetal fat deposition, diabetes mellitus, osteoporosis, and mediastinal lipomatosis. There have been several reported cases of "epidural lipomatosis" or compressive myelopathies due to excessive epidural fat deposition in patients receiving large doses of corticosteroids. In suspected cases, an appropriate diagnostic workup is essential to rule out epidural lipomatosis; a patient receiving long-term steroid treatment may suffer compression fractures or myelopathies. Suspected spinal cord compression is often treated with an even higher dose of steroids when, in fact, the dosage should be lowered.

Twenty patients have been reported to have neurological symptoms secondary to steroid-induced epidural lipomatosis. Nine of these presented with myelopathy, and one each with radiculopathy, cauda equina syndrome, and neurogenic claudication. All had myelographic evidence of an epidural mass, and all but one underwent laminectomy with the identification and removal of excess epidural fat. Histopathologically, the tissue removed was variously labeled "lipoma," "lipomatosis," and "normal fat." Brown fat was not noted in any of these five cases. The reports of the other seven cases made no mention of pathology.

Case Report

This 6-year-old boy was brought to Texas Children's Hospital in August, 1986, for evaluation of progressive loss of function in the lower extremities, bowels, and bladder. He had been diagnosed 4 years previously as having juvenile rheumatoid arthritis and was then started on a course of prednisone, 10 mg/day. Because of continued pain, liver abnormalities, and evidence of arthritis, the prednisone dosage was increased in September, 1984, to 20 mg/day. The development of diabetes mellitus necessitated the use of NPH insulin (isophane insulin). In June, 1986, the child's prednisone dose was increased to 30 mg/day because of progressive arthralgia and arthritis. In July, 1986, he complained of "soreness" of both legs, and bedwetting occurred. As renal function continued to deteriorate, the prednisone...
dosage was increased to 40 mg/day. Five days prior to admission, the patient developed severe thoracic pain and was unable to support himself. Films of the spine revealed severe osteoporosis with compression fractures.

**Examination.** Examination at the time of admission revealed an obese child with cushingoid characteristics, obviously suffering pain of an unrelenting nature which extended from the posterior thoracic region to the anterior sternum. Neurological examination revealed an absence of pinprick sensation below T-6. The child was paraplegic with increased tone and hyperreflexia of the lower extremities. Anal sphincter tone was poor. Metrizamide computerized tomography (CT) myelography showed attenuation of the subarachnoid space dorsally with a complete block at T-4; the dorsal epidural mass displaced the cord and thecal sac ventrally and appeared to have a CT density of fat (Fig. 1). The upper limit of the obstruction was not identified.

**Operation.** Laminectomy of T2–6 revealed an excessive amount of abnormal-appearing, tough adipose tissue occupying the dorsal epidural space and displacing the thecal sac anteriorly. With removal of this tissue, the dura became pulsatile and intradural exploration disclosed no further abnormality. Cultures for bacterial and fungal elements were negative.

**Postoperative Course.** Lower-extremity movement with gravity returned postoperatively. Prednisone doses were lowered to 20 mg/day. No worsening of the neurological symptoms has occurred in the follow-up period. Pathological examination of the excised specimen revealed vascular adipose tissue. Some of the fat cells had the appearance of brown fat, with central nuclei and finely vesicular eosinophilic cytoplasm (Fig. 2). The final diagnosis was epidural hibernoma, or brown-fat tumor.

**Discussion**

Brown fat is a specialized tissue present in many fetal animals, including man. Unless an animal hibernates, the brown fat rapidly diminishes in mass as the animal ages. Brown fat has been found almost everywhere in the human fetus; the primary deposits are in the subcutaneous tissues of the interscapular area, the neck, mediastinum, axilla, and periaortic and retroperitoneal areas. Vestigial in man, brown fat serves in hibernating animals as an important source of non-shivering heat production under cold stress. Brown fat is composed of varied cell types; it is tan to brown in color and vascular. The characteristic cell is eosinophilic and multivacuolated with granular cytoplasm and a central spherical nucleus. White adipose tissue is yellow, with the appearance of lard; the cells are larger than in brown fat and univacuolated with flattened peripheral nuclei.

Hibernomas (fatty tumors consisting primarily of brown adipose tissue) are rare, with fewer than 100 cases reported. They present as expanding soft-tissue masses with symptoms reflecting compression of adjacent organs, nerves, or vessels. They occur in anatomical areas where brown fat is most common in fetuses and newborns, the interscapular area, the neck, axilla, mediastinum, and, rarely, on the extremities. Sex incidence is equal and peak age incidence is in the fourth decade. One case of lumbar intradural hibernoma has been reported in a 14-year-old child with spina bifida. Epidural hibernoma has not been described prior to our case.
Epidural hibernoma after corticosteroid treatment

Three children and 10 adults with steroid-induced epidural lipomatosis have now been described (Table 1). All presented with back pain, 10 with myelopathy,7,14,15,21,26,28,30 and one each with radiculopathy,3 cauda equina syndrome,7 and neurogenic claudication.23 Daily prednisone doses varied from 15 to 150 mg, with the duration of treatment prior to the onset of neurological symptoms varying from 6 months to 14 years. Of the eight patients who had received steroid therapy for 15 months or less, all had taken at least 40 mg prednisone daily for a minimum of 4 months.7,14-16,21,22,28 Two patients took maximum daily doses of 15 mg prednisone and developed symptoms after 4 and 13 years, respectively.3,7 Five patients experienced the onset of symptoms following steroid dosage increases,5,7,14,16 whereas four developed symptoms when steroid dosage levels were lowered.7,21,23,30 Of the patients developing symptoms while dosage levels were being tapered down, all had taken 40 mg prednisone daily for at least 4 consecutive months.

Twelve of these 13 patients underwent decompressive laminectomy and epidural fat removal: 10 were neurologically improved, and two returned to normal.7,23 The unoperated patient, a 13-year-old boy with a renal transplant, was treated with rapidly tapered prednisone and a low-calorie low-carbohydrate diet.14 His pain resolved and his neurological function improved; a follow-up CT scan revealed marked reduction in the volume of epidural fat.

Although it had long been considered that glucocorticoids affected adipose tissue, it was not until 1977 that Feldman and Loose12 demonstrated the presence of glucocorticoid receptors on fat cells. Affinity of steroids to these receptors is directly related to glucocorticoid activity, with dexamethasone being most tightly bound, progesterone intermediate bound, and gonadotropins least tightly bound.11,12,24,27 Glucocorticoids affect white and brown fat tissue differently. They inhibit glucose uptake and activate lipolysis and free fatty acid release in white fat while increasing the amount of glycogen and lipid in brown fat; in effect, they decrease the white-fat mass while increasing the brown-fat mass.9,24,29 No difference, however, has been found in glucocorticoid receptor number or effect between central and peripheral white fat.10,12 Such a difference might have been expected since cushingoid patients lose peripheral fat and increase central fat deposition. Perhaps much of the increased centripetal fat, instead of being white fat, is actually brown fat expanding in response to excessive steroids. The "buffalo hump," the moon facies, and the mediastinal fat deposition characteristic of cushingoid patients all occur in areas where infants have prominent brown-fat deposits. While pathological studies of both mediastinal and epidural lipomatoses have been performed (although not in every case), no mention has been made of the presence of brown fat.2,4,5,7,16,23,28,31 A more detailed histopathological examination might reveal brown fat, or hibernoma, to be playing a larger role in steroid-induced adipose collections than may have been hitherto suspected.

In conclusion, it is important to consider epidural lipomatosis as a cause of spinal cord or nerve root-related symptoms in any patient taking corticosteroids. It should not be assumed that such symptoms are related solely to myelopathy or compression fractures. Although there is no definite relationship between dosage and disease onset, it does appear that patients on higher doses of steroids or with increasing dose schedules tend to develop epidural lipomatosis earlier than patients with low or tapering doses.

<table>
<thead>
<tr>
<th>Authors &amp; Year</th>
<th>Systemic Disease</th>
<th>Age (yrs)</th>
<th>Maximum Prednisone Dose (mg/day)</th>
<th>Onset After Steroids</th>
<th>Surgery</th>
<th>Spine Level</th>
<th>Pathology</th>
<th>Recovery</th>
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<tr>
<td>Lee, et al., 1975</td>
<td>renal transplant</td>
<td>16</td>
<td>55 for 9 mos</td>
<td>15 mos</td>
<td>yes</td>
<td>C7-L4</td>
<td>hypertrophied adipose tissue</td>
<td>partial</td>
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<tr>
<td>Butcher &amp; Sahn, 1979</td>
<td>asthma</td>
<td>47</td>
<td>150 for 15 mos</td>
<td>5 yrs</td>
<td>yes</td>
<td>T2-10</td>
<td>none</td>
<td>partial</td>
</tr>
<tr>
<td>George, et al., 1979</td>
<td>renal transplant</td>
<td>13</td>
<td>180 for 3 days</td>
<td>9 mos</td>
<td>no</td>
<td>T-1</td>
<td>partial</td>
<td>partial</td>
</tr>
<tr>
<td>Godeau, et al., 1979</td>
<td>polyarteritis</td>
<td>43</td>
<td>80 for 6 mos</td>
<td>6 mos</td>
<td>yes</td>
<td>T1-9</td>
<td>normal adipose tissue</td>
<td>partial</td>
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<tr>
<td>Lipson, et al., 1979</td>
<td>Graves' disease</td>
<td>53</td>
<td>150 for 2 mos</td>
<td>6 mos</td>
<td>yes</td>
<td>L4-5</td>
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<td>partial</td>
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<tr>
<td>Chapman, et al., 1981</td>
<td>renal transplant</td>
<td>42</td>
<td>60 for ?</td>
<td>7 mos</td>
<td>yes</td>
<td>T8-12</td>
<td>lipomatosis</td>
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<td>Archer &amp; Smith, 1982</td>
<td>asthma?</td>
<td>32</td>
<td>40 for 4 mos</td>
<td>11 mos</td>
<td>yes</td>
<td>T6-9</td>
<td>complete</td>
<td>partial</td>
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<td>Guegan, et al., 1982</td>
<td>hepatitis</td>
<td>63</td>
<td>15 for 4 yrs</td>
<td>4 yrs</td>
<td>yes</td>
<td>L5-83</td>
<td>partial</td>
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<td>Russell, et al., 1984</td>
<td>asthma</td>
<td>48</td>
<td>15 for 13 yrs</td>
<td>13 yrs</td>
<td>yes</td>
<td>L4-5</td>
<td>partial</td>
<td>partial</td>
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<tr>
<td>Pennisi, et al., 1985</td>
<td>lymphoma</td>
<td>30</td>
<td>120 for ?</td>
<td>15 mos</td>
<td>yes</td>
<td>T1-10</td>
<td>normal adipose tissue</td>
<td>partial</td>
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<tr>
<td>Perling, et al., 1987</td>
<td>juvenile rheumatoid</td>
<td>21</td>
<td>80 for 1 yr</td>
<td>14 yrs</td>
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<td>Lipson, et al., 1988</td>
<td>arthritis</td>
<td>34</td>
<td>110 for 6 mos</td>
<td>6 mos</td>
<td>yes</td>
<td>T4-10</td>
<td>lipoma</td>
<td>partial</td>
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<td>arthritis</td>
<td>6</td>
<td>40 for 1 mo</td>
<td>4 yrs</td>
<td>yes</td>
<td>T2-6</td>
<td>hibernoma</td>
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**TABLE 1**

Clinical summary of 13 patients with steroid-induced epidural lipomatosis

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References


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